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(54) **PEPTIDE REAGENTS AND METHOD FOR INHIBITING AUTOANTIBODY ANTIGEN BINDING**

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(57) **ABSTRACT**

The present disclosure provides immunoassays and kits for detection or quantification of an protein of interest in a test sample that potentially contains endogenously produced autoantibodies reactive with the analyte.

Ala Asp Gly Ser Ser Asp Ala Ala Arg Glu Pro Arg Pro Ala Pro Ala Pro Ile Arg Arg Arg Ser Ser Asn Tyr Arg Ala Tyr Ala Thr Glu Pro His Ala Lys Lys Lys Ser Lys Ile Ser Ala Ser Arg Lys Leu Gln Leu Lys Thr Leu Leu Leu Gln Ile Ala Lys Gln Glu Leu Glu Arg Glu Ala Glu Glu Arg Arg Gly Glu Lys Gly Arg Ala Leu Ser Thr Arg Cys Gln Pro Leu Glu Leu Ala Gly Leu Gly Phe Ala Glu Leu Gln Asp Leu Cys Arg Gln Leu His Ala Arg Val Asp Lys Val Asp Glu Glu Arg Tyr Asp Ile Glu Ala Lys Val Thr Lys Asn Ile Thr Glu Ile Ala Asp Leu Thr Gln Lys Ile Phe Asp Leu Arg Gly Lys Phe Lys Arg Pro Thr Leu Arg Arg Val Arg Ile Ser Ala Asp Ala Met Met Gln Ala Leu Leu Gly Ala Arg Ala Lys Glu Ser Leu Asp Leu Arg Ala His Leu Lys Gln Val Lys Lys Glu Asp Thr Glu Lys Glu Asn Arg Glu Val Gly Asp Trp Arg Lys Asn Ile Asp Ala Leu Ser Gly Met Glu Gly Arg Lys Lys Lys Phe Glu

FIG. 1

Ser Asp Ile Glu Glu Val Val Glu Glu Tyr Glu Glu Glu Glu Gln Glu Glu Ala Ala Val Glu
Glu Glu Glu Asp Trp Arg Glu Asp Glu Asp Glu Gln Glu Glu Ala Ala Glu Glu Asp Ala
Glu Ala Glu Ala Glu Thr Glu Glu Thr Arg Ala Glu Glu Asp Glu Glu Glu Glu Glu Ala
Lys Glu Ala Glu Asp Gly Pro Met Glu Glu Ser Lys Pro Lys Pro Arg Ser Phe Met
Pro Asn Leu Val Pro Pro Lys Ile Pro Asp Gly Glu Arg Val Asp Phe Asp Asp Ile His Arg
Lys Arg Met Glu Lys Asp Leu Asn Glu Leu Gln Ala Leu Ile Glu Ala His Phe Glu Asn
Arg Lys Lys Glu Glu Glu Glu Leu Val Ser Leu Lys Asp Arg Ile Glu Arg Arg Arg Ala
Glu Arg Ala Glu Gln Gln Arg Ile Arg Asn Glu Arg Glu Lys Glu Arg Gln Asn Arg
Leu Ala Glu Glu Arg Ala Arg Arg Glu Glu Glu Glu Asn Arg Arg Lys Ala Glu Asp Glu
Ala Arg Lys Lys Lys Ala Leu Ser Asn Met Met His Phe Gly Gly Tyr Ile Gln Lys Gln Ala
Gln Thr Glu Arg Lys Ser Gly Lys Arg Gln Thr Glu Arg Glu Lys Lys Lys Lys Ile Leu Ala
Glu Arg Arg Lys Val Leu Ala Ile Asp His Leu Asn Glu Asp Gln Leu Arg Glu Lys Ala
Lys Glu Leu Trp Gln Ser Ile Tyr Asn Leu Glu Ala Glu Lys Phe Asp Leu Gln Glu Lys
Phe Lys Gln Gln Lys Tyr Glu Ile Asn Val Leu Arg Asn Arg Ile Asn Asp Asn Gln Lys
Val Ser Lys Thr Arg Gly Lys Ala Lys Val Thr Gly Arg Trp Lys

FIG. 2

Thr Ala Leu Phe Leu Met Ser Met Leu Phe Gly Leu Ala Cys Gly Gln Ala Met Ser Phe Cys Ile Pro Thr Glu Tyr Thr Met His Ile Glu Arg Arg Glu Cys Ala Tyr Cys Leu Thr Ile Asn Thr Thr Ile Cys Ala Gly Tyr Cys Met Thr Arg Asp Ile Asn Gly Lys Leu Phe Leu Pro Lys Tyr Ala Leu Ser Gln Asp Val Cys Thr Tyr Arg Asp Phe Ile Tyr Arg Thr Val Glu Ile Pro Gly Cys Pro Leu His Val Ala Pro Tyr Phe Ser Tyr Pro Val Ala Leu Ser Cys Lys Cys Gly Lys Cys Asn Thr Asp Tyr Ser Asp Cys Ile His Glu Ala Ile Lys Thr Asn Tyr Cys Thr Lys Pro Gln Lys Ser Tyr Leu Val Gly Phe Ser Val

FIG. 3

Glu Met Phe Gln Gly Leu Leu Leu Leu Leu Leu Ser Met Gly Gly Thr Trp Ala Ser
Lys Glu Pro Leu Arg Pro Arg Cys Arg Pro Ile Asn Ala Thr Leu Ala Val Glu Lys Glu Gly
Cys Pro Val Cys Ile Thr Val Asn Thr Thr Ile Cys Ala Gly Tyr Cys Pro Thr Met Thr Arg
Val Leu Gln Gly Val Leu Pro Ala Leu Pro Gln Val Val Cys Asn Tyr Arg Asp Val Arg
Phe Glu Ser Ile Arg Leu Pro Gly Cys Pro Arg Gly Val Asn Pro Val Val Ser Tyr Ala Val
Ala Leu Ser Cys Gln Cys Ala Leu Cys Arg Arg Ser Thr Thr Asp Cys Gly Gly Pro Lys
Asp His Pro Leu Thr Cys Asp Asp Pro Arg Phe Gln Asp Ser Ser Ser Ser Lys Ala Pro Pro
Pro Ser Leu Pro Ser Pro Ser Arg Leu Pro Gly Pro Ser Asp Thr Pro Ile Leu Pro Gln

FIG. 4

Gly Val Pro Phe Phe Ser Ser Leu Arg Cys Met Val Asp Leu Gly Pro Cys Trp Ala Gly
Gly Leu Thr Ala Glu Met Lys Leu Leu Leu Ala Leu Ala Gly Leu Leu Ala Ile Leu Ala
Thr Pro Gln Pro Ser Glu Gly Ala Ala Pro Ala Val Leu Gly Glu Val Asp Thr Ser Leu Val
Leu Ser Ser Met Glu Glu Ala Lys Gln Leu Val Asp Lys Ala Tyr Lys Glu Arg Arg Glu
Ser Ile Lys Gln Arg Leu Arg Ser Gly Ser Ala Ser Pro Met Glu Leu Leu Ser Tyr Phe Lys
Gln Pro Val Ala Ala Thr Arg Thr Ala Val Arg Ala Ala Asp Tyr Leu His Val Ala Leu
Asp Leu Leu Glu Arg Lys Leu Arg Ser Leu Trp Arg Arg Pro Phe Asn Val Thr Asp Val
Leu Thr Pro Ala Gln Leu Asn Val Leu Ser Lys Ser Ser Gly Cys Ala Tyr Gln Asp Val Gly
Val Thr Cys Pro Glu Gln Asp Lys Tyr Arg Thr Ile Thr Gly Met Cys Asn Asn Arg Arg
Ser Pro Thr Leu Gly Ala Ser Asn Arg Ala Phe Val Arg Trp Leu Pro Ala Glu Tyr Glu Asp
Gly Phe Ser Leu Pro Tyr Gly Trp Thr Pro Gly Val Lys Arg Asn Gly Phe Pro Val Ala
Leu Ala Arg Ala Val Ser Asn Glu Ile Val Arg Phe Pro Thr Asp Gln Leu Thr Pro Asp Gln
Glu Arg Ser Leu Met Phe Met Gln Trp Gly Gln Leu Leu Asp His Asp Leu Asp Phe Thr
Pro Glu Pro Ala Ala Arg Ala Ser Phe Val Thr Gly Val Asn Cys Glu Thr Ser Cys Val Gln
Gln Pro Pro Cys Phe Pro Leu Lys Ile Pro Pro Asn Asp Pro Arg Ile Lys Asn Gln Ala Asp
Cys Ile Pro Phe Phe Arg Ser Cys Pro Ala Cys Pro Gly Ser Asn Ile Thr Ile Arg Asn Gln
Ile Asn Ala Leu Thr Ser Phe Val Asp Ala Ser Met Val Tyr Gly Ser Glu Glu Pro Leu Ala
Arg Asn Leu Arg Asn Met Ser Asn Gln Leu Gly Leu Leu Ala Val Asn Gln Arg Phe Gln
Asp Asn Gly Arg Ala Leu Leu Pro Phe Asp Asn Leu His Asp Asp Pro Cys Leu Leu Thr
Asn Arg Ser Ala Arg Ile Pro Cys Phe Leu Ala Gly Asp Thr Arg Ser Ser Glu Met Pro Glu
Leu Thr Ser Met His Thr Leu Leu Leu Arg Glu His Asn Arg Leu Ala Thr Glu Leu Lys
Ser Leu Asn Pro Arg Trp Asp Gly Glu Arg Leu Tyr Gln Glu Ala Arg Lys Ile Val Gly Ala
Met Val Gln Ile Ile Thr Tyr Arg Asp Tyr Leu Pro Leu Val Leu Gly Pro Thr Ala Met Arg
Lys Tyr Leu Pro Thr Tyr Arg Ser Tyr Asn Asp Ser Val Asp Pro Arg Ile Ala Asn Val Phe
Thr Asn Ala Phe Arg Tyr Gly His Thr Leu Ile Gln Pro Phe Met Phe Arg Leu Asp Asn
Arg Tyr Gln Pro Met Glu Pro Asn Pro Arg Val Pro Leu Ser Arg Val Phe Phe Ala Ser Trp
Arg Val Val Leu Glu Gly Gly Ile Asp Pro Ile Leu Arg Gly Leu Met Ala Thr Pro Ala Lys
Leu Asn Arg Gln Asn Gln Ile Ala Val Asp Glu Ile Arg Glu Arg Leu Phe Glu Gln Val
Met Arg Ile Gly Leu Asp Leu Pro Ala Leu Asn Met Gln Arg Ser Arg Asp His Gly Leu
Pro Gly Tyr Asn Ala Trp Arg Arg Phe Cys Gly Leu Pro Gln Pro Glu Thr Val Gly Gln
Leu Gly Thr Val Leu Arg Asn Leu Lys Leu Ala Arg Lys Leu Met Glu Gln Tyr Gly Thr
Pro Asn Asn Ile Asp Ile Trp Met Gly Gly Val Ser Glu Pro Leu Lys Arg Lys Gly Arg Val
Gly Pro Leu Leu Ala Cys Ile Ile Gly Thr Gln Phe Arg Lys Leu Arg Asp Gly Asp Arg Phe
Trp Trp Glu Asn Glu Gly Val Phe Ser Met Gln Gln Arg Gln Ala Leu Ala Gln Ile Ser Leu
Pro Arg Ile Ile Cys Asp Asn Thr Gly Ile Thr Thr Val Ser Lys Asn Asn Ile Phe Met Ser
Asn Ser Tyr Pro Arg Asp Phe Val Asn Cys Ser Thr Leu Pro Ala Leu Asn Leu Ala Ser
Trp Arg Glu Ala Ser

FIG. 5

Trp Val Pro Val Val Phe Leu Thr Leu Ser Val Thr Trp Ile Gly Ala Ala Pro Leu Ile Leu Ser Arg Ile Val Gly Gly Trp Glu Cys Glu Lys His Ser Gln Pro Trp Gln Val Leu Val Ala Ser Arg Gly Arg Ala Val Cys Gly Gly Val Leu Val His Pro Gln Trp Val Leu Thr Ala Ala His Cys Ile Arg Asn Lys Ser Val Ile Leu Leu Gly Arg His Ser Leu Phe His Pro Glu Asp Thr Gly Gln Val Phe Gln Val Ser His Ser Phe Pro His Pro Leu Tyr Asp Met Ser Leu Leu Lys Asn Arg Phe Leu Arg Pro Gly Asp Asp Ser Ser His Asp Leu Met Leu Leu Arg Leu Ser Glu Pro Ala Glu Leu Thr Asp Ala Val Lys Val Met Asp Leu Pro Thr Gln Glu Pro Ala Leu Gly Thr Thr Cys Tyr Ala Ser Gly Trp Gly Ser Ile Glu Pro Glu Glu Phe Leu Thr Pro Lys Lys Leu Gln Cys Val Asp Leu His Val Ile Ser Asn Asp Val Cys Ala Gln Val His Pro Gln Lys Val Thr Lys Phe Met Leu Cys Ala Gly Arg Trp Thr Gly Gly Lys Ser Thr Cys Ser Gly Asp Ser Gly Gly Pro Leu Val Cys Asn Gly Val Leu Gln Gly Ile Thr Ser Trp Gly Ser Glu Pro Cys Ala Leu Pro Glu Arg Pro Ser Leu Tyr Thr Lys Val Val His Tyr Arg Lys Trp Ile Lys Asp Thr Ile Val Ala Asn Pro

FIG. 6

Asp Pro Gln Thr Ala Pro Ser Arg Ala Leu Leu Leu Leu Leu Phe Leu His Leu Ala Phe Leu Gly Gly Arg Ser His Pro Leu Gly Ser Pro Gly Ser Ala Ser Asp Leu Glu Thr Ser Gly Leu Gln Glu Gln Arg Asn His Leu Gln Gly Lys Leu Ser Glu Leu Gln Val Glu Gln Thr Ser Leu Glu Pro Leu Gln Glu Ser Pro Arg Pro Thr Gly Val Trp Lys Ser Arg Glu Val Ala Thr Glu Gly Ile Arg Gly His Arg Lys Met Val Leu Tyr Thr Leu Arg Ala Pro Arg Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys Val Leu Arg Arg His

FIG. 7

Ala Pro Lys Lys Ala Lys Lys Arg Ala Gly Gly Ala Asn Ser Asn Val Phe Ser Met Phe Glu Gln Thr Gln Ile Gln Glu Phe Lys Glu Ala Phe Thr Ile Met Asp Gln Asn Arg Asp Gly Phe Ile Asp Lys Asn Asp Leu Arg Asp Thr Phe Ala Ala Leu Gly Arg Val Asn Val Lys Asn Glu Glu Ile Asp Glu Met Ile Lys Glu Ala Pro Gly Pro Ile Asn Phe Thr Val Phe Leu Thr Met Phe Gly Glu Lys Leu Lys Gly Ala Asp Pro Glu Glu Thr Ile Leu Asn Ala Phe Lys Val Phe Asp Pro Glu Gly Lys Gly Val Leu Lys Ala Asp Tyr Val Arg Glu Met Leu Thr Thr Gln Ala Glu Arg Phe Ser Lys Glu Glu Val Asp Gln Met Phe Ala Ala Phe Pro Pro Asp Val Thr Gly Asn Leu Asp Tyr Lys Asn Leu Val His Ile Ile Thr His Gly Glu Glu Lys Asp

FIG. 8

Thr Asp Ala Gln Met Ala Asp Phe Gly Ala Ala Ala Gln Tyr Leu Arg Lys Ser Glu Lys
Glu Arg Leu Glu Ala Gln Thr Arg Pro Phe Asp Ile Arg Thr Glu Cys Phe Val Pro Asp
Asp Lys Glu Glu Phe Val Lys Ala Lys Ile Leu Ser Arg Glu Gly Gly Lys Val Ile Ala Glu
Thr Glu Asn Gly Lys Thr Val Thr Val Lys Glu Asp Gln Val Leu Gln Gln Asn Pro Pro
Lys Phe Asp Lys Ile Gln Asp Met Ala Met Leu Thr Phe Leu His Glu Pro Ala Val Leu
Phe Asn Leu Lys Glu Arg Tyr Ala Ala Trp Met Ile Tyr Thr Tyr Ser Gly Leu Phe Cys Val
Thr Val Asn Pro Tyr Lys Trp Leu Pro Val Tyr Asn Ala Glu Val Val Ala Ala Tyr Arg Gly
Lys Lys Arg Ser Glu Ala Pro Pro His Ile Phe Ser Ile Ser Asp Asn Ala Tyr Gln Tyr Met
Leu Thr Asp Arg Glu Asn Gln Ser Ile Leu Ile Thr Gly Glu Ser Gly Ala Gly Lys Thr Val
Asn Thr Lys Arg Val Ile Gln Tyr Phe Ala Ser Ile Ala Ala Ile Gly Asp Arg Gly Lys Lys
Asp Asn Ala Asn Ala Asn Lys Gly Thr Leu Glu Asp Gln Ile Ile Gln Ala Asn Pro Ala Leu
Glu Ala Phe Gly Asn Ala Lys Thr Val Arg Asn Asp Asn Ser Ser Arg Phe Gly Lys Phe
Ile Arg Ile His Phe Gly Ala Thr Gly Lys Leu Ala Ser Ala Asp Ile Glu Thr Tyr Leu Leu
Glu Lys Ser Arg Val Ile Phe Gln Leu Lys Ala Glu Arg Asn Tyr His Ile Phe Tyr Gln Ile
Leu Ser Asn Lys Lys Pro Glu Leu Leu Asp Met Leu Leu Val Thr Asn Asn Pro Tyr Asp
Tyr Ala Phe Val Ser Gln Gly Glu Val Ser Val Ala Ser Ile Asp Asp Ser Glu Glu Leu Met
Ala Thr Asp Ser Ala Phe Asp Val Leu Gly Phe Thr Ser Glu Glu Lys Ala Gly Val Tyr Lys
Leu Thr Gly Ala Ile Met His Tyr Gly Asn Met Lys Phe Lys Gln Lys Gln Arg Glu Glu
Gln Ala Glu Pro Asp Gly Thr Glu Asp Ala Asp Lys Ser Ala Tyr Leu Met Gly Leu Asn
Ser Ala Asp Leu Leu Lys Gly Leu Cys His Pro Arg Val Lys Val Gly Asn Glu Tyr Val
Thr Lys Gly Gln Ser Val Gln Gln Val Tyr Tyr Ser Ile Gly Ala Leu Ala Lys Ala Val Tyr
Glu Lys Met Phe Asn Trp Met Val Thr Arg Ile Asn Ala Thr Leu Glu Thr Lys Gln Pro
Arg Gln Tyr Phe Ile Gly Val Leu Asp Ile Ala Gly Phe Glu Ile Phe Asp Phe Asn Ser Phe
Glu Gln Leu Cys Ile Asn Phe Thr Asn Glu Lys Leu Gln Gln Phe Phe Asn His His Met
Phe Val Leu Glu Gln Glu Glu Tyr Lys Lys Glu Gly Ile Glu Trp Thr Phe Ile Asp Phe Gly
Met Asp Leu Gln Ala Cys Ile Asp Leu Ile Glu Lys Pro Met Gly Ile Met Ser Ile Leu Glu
Glu Glu Cys Met Phe Pro Lys Ala Thr Asp Met Thr Phe Lys Ala Lys Leu Tyr Asp Asn
His Leu Gly Lys Ser Asn Asn Phe Gln Lys Pro Arg Asn Ile Lys Gly Lys Gln Glu Ala His
Phe Ser Leu Ile His Tyr Ala Gly Thr Val Asp Tyr Asn Ile Leu Gly Trp Leu Glu Lys Asn
Lys Asp Pro Leu Asn Glu Thr Val Val Ala Leu Tyr Gln Lys Ser Ser Leu Lys Leu Met
Ala Thr Leu Phe Ser Ser Tyr Ala Thr Ala Asp Thr Gly Asp Ser Gly Lys Ser Lys Gly Gly
Lys Lys Lys Gly Ser Ser Phe Gln Thr Val Ser Ala Leu His Arg Glu Asn Leu Asn Lys
Leu Met Thr Asn Leu Arg Thr Thr His Pro His Phe Val Arg Cys Ile Ile Pro Asn Glu Arg
Lys Ala Pro Gly Val Met Asp Asn Pro Leu Val Met His Gln Leu Arg Cys Asn Gly Val
Leu Glu Gly Ile Arg Ile Cys Arg Lys Gly Phe Pro Asn Arg Ile Leu Tyr Gly Asp Phe Arg
Gln Arg Tyr Arg Ile Leu Asn Pro Val Ala Ile Pro Glu Gly Gln Phe Ile Asp Ser Arg Lys
Gly Thr Glu Lys Leu Leu Ser Ser Leu Asp Ile Asp His Asn Gln Tyr Lys Phe Gly His Thr
Lys Val Phe Phe Lys Ala Gly Leu Leu Gly Leu Leu Glu Glu Met Arg Asp Glu Arg Leu
Ser Arg Ile Ile Thr Arg Met Gln Ala Gln Ala Arg Gly Gln Leu Met Arg Ile Glu Phe Lys
Lys Ile Val Glu Arg Arg Asp Ala Leu Leu Val Ile Gln Trp Asn Ile Arg Ala Phe Met Gly

FIG. 9A

Val Lys Asn Trp Pro Trp Met Lys Leu Tyr Phe Lys Ile Lys Pro Leu Leu Lys Ser Ala Glu Thr Glu Lys Glu Met Ala Thr Met Lys Glu Glu Phe Gly Arg Ile Lys Glu Thr Leu Glu Lys Ser Glu Ala Arg Arg Lys Glu Leu Glu Glu Lys Met Val Ser Leu Leu Gln Glu Lys Asn Asp Leu Gln Leu Gln Val Gln Ala Glu Gln Asp Asn Leu Asn Asp Ala Glu Glu Arg Cys Asp Gln Leu Ile Lys Asn Lys Ile Gln Leu Glu Ala Lys Val Lys Glu Met Asn Glu Arg Leu Glu Asp Glu Glu Glu Met Asn Ala Glu Leu Thr Ala Lys Lys Arg Lys Leu Glu Asp Glu Cys Ser Glu Leu Lys Lys Asp Ile Asp Asp Leu Glu Leu Thr Leu Ala Lys Val Glu Lys Glu Lys His Ala Thr Glu Asn Lys Val Lys Asn Leu Thr Glu Glu Met Ala Gly Leu Asp Glu Ile Ile Ala Lys Leu Thr Lys Glu Lys Lys Ala Leu Gln Glu Ala His Gln Gln Ala Leu Asp Asp Leu Gln Val Glu Glu Asp Lys Val Asn Ser Leu Ser Lys Ser Lys Val Lys Leu Glu Gln Gln Val Asp Asp Leu Glu Gly Ser Leu Glu Gln Glu Lys Lys Val Arg Met Asp Leu Glu Arg Ala Lys Arg Lys Leu Glu Gly Asp Leu Lys Leu Thr Gln Glu Ser Ile Met Asp Leu Glu Asn Asp Lys Leu Gln Leu Glu Glu Lys Leu Lys Lys Lys Glu Phe Asp Ile Asn Gln Gln Asn Ser Lys Ile Glu Asp Glu Gln Ala Leu Ala Leu Gln Leu Gln Lys Lys Leu Lys Glu Asn Gln Ala Arg Ile Glu Glu Leu Glu Glu Glu Leu Glu Ala Glu Arg Thr Ala Arg Ala Lys Val Glu Lys Leu Arg Ser Asp Leu Ser Arg Glu Leu Glu Glu Ile Ser Glu Arg Leu Glu Glu Ala Gly Gly Ala Thr Ser Val Gln Ile Glu Met Asn Lys Lys Arg Glu Ala Glu Phe Gln Lys Met Arg Arg Asp Leu Glu Glu Ala Thr Leu Gln His Glu Ala Thr Ala Ala Ala Leu Arg Lys Lys His Ala Asp Ser Val Ala Glu Leu Gly Glu Gln Ile Asp Asn Leu Gln Arg Val Lys Gln Lys Leu Glu Lys Glu Lys Ser Glu Phe Lys Leu Glu Leu Asp Asp Val Thr Ser Asn Met Glu Gln Ile Ile Lys Ala Lys Ala Asn Leu Glu Lys Val Ser Arg Thr Leu Glu Asp Gln Ala Asn Glu Tyr Arg Val Lys Leu Glu Glu Ala Gln Arg Ser Leu Asn Asp Phe Thr Thr Gln Arg Ala Lys Leu Gln Thr Glu Asn Gly Glu Leu Ala Arg Gln Leu Glu Glu Lys Glu Ala Leu Ile Ser Gln Leu Thr Arg Gly Lys Leu Ser Tyr Thr Gln Gln Met Glu Asp Leu Lys Arg Gln Leu Glu Glu Glu Gly Lys Ala Lys Asn Ala Leu Ala His Ala Leu Gln Ser Ala Arg His Asp Cys Asp Leu Leu Arg Glu Gln Tyr Glu Glu Glu Thr Glu Ala Lys Ala Glu Leu Gln Arg Val Leu Ser Lys Ala Asn Ser Glu Val Ala Gln Trp Arg Thr Lys Tyr Glu Thr Asp Ala Ile Gln Arg Thr Glu Glu Leu Glu Glu Ala Lys Lys Lys Leu Ala Gln Arg Leu Gln Asp Ala Glu Glu Ala Val Glu Ala Val Asn Ala Lys Cys Ser Ser Leu Glu Lys Thr Lys His Arg Leu Gln Asn Glu Ile Glu Asp Leu Met Val Asp Val Glu Arg Ser Asn Ala Ala Ala Ala Ala Leu Asp Lys Lys Gln Arg Asn Phe Asp Lys Ile Leu Ala Glu Trp Lys Gln Lys Tyr Glu Glu Ser Gln Ser Glu Leu Glu Ser Ser Gln Lys Glu Ala Arg Ser Leu Ser Thr Glu Leu Phe Lys Leu Lys Asn Ala Tyr Glu Glu Ser Leu Glu His Leu Glu Thr Phe Lys Arg Glu Asn Lys Asn Leu Gln Glu Glu Ile Ser Asp Leu Thr Glu Gln Leu Gly Glu Gly Gly Lys Asn Val His Glu Leu Glu Lys Val Arg Lys Gln Leu Glu Val Glu Lys Leu Glu Leu Gln Ser Ala Leu Glu Glu Ala Glu Ala Ser Leu Glu His Glu Glu Gly Lys Ile Leu Arg Ala Gln Leu Glu Phe Asn Gln Ile Lys Ala Glu Ile Glu Arg Lys Leu Ala Glu Lys Asp Glu Glu Met Glu Gln Ala Lys Arg Asn His Gln Arg Val Val Asp Ser Leu Gln Thr Ser Leu Asp Ala Glu Thr Arg Ser Arg Asn Glu Val Leu Arg Val Lys Lys Lys Met Glu Gly

FIG. 9B

Asp Leu Asn Glu Met Glu Ile Gln Leu Ser His Ala Asn Arg Met Ala Ala Glu Ala Gln
Lys Gln Val Lys Ser Leu Gln Ser Leu Leu Lys Asp Thr Gln Ile Gln Leu Asp Asp Ala
Val Arg Ala Asn Asp Asp Leu Lys Glu Asn Ile Ala Ile Val Glu Arg Arg Asn Asn Leu
Leu Gln Ala Glu Leu Glu Glu Leu Arg Ala Val Val Glu Gln Thr Glu Arg Ser Arg Lys
Leu Ala Glu Gln Glu Leu Ile Glu Thr Ser Glu Arg Val Gln Leu Leu His Ser Gln Asn
Thr Ser Leu Ile Asn Gln Lys Lys Lys Met Glu Ala Asp Leu Thr Gln Leu Gln Ser Glu
Val Glu Glu Ala Val Gln Glu Cys Arg Asn Ala Glu Glu Lys Ala Lys Lys Ala Ile Thr
Asp Ala Ala Met Met Ala Glu Glu Leu Lys Lys Glu Gln Asp Thr Ser Ala His Leu Glu
Arg Met Lys Lys Asn Met Glu Gln Thr Ile Lys Asp Leu Gln His Arg Leu Asp Glu Ala
Glu Gln Ile Ala Leu Lys Gly Gly Lys Lys Gln Leu Gln Lys Leu Glu Ala Arg Val Arg
Glu Leu Glu Gly Glu Leu Glu Ala Glu Gln Lys Arg Asn Ala Glu Ser Val Lys Gly Met
Arg Lys Ser Glu Arg Arg Ile Lys Glu Leu Thr Tyr Gln Thr Glu Glu Asp Lys Lys Asn
Leu Leu Arg Leu Gln Asp Leu Val Asp Lys Leu Gln Leu Lys Val Lys Ala Tyr Lys
Arg Gln Ala Glu Glu Ala Glu Glu Gln Ala Asn Thr Asn Leu Ser Lys Phe Arg Lys Val
Gln His Glu Leu Asp Glu Ala Glu Glu Arg Ala Asp Ile Ala Glu Ser Gln Val Asn Lys
Leu Arg Ala Lys Ser Arg Asp Ile Gly Ala Lys Gln Lys Met His Asp Glu Glu

FIG. 9C

Gly Asp Ser Glu Met Ala Val Phe Gly Ala Ala Ala Pro Tyr Leu Arg Lys Ser Glu Lys
Glu Arg Leu Glu Ala Gln Thr Arg Pro Phe Asp Leu Lys Lys Asp Val Phe Val Pro Asp
Asp Lys Gln Glu Phe Val Lys Ala Lys Ile Val Ser Arg Glu Gly Gly Lys Val Thr Ala Glu
Thr Glu Tyr Gly Lys Thr Val Thr Val Lys Glu Asp Gln Val Met Gln Gln Asn Pro Pro
Lys Phe Asp Lys Ile Glu Asp Met Ala Met Leu Thr Phe Leu His Glu Pro Ala Val Leu
Tyr Asn Leu Lys Asp Arg Tyr Gly Ser Trp Met Ile Tyr Thr Tyr Ser Gly Leu Phe Cys Val
Thr Val Asn Pro Tyr Lys Trp Leu Pro Val Tyr Thr Pro Glu Val Val Ala Ala Tyr Arg Gly
Lys Lys Arg Ser Glu Ala Pro Pro His Ile Phe Ser Ile Ser Asp Asn Ala Tyr Gln Tyr Met
Leu Thr Asp Arg Glu Asn Gln Ser Ile Leu Ile Thr Gly Glu Ser Gly Ala Gly Lys Thr Val
Asn Thr Lys Arg Val Ile Gln Tyr Phe Ala Val Ile Ala Ala Ile Gly Asp Arg Ser Lys Lys
Asp Gln Ser Pro Gly Lys Gly Thr Leu Glu Asp Gln Ile Ile Gln Ala Asn Pro Ala Leu Glu
Ala Phe Gly Asn Ala Lys Thr Val Arg Asn Asp Asn Ser Ser Arg Phe Gly Lys Phe Ile
Arg Ile His Phe Gly Ala Thr Gly Lys Leu Ala Ser Ala Asp Ile Glu Thr Tyr Leu Leu Glu
Lys Ser Arg Val Ile Phe Gln Leu Lys Ala Glu Arg Asp Tyr His Ile Phe Tyr Gln Ile
Leu Ser Asn Lys Lys Pro Glu Leu Leu Asp Met Leu Leu Ile Thr Asn Asn Pro Tyr Asp
Tyr Ala Phe Ile Ser Gln Gly Glu Thr Thr Val Ala Ser Ile Asp Asp Ala Glu Glu Leu Met
Ala Thr Asp Asn Ala Phe Asp Val Leu Gly Phe Thr Ser Glu Glu Lys Asn Ser Met Tyr
Lys Leu Thr Gly Ala Ile Met His Phe Gly Asn Met Lys Phe Lys Leu Lys Gln Arg
Glu Glu Gln Ala Glu Pro Asp Gly Thr Glu Glu Ala Asp Lys Ser Ala Tyr Leu Met Gly
Leu Asn Ser Ala Asp Leu Leu Lys Gly Leu Cys His Pro Arg Val Lys Val Gly Asn Glu
Tyr Val Thr Lys Gly Gln Asn Val Gln Gln Val Ile Tyr Ala Thr Gly Ala Leu Ala Lys Ala
Val Tyr Glu Arg Met Phe Asn Trp Met Val Thr Arg Ile Asn Ala Thr Leu Glu Thr
Lys Gln Pro Arg Gln Tyr Phe Ile Gly Val Leu Asp Ile Ala Gly Phe Glu Ile Phe Asp Phe
Asn Ser Phe Glu Gln Leu Cys Ile Asn Phe Thr Asn Glu Lys Leu Gln Gln Phe Phe Asn
His His Met Phe Val Leu Glu Gln Glu Glu Tyr Lys Lys Glu Gly Ile Glu Trp Thr Phe Ile
Asp Phe Gly Met Asp Leu Gln Ala Cys Ile Asp Leu Ile Glu Lys Pro Met Gly Ile Met Ser
Ile Leu Glu Glu Glu Cys Met Phe Pro Lys Ala Thr Asp Met Thr Phe Lys Ala Lys Leu
Phe Asp Asn His Leu Gly Lys Ser Ala Asn Phe Gln Lys Pro Arg Asn Ile Lys Gly Lys
Pro Glu Ala His Phe Ser Leu Ile His Tyr Ala Gly Ile Val Asp Tyr Asn Ile Ile Gly Trp
Leu Gln Lys Asn Lys Asp Pro Leu Asn Glu Thr Val Val Gly Leu Tyr Gln Lys Ser Ser
Leu Lys Leu Leu Ser Thr Leu Phe Ala Asn Tyr Ala Gly Ala Asp Ala Pro Ile Glu Lys Gly
Lys Gly Lys Ala Lys Lys Gly Ser Ser Phe Gln Thr Val Ser Ala Leu His Arg Glu Asn Leu
Asn Lys Leu Met Thr Asn Leu Arg Ser Thr His Pro His Phe Val Arg Cys Ile Ile Pro Asn
Glu Thr Lys Ser Pro Gly Val Met Asp Asn Pro Leu Val Met His Gln Leu Arg Cys Asn
Gly Val Leu Glu Gly Ile Arg Ile Cys Arg Lys Gly Phe Pro Asn Arg Ile Leu Tyr Gly Asp
Phe Arg Gln Arg Tyr Arg Ile Leu Asn Pro Ala Ala Ile Pro Glu Gly Gln Phe Ile Asp
Ser Arg Lys Gly Ala Glu Lys Leu Leu Ser Ser Leu Asp Ile Asp His Asn Gln Tyr Lys Phe
Gly His Thr Lys Val Phe Phe Lys Ala Gly Leu Leu Gly Leu Leu Glu Glu Met Arg Asp
Glu Arg Leu Ser Arg Ile Ile Thr Arg Ile Gln Ala Gln Ser Arg Gly Val Leu Ala Arg Met

FIG. 10A

Glu Tyr Lys Lys Leu Leu Glu Arg Arg Asp Ser Leu Leu Val Ile Gln Trp Asn Ile Arg Ala
Phe Met Gly Val Lys Asn Trp Pro Trp Met Lys Leu Tyr Phe Lys Ile Lys Pro Leu Leu
Lys Ser Ala Glu Arg Glu Lys Glu Met Ala Ser Met Lys Glu Glu Phe Thr Arg Leu Lys
Glu Ala Leu Glu Lys Ser Glu Ala Arg Arg Lys Glu Leu Glu Glu Lys Met Val Ser Leu
Leu Gln Glu Lys Asn Asp Leu Gln Leu Gln Val Gln Ala Glu Gln Asp Asn Leu Ala Asp
Ala Glu Glu Arg Cys Asp Gln Leu Ile Lys Asn Lys Ile Gln Leu Glu Ala Lys Val Lys Glu
Met Asn Glu Arg Leu Glu Asp Glu Glu Glu Met Asn Ala Glu Leu Thr Ala Lys Lys Arg
Lys Leu Glu Asp Glu Cys Ser Glu Leu Lys Arg Asp Ile Asp Asp Leu Glu Leu Thr Leu
Ala Lys Val Glu Lys Glu Lys His Ala Thr Glu Asn Lys Val Lys Asn Leu Thr Glu Glu
Met Ala Gly Leu Asp Glu Ile Ile Ala Lys Leu Thr Lys Glu Lys Lys Ala Leu Gln Glu Ala
His Gln Gln Ala Leu Asp Asp Leu Gln Ala Glu Glu Asp Lys Val Asn Thr Leu Thr Lys
Ala Lys Val Lys Leu Glu Gln Gln Val Asp Asp Leu Glu Gly Ser Leu Glu Gln Glu Lys
Lys Val Arg Met Asp Leu Glu Arg Ala Lys Arg Lys Leu Glu Gly Asp Leu Lys Leu
Thr Gln Glu Ser Ile Met Asp Leu Glu Asn Asp Lys Gln Gln Leu Asp Glu Arg Leu Lys
Lys Lys Asp Phe Glu Leu Asn Ala Leu Asn Ala Arg Ile Glu Asp Glu Gln Ala Leu Gly
Ser Gln Leu Gln Lys Lys Leu Lys Glu Leu Gln Ala Arg Ile Glu Glu Leu Glu Glu Glu
Leu Glu Ala Glu Arg Thr Ala Arg Ala Lys Val Glu Lys Leu Arg Ser Asp Leu Ser Arg
Glu Leu Glu Glu Ile Ser Glu Arg Leu Glu Glu Ala Gly Gly Ala Thr Ser Val Gln Ile
Glu Met Asn Lys Lys Arg Glu Ala Glu Phe Gln Lys Met Arg Arg Asp Leu Glu Glu
Ala Thr Leu Gln His Glu Ala Thr Ala Ala Ala Leu Arg Lys Lys His Ala Asp Ser Val
Ala Glu Leu Gly Glu Gln Ile Asp Asn Leu Gln Arg Val Lys Gln Lys Leu Glu Lys
Glu Lys Ser Glu Phe Lys Leu Glu Leu Asp Asp Val Thr Ser Asn Met Glu Gln Ile Ile
Lys Ala Lys Ala Asn Leu Glu Lys Met Cys Arg Thr Leu Glu Asp Gln Met Asn Glu
His Arg Ser Lys Ala Glu Glu Thr Gln Arg Ser Val Asn Asp Leu Thr Ser Gln Arg Ala
Lys Leu Gln Thr Glu Asn Gly Glu Leu Ser Arg Gln Leu Asp Glu Lys Glu Ala Leu Ile
Ser Gln Leu Thr Arg Gly Lys Leu Thr Tyr Thr Gln Gln Leu Glu Asp Leu Lys Arg Gln
Leu Glu Glu Glu Val Lys Ala Lys Asn Ala Leu Ala His Ala Leu Gln Ser Ala Arg His
Asp Cys Asp Leu Leu Arg Glu Gln Tyr Glu Glu Glu Thr Glu Ala Lys Ala Glu Leu
Gln Arg Val Leu Ser Lys Ala Asn Ser Glu Val Ala Gln Trp Arg Thr Lys Tyr Glu Thr
Asp Ala Ile Gln Arg Thr Glu Glu Leu Glu Glu Ala Lys Lys Lys Leu Ala Gln Arg Leu
Gln Glu Ala Glu Glu Ala Val Glu Ala Val Asn Ala Lys Cys Ser Ser Leu Glu Lys Thr
Lys His Arg Leu Gln Asn Glu Ile Glu Asp Leu Met Val Asp Val Glu Arg Ser Asn Ala
Ala Ala Ala Ala Ala Leu Asp Lys Lys Gln Arg Asn Phe Asp Lys Ile Leu Ala Glu Trp Lys
Gln Lys Tyr Glu Glu Ser Gln Ser Glu Leu Glu Ser Ser Gln Lys Glu Ala Arg Ser Leu
Ser Thr Glu Leu Phe Lys Leu Lys Asn Ala Tyr Glu Glu Ser Leu Glu His Leu Glu Thr
Phe Lys Arg Glu Asn Lys Asn Leu Gln Glu Glu Ile Ser Asp Leu Thr Glu Gln Leu Gly
Ser Ser Gly Lys Thr Ile His Glu Leu Glu Lys Val Arg Lys Gln Leu Glu Ala Glu Lys
Met Glu Leu Gln Ser Ala Leu Glu Glu Ala Glu Ala Ser Leu Glu His Glu Glu Gly Lys

FIG. 10B

Ile Leu Arg Ala Gln Leu Glu Phe Asn Gln Ile Lys Ala Glu Ile Glu Arg Lys Leu Ala Glu Lys Asp Glu Glu Met Glu Gln Ala Lys Arg Asn His Leu Arg Val Val Asp Ser Leu Gln Thr Ser Leu Asp Ala Glu Thr Arg Ser Arg Asn Glu Ala Leu Arg Val Lys Lys Lys Met Glu Gly Asp Leu Asn Glu Met Glu Ile Gln Leu Ser His Ala Asn Arg Met Ala Ala Glu Ala Gln Lys Gln Val Lys Ser Leu Gln Ser Leu Leu Lys Asp Thr Gln Ile Gln Leu Asp Asp Ala Val Arg Ala Asn Asp Asp Leu Lys Glu Asn Ile Ala Ile Val Glu Arg Arg Asn Asn Leu Leu Gln Ala Glu Leu Glu Glu Leu Arg Ala Val Val Glu Gln Thr Glu Arg Ser Arg Lys Leu Ala Glu Gln Glu Leu Ile Glu Thr Ser Glu Arg Val Gln Leu Leu His Ser Gln Asn Thr Ser Leu Ile Asn Gln Lys Lys Lys Met Asp Ala Asp Leu Ser Gln Leu Gln Thr Glu Val Glu Glu Ala Val Gln Glu Cys Arg Asn Ala Glu Glu Lys Ala Lys Lys Ala Ile Thr Asp Ala Ala Met Met Ala Glu Glu Leu Lys Lys Glu Gln Asp Thr Ser Ala His Leu Glu Arg Met Lys Lys Asn Met Glu Gln Thr Ile Lys Asp Leu Gln His Arg Leu Asp Glu Ala Glu Gln Ile Ala Leu Lys Gly Gly Lys Lys Gln Leu Gln Lys Leu Glu Ala Arg Val Arg Glu Leu Glu Asn Glu Leu Glu Ala Glu Gln Lys Arg Asn Ala Glu Ser Val Lys Gly Met Arg Lys Ser Glu Arg Arg Ile Lys Glu Leu Thr Tyr Gln Thr Glu Glu Asp Arg Lys Asn Leu Leu Arg Leu Gln Asp Leu Val Asp Lys Leu Gln Leu Lys Val Lys Ala Tyr Lys Arg Gln Ala Glu Glu Ala Glu Glu Gln Ala Asn Thr Asn Leu Ser Lys Phe Arg Lys Val Gln His Glu Leu Asp Glu Ala Glu Glu Arg Ala Asp Ile Ala Glu Ser Gln Val Asn Lys Leu Arg Ala Lys Ser Arg Asp Ile Gly Thr Lys Gly Leu Asn Glu Glu

FIG. 10C

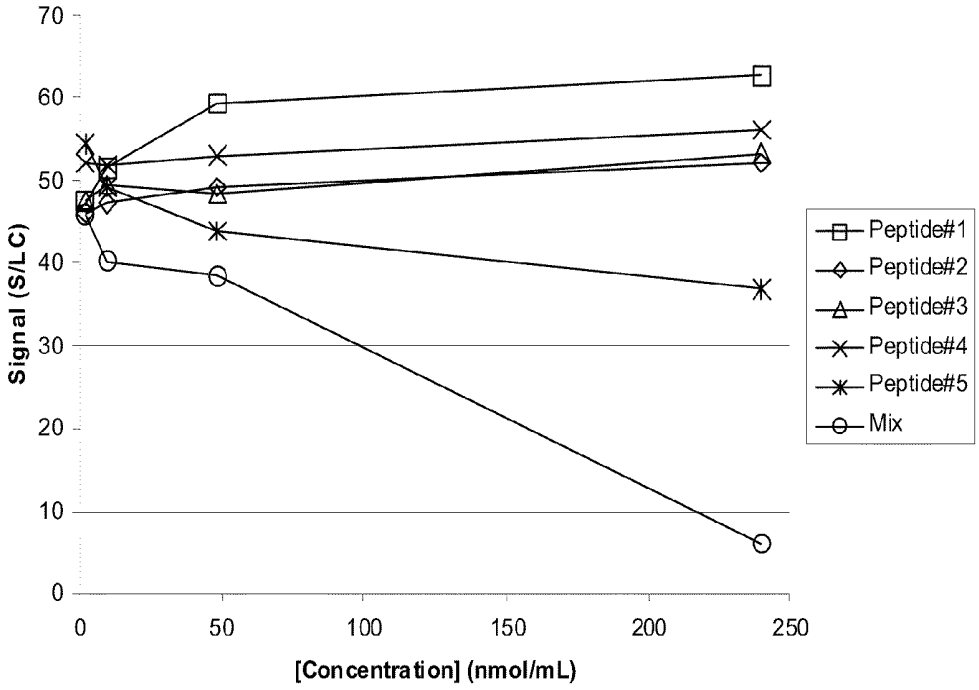

70
60
50
40
30
20
10
0
Signal (S/LC)
0
50
100
150
200
250
[Concentration] (nmol/mL)
Peptide#1
Peptide#2
Peptide#3
Peptide#4
Peptide#5
Mix

FIG. 11

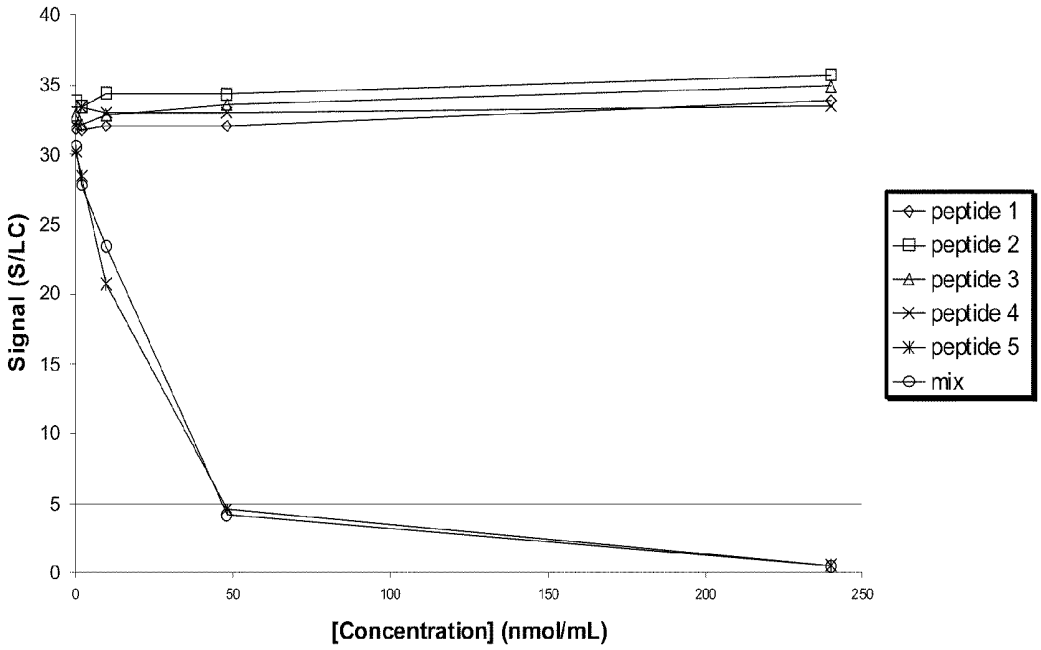

40
35
30
25
20
15
10
5
0
Signal (S/LC)
0
50
100
150
200
250
[Concentration] (nmol/mL)
peptide 1
peptide 2
peptide 3
peptide 4
peptide 5
mix

FIG. 12

PEPTIDE REAGENTS AND METHOD FOR INHIBITING AUTOANTIBODY ANTIGEN BINDING

RELATED APPLICATION INFORMATION

[0001] None.

INCORPORATION OF SEQUENCE LISTING

[0002] The entire contents of a paper copy of the "Sequence Listing" and a computer readable form of the sequence listing on diskette, containing the file named 400797_SequenceListing_ST25.txt, which is 56 kilobytes in size and was created on Dec. 3, 2009, 2009, are herein incorporated by reference.

TECHNICAL FIELD

[0003] The present disclosure relates to methods and kits for detecting a protein of interest in a test sample, and in particular to methods and kits for detecting the protein in a human test sample that may contain endogenous anti-analyte antibodies.

BACKGROUND

[0004] Immunoassay techniques have been known for the last few decades and are now commonly used in medicine for a wide variety of diagnostic purposes to detect target analytes in a biological sample. Immunoassays exploit the highly specific binding of an antibody to its corresponding antigen, wherein the antigen is the target analyte. Typically, quantification of either the antibody or antigen is achieved through some form of labeling such as radio- or fluorescence-labeling. Sandwich immunoassays involve binding the target analyte in the sample to the antibody site (which is frequently bound to a solid support), binding labeled antibody to the captured analyte, and then measuring the amount of bound labeled antibody, wherein the label generates a signal proportional to the concentration of the target analyte inasmuch as labeled antibody does not bind unless the analyte is present in the sample.

[0005] A problem with this general approach is that many patients have circulating endogenous antibodies, or "autoantibodies" against an analyte of clinical interest. For example, autoantibodies have been described for cardiac troponin, myeloperoxidase (MPO), prostate specific antigen (PSA), and thyroid stimulating hormone (TSH), and other clinically significant analytes. Autoantibodies create interference in typical sandwich immunoassays that are composed of two or more analyte-specific antibodies. For example, cardiac troponin-reactive autoantibodies may interfere with the measurement of cTnI using conventional midfragment-specific immunoassays. Thus, interference from autoantibodies can produce erroneous results, particularly near the cut-off values established for clinical diagnoses, and increases the risk of false negative diagnostic results and the risk that individuals will not obtain a timely diagnosis.

[0006] One approach to addressing this problem is to choose analyte-specific antibodies that bind to specific epitopes distinct from the analyte epitopes that react with the autoantibodies. Following this general approach, efforts have focused on exploring the use of thousands of different combinations of two, three and even four analyte-specific antibodies to avoid interference from autoantibodies. However, this effort has been largely unsuccessful. It is now evident that autoantibodies against complex protein analytes are likely to be polyclonal within a particular sample, and may be even more diverse among samples from different individuals. Interference from diverse polyclonal autoantibodies may explain the observation that as little as 25% or even less of an analyte protein sequence binds to analyte-specific antibodies, which may in turn explain the lack of success using this approach.

[0007] A need exists in the art for new immunoassay methods that compensate for interference by autoantibodies in a sample, and in particular for such methods that do so without involving redesign of the analyte detection or capture antibodies.

SUMMARY

[0008] In one embodiment, the present disclosure relates to a reagent for use in an immunoassay for determining the presence or amount of at least one protein in a test sample, the reagent comprising at least one peptide comprising at least 5 consecutive amino acid residues wherein the peptide is derived from the protein and further wherein the reagent is used to block the interaction between an endogenous antibody and the protein in the test sample.

[0009] In certain embodiments, the protein from which the reagent is derived may be selected from the group consisting of: cardiac troponin I (SEQ ID NO:1), cardiac troponin T (SEQ ID NO:2), thyroid stimulating hormone (TSH) (SEQ ID NO:3), beta-human chorionic gonadotropin (beta-HCG) (SEQ ID NO:4), myeloperoxidase (MPO) (SEQ ID NO:5), prostate specific antigen (PSA) (SEQ ID NO:6), human B-type natriuretic peptide (hBNP) (SEQ ID NO:7), myosin light chain 2 (SEQ ID NO:8), myosin-6 (SEQ ID NO:9) and myosin-7 (SEQ ID NO:10).

[0010] The peptide can have, for example, an amino acid sequence of five (5) consecutive amino acid residues to fifteen (15) consecutive amino acid residues from the amino acid sequence of the protein from which the reagent is derived. In one embodiment, for example, the protein from which the reagent is derived is cardiac troponin I, and the reagent has an amino acid sequence comprising at least five consecutive amino acid residues from the full amino acid sequence of cardiac troponin I (SEQ ID NO: 1). In certain embodiments, the peptide reagent has a sequence selected from the group consisting of SSDAAREPRPAPAPI (SEQ ID NO:11), VDEERYDIEAKVTKN (SEQ ID NO:12), DIEAKVTKNITEIAD (SEQ ID NO:13), LDLRAHLKQVKKEDT (SEQ ID NO:14), and ALSGMEGRKKKFES (SEQ ID NO:15), or any subsequence thereof consisting of at least 5 consecutive amino acid residues.

[0011] In another embodiment, the present disclosure relates to a reagent for use in an immunoassay for determining the presence or amount of a cardiac troponin I in a test sample, the reagent comprising a peptide having a sequence comprising at least five consecutive amino acid residues from a sequence selected from the group consisting of SSDAAREPRPAPAPI (SEQ ID NO:11), VDEERYDIEAKVTKN (SEQ ID NO:12), DIEAKVTKNITEIAD (SEQ ID NO:13), LDLRAHLKQVKKEDT (SEQ ID NO:14), and ALSGMEGRKKKFES (SEQ ID NO:15).

[0012] In another embodiment, the present disclosure relates to a method of detecting at least one protein of interest in a test sample, the method comprising the steps of:

[0013] a. preparing a first mixture comprising a test sample suspected of containing at least one protein of interest and at least one reagent, wherein said reagent (1) is at least one peptide comprising at least 5 consecutive amino acid residues derived from said protein that binds to the antibody of interest; and (2) disrupts the interaction between an endogenous antibody in the test sample and the antigen;

[0014] b. preparing a second mixture comprising the first mixture and a first specific binding partner, wherein the first specific binding partner comprises an antibody, wherein the antibody binds with the protein of interest to form a first specific binding partner-protein complex; and

[0015] c. contacting the second mixture with a second specific binding partner, wherein the second specific binding partner comprises an antibody that has been conjugated to a detectable label and further wherein the second specific binding partner binds to the first specific binding partner-protein complex to form a first specific binding partner-protein-second specific binding partner complex; and

[0016] d. measuring the signal generated by or emitted from the detectable label and detecting the protein of interest in the test sample.

[0017] In the above-described method, the protein can be selected for example from the group consisting of: cardiac troponin I, cardiac troponin T, thyroid stimulating hormone (TSH), beta-human chorionic gonadotropin (beta-HCG), myeloperoxidase (MPO), prostate specific antigen (PSA), human B-type natriuretic peptide (hBNP), myosin light chain 2, myosin-6 and myosin

[0018] In the above-described method the test sample can be whole blood, serum or plasma.

[0019] In one embodiment of the method, the first specific binding partner can be immobilized to a solid phase either before or after the formation of the first specific binding partner-protein complex. Additionally, the second specific binding partner can be immobilized to a solid phase either before or after formation of the first specific binding partner-protein-second specific binding partner complex.

[0020] In the above-described method the detectable label can be selected from the group consisting of a radioactive label, an enzymatic label, a chemiluminescent label, a fluorescence label, a thermometric label, and an immuno-polymerase chain reaction label.

[0021] In one embodiment of the method the detectable label is an acridinium compound. When an acridinium compound is used, the method may further include:

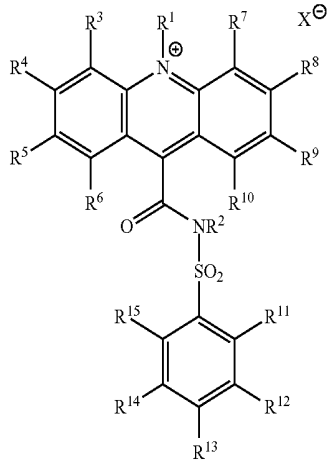
[0022] a. generating or providing a source of hydrogen peroxide to the second mixture contacted with a second specific binding partner;

[0023] b. adding a basic solution to the mixture of step (a); and

[0024] c. measuring the light signal generated or emitted in step (b) and detecting the protein of interest in the sample.

[0025] Any acridinium compound can be used in the above-described method. For example, the acridinium compound can be an acridinium-9-carboxamide having a structure according to formula I:

I

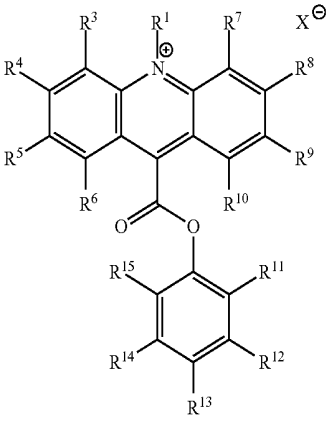


[0026] wherein R1 and R2 are each independently selected from the group consisting of: alkyl, alkenyl, alkynyl, aryl or aralkyl, sulfoalkyl, carboxyalkyl and oxoalkyl, and

[0027] wherein R3 through R15 are each independently selected from the group consisting of: hydrogen, alkyl, alkenyl, alkynyl, aryl or aralkyl, amino, amido, acyl, alkoxyl, hydroxyl, carboxyl, halogen, halide, nitro, cyano, sulfo, sulfoalkyl, carboxyalkyl and oxoalkyl; and optionally, if present, XΘ is an anion.

[0028] Alternatively, the acridinium compound can be an acridinium-9-carboxylate aryl ester having a structure according to formula II:

II



[0029] wherein R1 is an alkyl, alkenyl, alkynyl, aryl or aralkyl, sulfoalkyl, carboxyalkyl and oxoalkyl; and

[0030] wherein R3 through R15 are each independently selected from the group consisting of: hydrogen, alkyl, alkenyl, alkynyl, aryl or aralkyl, amino, amido, acyl, alkoxyl, hydroxyl, carboxyl, halogen, halide, nitro, cyano, sulfo, sulfoalkyl, carboxyalkyl and oxoalkyl; and

[0031] optionally, if present, XΘ is an anion.

[0032] In the above-described method, the reagent can be a peptide having a length of 5 consecutive amino acids to 15 consecutive amino acids.

[0033] In one embodiment of the method, the protein from which the peptide is derived is cardiac troponin I, and the peptide has a sequence comprising at least five consecutive amino acid residues from a sequence selected from the group consisting of SSDAAREPRPAPAPI (SEQ ID NO:11), VDEERYDIEAKVTKN (SEQ ID NO:12), DIEAKVTKNITEIAD (SEQ ID NO:13), LDLRAHLKQVKKEDT (SEQ ID NO:14), and ALSGMEGRKKKFES (SEQ ID NO:15).

[0034] The above-described method may further include the step of quantifying the amount of protein of interest in the test sample by relating the amount of signal in step (c) to the amount of the one or more proteins of interest in the test sample either by use of a standard curve for the protein of interest or by comparison to a reference standard.

[0035] The above-described method may be adapted for use in an automated system or semi-automated system.

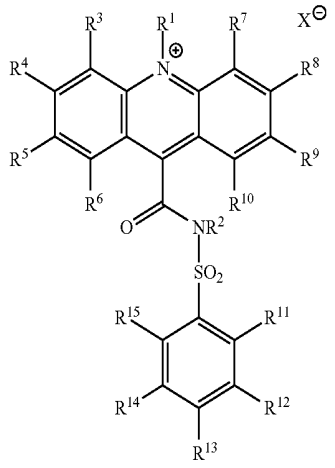
[0036] In still another embodiment, the present disclosure relates to a kit for detecting and/or quantifying at least one protein of interest in a test sample, the kit comprising the above-described peptide reagent, a capture reagent comprising an antibody that binds to the protein of interest, and instructions for detecting and/or quantifying at least one protein of interest in a test sample.

[0037] The above-described kit may further include a conjugate comprising an antibody conjugated to a detectable label.

[0038] In one embodiment of the kit, the detectable label can be selected from the group consisting of a radioactive label, an enzymatic label, a chemiluminescent label, a fluorescence label, a thermometric label, and an immuno-polymerase chain reaction label.

[0039] The detectable label used in the above-described kit can be an acridinium compound. Any acridinium compound can be used. For example the acridinium compound can be an acridinium-9-carboxamide having a structure according to formula I:

I



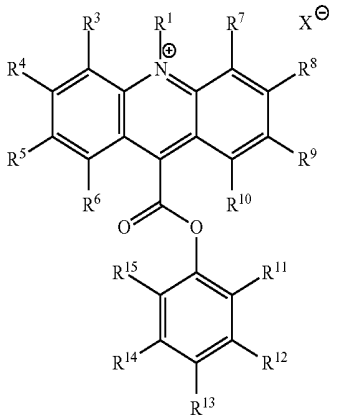
[0040] wherein R1 and R2 are each independently selected from the group consisting of: alkyl, alkenyl, alkynyl, aryl or aralkyl, sulfoalkyl, carboxyalkyl and oxoalkyl, and

[0041] wherein R3 through R15 are each independently selected from the group consisting of: hydrogen, alkyl, alkenyl, alkynyl, aryl or aralkyl, amino, amido, acyl, alkoxyl, hydroxyl, carboxyl, halogen, halide, nitro, cyano, sulfo, sulfoalkyl, carboxyalkyl and oxoalkyl; and

[0042] optionally, if present, $X^{\ominus}$ is an anion.

[0043] Alternatively, the acridinium compound can be an acridinium-9-carboxylate aryl ester having a structure according to formula II:

II



wherein R1 is an alkyl, alkenyl, alkynyl, aryl or aralkyl, sulfoalkyl, carboxyalkyl and oxoalkyl; and

[0044] wherein R3 through R15 are each independently selected from the group consisting of: hydrogen, alkyl, alkenyl, alkynyl, aryl or aralkyl, amino, amido, acyl, alkoxyl, hydroxyl, carboxyl, halogen, halide, nitro, cyano, sulfo, sulfoalkyl, carboxyalkyl and oxoalkyl; and

[0045] optionally, if present, XΘ is an anion.

[0046] When an acridinium compound is included as the detectable label in the above-described kit, the kit optionally further includes a basic solution. The basic solution can be for example a solution having a pH of at least about 10.

[0047] The above kit may further include a hydrogen peroxide source, which can be a buffer, a solution containing hydrogen peroxide, or a hydrogen peroxide generating enzyme. In kits containing a hydrogen peroxide generating enzyme, the enzyme can be selected from the group consisting of: (R)-6-hydroxynicotine oxidase, (S)-2-hydroxy acid oxidase, (S)-6-hydroxynicotine oxidase, 3-aci-nitropropanoate oxidase, 3-hydroxyanthranilate oxidase, 4-hydroxymandelate oxidase, 6-hydroxynicotinate dehydrogenase, abscisic-aldehyde oxidase, acyl-CoA oxidase, alcohol oxidase, aldehyde oxidase, amine oxidase, amine oxidase (copper-containing), amine oxidase (flavin-containing), aryl-alcohol oxidase, aryl-aldehyde oxidase, catechol oxidase, cholesterol oxidase, choline oxidase, columbamine oxidase, cyclohexylamine oxidase, cytochrome c oxidase, D-amino-acid oxidase, D-arabinono-1,4-lactone oxidase, D-arabinono-1,4-lactone oxidase, D-aspartate oxidase, D-glutamate oxidase, D-glutamate(D-aspartate) oxidase, dihydrobenzophenanthridine oxidase, dihydroorotate oxidase, dihydrouracil oxidase, dimethylglycine oxidase, D-mannitol oxidase, ecdysone oxidase, ethanolamine oxidase, galactose oxidase, glucose oxidase, glutathione oxidase, glycerol-3-phosphate oxidase, glycine oxidase, glyoxylate oxidase, hexose oxidase, hydroxyphytanate oxidase, indole-3-acetaldehyde oxidase, lactic acid oxidase, L-amino-acid oxidase, L-aspartate oxidase, L-galactonolactone oxidase, L-glutamate oxidase, L-gulonolactone oxidase,

L-lysine 6-oxidase, L-lysine oxidase, long-chain-alcohol oxidase, L-pipecolate oxidase, L-sorbose oxidase, malate oxidase, methanethiol oxidase, monoamino acid oxidase, N6-methyl-lysine oxidase, N-acylhexosamine oxidase, NAD (P)H oxidase, nitroalkane oxidase, N-methyl-L-amino-acid oxidase, nucleoside oxidase, oxalate oxidase, polyamine oxidase, polyphenol oxidase, polyvinyl-alcohol oxidase, prenylcysteine oxidase, protein-lysine 6-oxidase, putrescine oxidase, pyranose oxidase, pyridoxal 5'-phosphate synthase, pyridoxine 4-oxidase, pyrroloquinoline-quinone synthase, pyruvate oxidase, pyruvate oxidase (CoA-acetylating), reticuline oxidase, retinal oxidase, rifamycin-B oxidase, sarcosine oxidase, secondary-alcohol oxidase, sulfite oxidase, superoxide dismutase, superoxide reductase, tetrahydroberberine oxidase, thiamine oxidase, tryptophan α,β-oxidase, urate oxidase (uricase, uric acid oxidase), vanillyl-alcohol oxidase, xanthine oxidase, xylitol oxidase and combinations thereof.

[0048] In one embodiment, the above-described kit includes a reagent derived from a protein selected from the group consisting of: cardiac troponin I, cardiac troponin T, thyroid stimulating hormone (TSH), beta-human chorionic gonadotropin (beta-HCG), myeloperoxidase (MPO), prostate specific antigen (PSA), human B-type natriuretic peptide (hBNP), myosin light chain 2, myosin-6 and myosin-7.

[0049] In the above-described kit, the reagent can be a peptide having a length of 5 consecutive amino acids to 15 consecutive amino acids.

[0050] In one embodiment of the above-described kit, the protein from which the reagent is derived is cardiac troponin I, and the peptide has a sequence comprising at least five consecutive amino acid residues from a sequence selected from the group consisting of SSDAAREPRPAPAPI (SEQ ID NO:11), VDEERYDIEAKVTKN (SEQ ID NO:12), DIEAKVTKNITEIAD (SEQ ID NO:13), LDLRAHLKQVKKEDT (SEQ ID NO:14), and ALSGMEGRKKKFES (SEQ ID NO:15).

BRIEF DESCRIPTION OF THE FIGURES

[0051] FIG. **1** shows the amino acid sequence of cardiac troponin I;

[0052] FIG. **2** shows the amino acid sequence of cardiac troponin T;

[0053] FIG. **3** shows the amino acid sequence of thyroid stimulating hormone (TSH);

[0054] FIG. **4** shows the amino acid sequence of the beta subunit of human chorionic gonadotropin (beta-HCG);

[0055] FIG. **5** shows the amino acid sequence of myeloperoxidase (MPO);

[0056] FIG. **6** shows the amino acid sequence of prostate specific antigen (PSA);

[0057] FIG. **7** shows the amino acid sequence of human B-type natriuretic peptide (hBNP);

[0058] FIG. **8** shows the amino acid sequence of myosin light chain 2;

[0059] FIG. **9** A-C shows the amino acid sequence of myosin-6;

[0060] FIG. **10** A-C shows the amino acid sequence of myosin-7;

[0061] FIG. **11** shows a graph of the ratio of the signal to the low control (S/LC) against concentration (nmol/mL) for each of five different peptide reagents and a combination thereof; and

[0062] FIG. **12** shows a graph of the ratio of the signal to the low control (S/LC) against concentration (nmol/mL) for each of five different peptide reagents and a combination thereof.

DETAILED DESCRIPTION

[0063] The present disclosure relates to immunoassay methods and kits for detecting a protein of interest in a test sample, and more particularly to methods and kits for detecting a protein in a human test sample that may contain endogenous antibodies against the protein of interest. Specifically, the inventors have discovered an alternative approach to address the problem of interference by autoantibodies in immunodetection of clinically significant analytes in a sample. Such analytes include self-antigens such as for example cardiac troponin, myeloperoxidase, prostate specific antigen and thyroid stimulating hormone. More specifically, the alternative approach includes use of a peptide reagent that is derived from the protein, especially a self-antigen, of interest. The peptide reagent inhibits binding of autoantibodies to the protein, and thus prevents interference by autoantibodies with immunodetection of the protein. This approach compensates for the presence of autoantibodies that may be in the sample without need for a redesign of the specific detection antibodies or the capture antibodies, does not require use of an extra anti-human IgG detection conjugate, and avoids the need of a second assay to identify problematic samples.

A. Definitions

[0064] Section headings as used in this section and the entire disclosure herein are not intended to be limiting.

[0065] As used herein, the singular forms "a," "an" and "the" include plural referents unless the context clearly dictates otherwise. For the recitation of numeric ranges herein, each intervening number there between with the same degree of precision is explicitly contemplated. For example, for the range 6-9, the numbers 7 and 8 are contemplated in addition to 6 and 9, and for the range 6.0-7.0, the numbers 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9 and 7.0 are explicitly contemplated.

[0066] a) Acyl (and Other Chemical Structural Group Definitions)

[0067] As used herein, the term "acyl" refers to a —C(O)R_a group where R_a is hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, phenyl or phenylalkyl. Representative examples of acyl include, but are not limited to, formyl, acetyl, cylcohexylcarbonyl, cyclohexylmethylcarbonyl, benzoyl, benzylcarbonyl and the like.

[0068] As used herein, the term "alkenyl" means a straight or branched chain hydrocarbon containing from 2 to 10 carbons and containing at least one carbon-carbon double bond formed by the removal of two hydrogens. Representative examples of alkenyl include, but are not limited to, ethenyl, 2-propenyl, 2-methyl-2-propenyl, 3-butenyl, 4-pentenyl, 5-hexenyl, 2-heptenyl, 2-methyl-1-heptenyl, and 3-decenyl.

[0069] As used herein, the term "alkyl" means a straight or branched chain hydrocarbon containing from 1 to 10 carbon atoms. Representative examples of alkyl include, but are not limited to, methyl, ethyl, n-propyl, iso-propyl, n-butyl, sec-butyl, iso-butyl, tert-butyl, n-pentyl, isopentyl, neopentyl, n-hexyl, 3-methylhexyl, 2,2-dimethylpentyl, 2,3-dimethylpentyl, n-heptyl, n-octyl, n-nonyl, and n-decyl.

[0070] As used herein, the term "alkyl radical" means any of a series of univalent groups of the general formula C_nH_{2n+1} derived from straight or branched chain hydrocarbons.

[0071] As used herein, the term "alkoxy" means an alkyl group, as defined herein, appended to the parent molecular moiety through an oxygen atom. Representative examples of alkoxy include, but are not limited to, methoxy, ethoxy, propoxy, 2-propoxy, butoxy, tert-butoxy, pentyloxy, and hexyloxy.

[0072] As used herein, the term "alkynyl" means a straight or branched chain hydrocarbon group containing from 2 to 10 carbon atoms and containing at least one carbon-carbon triple bond. Representative examples of alkynyl include, but are not limited, to acetylenyl, 1-propynyl, 2-propynyl, 3-butynyl, 2-pentynyl, and 1-butynyl.

[0073] As used herein, the term "amido" refers to an amino group attached to the parent molecular moiety through a carbonyl group (wherein the term "carbonyl group" refers to a —C(O)— group).

[0074] As used herein, the term "amino" means $—NR_bR_c$, wherein R_b and R_c are independently selected from the group consisting of hydrogen, alkyl and alkylcarbonyl.

[0075] As used herein, the term "aralkyl" means an aryl group appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of arylalkyl include, but are not limited to, benzyl, 2-phenylethyl, 3-phenylpropyl, and 2-naphth-2-ylethyl.

[0076] As used herein, the term "aryl" means a phenyl group, or a bicyclic or tricyclic fused ring system wherein one or more of the fused rings is a phenyl group. Bicyclic fused ring systems are exemplified by a phenyl group fused to a cycloalkenyl group, a cycloalkyl group, or another phenyl group. Tricyclic fused ring systems are exemplified by a bicyclic fused ring system fused to a cycloalkenyl group, a cycloalkyl group, as defined herein or another phenyl group. Representative examples of aryl include, but are not limited to, anthracenyl, azulenyl, fluorenyl, indanyl, indenyl, naphthyl, phenyl, and tetrahydronaphthyl. The aryl groups of the present disclosure can be optionally substituted with one-, two, three, four, or five substituents independently selected from the group consisting of alkoxy, alkyl, carboxyl, halo, and hydroxyl.

[0077] As used herein, the term "carboxy" or "carboxyl" refers to $—CO_2H$ or $—CO_2$.

[0078] As used herein, the term "carboxyalkyl" refers to a $—(CH_2)_nCO_2H$ or $—(CH_2)_nCO_2^-$ group where n is from 1 to 10.

[0079] As used herein, the term "cyano" means a —CN group.

[0080] As used herein, the term "cycloalkenyl" refers to a non-aromatic cyclic or bicyclic ring system having from three to ten carbon atoms and one to three rings, wherein each five-membered ring has one double bond, each six-membered ring has one or two double bonds, each seven- and eight-membered ring has one to three double bonds, and each nine-to ten-membered ring has one to four double bonds. Representative examples of cycloalkenyl groups include cyclohexenyl, octahydronaphthalenyl, norbornylenyl, and the like. The cycloalkenyl groups can be optionally substituted with one, two, three, four, or five substituents independently selected from the group consisting of alkoxy, alkyl, carboxyl, halo, and hydroxyl.

[0081] As used herein, the term "cycloalkyl" refers to a saturated monocyclic, bicyclic, or tricyclic hydrocarbon ring system having three to twelve carbon atoms. Representative examples of cycloalkyl groups include cyclopropyl, cyclopentyl, bicyclo[3.1.1]heptyl, adamantyl, and the like. The cycloalkyl groups of the present disclosure can be optionally substituted with one, two, three, four, or five substituents independently selected from the group consisting of alkoxy, alkyl, carboxyl, halo, and hydroxyl.

[0082] As used herein, the term "cycloalkylalkyl" means a $—R_dR_e$ group where R_d is an alkylene group and R_e is cycloalkyl group. A representative example of a cycloalkylalkyl group is cyclohexylmethyl and the like.

[0083] As used herein, the term "halogen" means a —Cl, —Br, —I or —F; the term "halide" means a binary compound, of which one part is a halogen atom and the other part is an element or radical that is less electronegative than the halogen, e.g., an alkyl radical.

[0084] As used herein, the term "hydroxyl" means an —OH group.

[0085] As used herein, the term "nitro" means a $—NO_2$ group.

[0086] As used herein, the term "oxoalkyl" refers to $—(CH_2)_nC(O)R_a$, where R_a is hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, phenyl or phenylalkyl and where n is from 1 to 10.

[0087] As used herein, the term "phenylalkyl" means an alkyl group which is substituted by a phenyl group.

[0088] As used herein, the term "sulfo" means a $—SO_3H$ group.

[0089] As used herein, the term "sulfoalkyl" refers to a $—(CH_2)_nSO_3H$ or $—(CH_2)_nSO_3^-$ group where n is from 1 to 10.

[0090] b) Anion

[0091] As used herein, the term "anion" refers to an anion of an inorganic or organic acid, such as, but not limited to, hydrochloric acid, hydrobromic acid, sulfuric acid, methane sulfonic acid, formic acid, acetic acid, oxalic acid, succinic acid, tartaric acid, mandelic acid, fumaric acid, lactic acid, citric acid, glutamic acid, aspartic acid, phosphate, trifluoromethansulfonic acid, trifluoroacetic acid and fluorosulfonic acid and any combinations thereof.

[0092] c) Antibody

[0093] As used herein, the term "antibody" refers to a protein consisting of one or more polypeptides substantially encoded by immunoglobulin genes or fragments of immunoglobulin genes, and encompasses polyclonal antibodies, monoclonal antibodies, and fragments thereof, as well as molecules engineered from immunoglobulin gene sequences. The recognized immunoglobulin genes include the kappa, lambda, alpha, gamma, delta, epsilon and mu constant region genes, as well as myriad immunoglobulin variable region genes. Light chains are classified as either kappa or lambda. Heavy chains are classified as gamma, mu, alpha, delta, or epsilon, which in turn define the immunoglobulin classes, IgG, IgM, IgA, IgD and IgE, respectively.

[0094] d) Hydrogen Peroxide Generating Enzyme

[0095] As used herein, the term "hydrogen peroxide generating enzyme" refers to an enzyme that is capable of producing as a reaction product the chemical compound having the molecular formula H_2O_2, i.e. hydrogen peroxide. Non-limiting examples of hydrogen peroxide generating enzymes are listed below in Table 1.

TABLE 1

ACCEPTED COMMON NAME	IUBMB ENZYME NOMENCLATURE	PREFERRED SUBSTRATE
(R)-6-hydroxynicotine oxidase	EC 1.5.3.6	(R)-6-hydroxynicotine
(S)-2-hydroxy acid oxidase	EC 1.1.3.15	S)-2-hydroxy acid
(S)-6-hydroxynicotine oxidase	EC 1.5.3.5	(S)-6-hydroxynicotine
3-aci-nitropropanoate oxidase	EC 1.7.3.5	3-aci-nitropropanoate
3-hydroxyanthranilate oxidase	EC 1.10.3.5	3-hydroxyanthranilate
4-hydroxymandelate oxidase	EC 1.1.3.19	(S)-2-hydroxy-2-(4-hydroxyphenyl)acetate
6-hydroxynicotinate dehydrogenase	EC 1.17.3.3	6-hydroxynicotinate
Abscisic-aldehyde oxidase	EC 1.2.3.14	abscisic aldehyde
acyl-CoA oxidase	EC 1.3.3.6	acyl-CoA
Alcohol oxidase	EC 1.1.3.13	a primary alcohol
Aldehyde oxidase	EC 1.2.3.1	an aldehyde
amine oxidase		
amine oxidase (copper-containing)	EC 1.4.3.6	primary monoamines, diamines and histamine
amine oxidase (flavin-containing)	EC 1.4.3.4	a primary amine
aryl-alcohol oxidase	EC 1.1.3.7	an aromatic primary alcohol (2-naphthyl)methanol 3-methoxybenzyl alcohol
aryl-aldehyde oxidase	EC 1.2.3.9	an aromatic aldehyde
Catechol oxidase	EC 1.1.3.14	Catechol
cholesterol oxidase	EC 1.1.3.6	Cholesterol
Choline oxidase	EC 1.1.3.17	Choline
columbamine oxidase	EC 1.21.3.2	Columbamine
cyclohexylamine oxidase	EC 1.4.3.12	Cyclohexylamine
cytochrome c oxidase	EC 1.9.3.1	
D-amino-acid oxidase	EC 1.4.3.3	a D-amino acid
D-arabinono-1,4-lactone oxidase	EC 1.1.3.37	D-arabinono-1,4-lactone
D-arabinono-1,4-lactone oxidase	EC 1.1.3.37	D-arabinono-1,4-lactone
D-aspartate oxidase	EC 1.4.3.1	D-aspartate
D-glutamate oxidase	EC 1.4.3.7	D-glutamate
D-glutamate(D-aspartate) oxidase	EC 1.4.3.15	D-glutamate
dihydrobenzophenanthridine oxidase	EC 1.5.3.12	dihydrosanguinarine
dihydroorotate oxidase	EC 1.3.3.1	(S)-dihydroorotate
dihydrouracil oxidase	EC 1.3.3.7	5,6-dihydrouracil
dimethylglycine oxidase	EC 1.5.3.10	N,N-dimethylglycine
D-mannitol oxidase	EC 1.1.3.40	Mannitol
Ecdysone oxidase	EC 1.1.3.16	Ecdysone
ethanolamine oxidase	EC 1.4.3.8	Ethanolamine
Galactose oxidase	EC 1.1.3.9	D-galactose
Glucose oxidase	EC 1.1.3.4	β-D-glucose
glutathione oxidase	EC 1.8.3.3	Glutathione
Glycerol-3-phosphate oxidase	EC 1.1.3.21	sn-glycerol 3-phosphate
Glycine oxidase	EC 1.4.3.19	Glycine
glyoxylate oxidase	EC 1.2.3.5	Glyoxylate
hexose oxidase	EC 1.1.3.5	D-glucose, D-galactose D-mannose maltose lactose cellobiose
hydroxyphytanate oxidase	EC 1.1.3.27	L-2-hydroxyphytanate
indole-3-acetaldehyde oxidase	EC 1.2.3.7	(indol-3-yl)acetaldehyde
lactic acid oxidase		Lactic acid
L-amino-acid oxidase	EC 1.4.3.2	an L-amino acid
L-aspartate oxidase	EC 1.4.3.16	L-aspartate
L-galactonolactone oxidase	EC 1.3.3.12	L-galactono-1,4-lactone
L-glutamate oxidase	EC 1.4.3.11	L-glutamate
L-gulonolactone oxidase	EC 1.1.3.8	L-gulono-1,4-lactone
L-lysine 6-oxidase	EC 1.4.3.20	L-lysine
L-lysine oxidase	EC 1.4.3.14	L-lysine
long-chain-alcohol oxidase	EC 1.1.3.20	A long-chain-alcohol
L-pipecolate oxidase	EC 1.5.3.7	L-pipecolate
L-sorbose oxidase	EC 1.1.3.11	L-sorbose
malate oxidase	EC 1.1.3.3	(S)-malate
methanethiol oxidase	EC 1.8.3.4	Methanethiol
monoamino acid oxidase		

TABLE 1-continued

ACCEPTED COMMON NAME	IUBMB ENZYME NOMENCLATURE	PREFERRED SUBSTRATE
N^6-methyl-lysine oxidase	EC 1.5.3.4	6-N-methyl-L-lysine
N-acylhexosamine oxidase	EC 1.1.3.29	N-acetyl-D-glucosamine N-glycolylglucosamine N-acetylgalactosamine N-acetylmannosamine.
NAD(P)H oxidase	EC 1.6.3.1	NAD(P)H
nitroalkane oxidase	EC 1.7.3.1	a nitroalkane
N-methyl-L-amino-acid oxidase	EC 1.5.3.2	an N-methyl-L-amino acid
nucleoside oxidase	EC 1.1.3.39	Adenosine
Oxalate oxidase	EC 1.2.3.4	Oxalate
polyamine oxidase	EC 1.5.3.11	1-N-acetylspermine
polyphenol oxidase	EC 1.14.18.1	
Polyvinyl-alcohol oxidase	EC 1.1.3.30	polyvinyl alcohol
prenylcysteine oxidase	EC 1.8.3.5	an S-prenyl-L-cysteine
Protein-lysine 6-oxidase	EC 1.4.3.13	peptidyl-L-lysyl-peptide
putrescine oxidase	EC 1.4.3.10	butane-1,4-diamine
Pyranose oxidase	EC 1.1.3.10	D-glucose D-xylose L-sorbose D-glucono-1,5-lactone
Pyridoxal 5'-phosphate synthase	EC 1.4.3.5	pyridoxamine 5'-phosphate
pyridoxine 4-oxidase	EC 1.1.3.12	Pyridoxine
pyrroloquinoline-quinone synthase	EC 1.3.3.11	6-(2-amino-2-carboxyethyl)-7,8-dioxo-1,2,3,4,5,6,7,8-octahydroquinoline-2,4-dicarboxylate
Pyruvate oxidase	EC 1.2.3.3	Pyruvate
Pyruvate oxidase (CoA-acetylating)	EC 1.2.3.6	Pyruvate
Reticuline oxidase	EC 1.21.3.3	Reticuline
retinal oxidase	EC 1.2.3.11	Retinal
Rifamycin-B oxidase	EC 1.10.3.6	rifamycin-B
Sarcosine oxidase	EC 1.5.3.1	Sarcosine
secondary-alcohol oxidase	EC 1.1.3.18	a secondary alcohol
sulfite oxidase	EC 1.8.3.1	Sulfite
superoxide dismutase	EC 1.15.1.1	Superoxide
superoxide reductase	EC 1.15.1.2	Superoxide
tetrahydroberberine oxidase	EC 1.3.3.8	(S)-tetrahydroberberine
Thiamine oxidase	EC 1.1.3.23	Thiamine
tryptophan α,β-oxidase	EC 1.3.3.10	L-tryptophan
urate oxidase (uricase, uric acid oxidase)	EC 1.7.3.3	uric acid
Vanillyl-alcohol oxidase	EC 1.1.3.38	vanillyl alcohol
Xanthine oxidase	EC 1.17.3.2	Xanthine
xylitol oxidase	EC 1.1.3.41	Xylitol

[0096] e) Autoantibody

[0097] As used herein, the phrase "autoantibody" refers to an antibody that binds to an analyte that is endogenously produced in the subject in which the antibody is produced.

[0098] f) Specific Binding Partner

[0099] As used herein, the phrase "specific binding partner," as used herein, is a member of a specific binding pair. That is, two different molecules where one of the molecules, through chemical or physical means, specifically binds to the second molecule. Therefore, in addition to antigen and antibody specific binding pairs of common immunoassays, other specific binding pairs can include biotin and avidin, carbohydrates and lectins, complementary nucleotide sequences, effector and receptor molecules, cofactors and enzymes, enzyme inhibitors, and enzymes and the like. Furthermore, specific binding pairs can include members that are analogs of the original specific binding members, for example, an analyte-analog. Immunoreactive specific binding members include antigens, antigen fragments, antibodies and antibody fragments, both monoclonal and polyclonal and complexes thereof, including those formed by recombinant DNA molecules.

[0100] g) Specific Binding Partner-Protein Complex

[0101] As used herein, the phrase "specific binding partner-protein complex" refers to a combination of an antibody and an antigen, in which the antigen is a protein of interest, and the antibody and protein are bound by specific, noncovalent interactions between an antigen-combining site on the antibody and an antigen epitope.

[0102] h) Detectable Label

[0103] As used herein the term "detectable label" refers to any moiety that generates a measurable signal via optical, electrical, or other physical indication of a change of state of a molecule or molecules coupled to the moiety. Such physical indicators encompass spectroscopic, photochemical, biochemical, immunochemical, electromagnetic, radiochemical, and chemical means, such as but not limited to fluorescence, chemifluorescence, chemiluminescence, and the like. Preferred detectable labels include acridinium compounds

such as an acridinium-9-carboximide having a structure according to Formula I as set forth in section B herein below, and an acridinium-9-carboxylate aryl ester having a structure according to Formula II as also set forth in section B herein below.

[0104] i) Subject

[0105] As used herein, the terms "subject" and "patient" are used interchangeably irrespective of whether the subject has or is currently undergoing any form of treatment. As used herein, the terms "subject" and "subjects" refer to any vertebrate, including, but not limited to, a mammal (e.g., cow, pig, camel, llama, horse, goat, rabbit, sheep, hamsters, guinea pig, cat, dog, rat, and mouse, a non-human primate (for example, a monkey, such as a cynomolgous monkey, chimpanzee, etc) and a human). Preferably, the subject is a human.

[0106] j) Test Sample

[0107] As used herein, the term "test sample" generally refers to a biological material being tested for and/or suspected of containing an protein of interest and which may also include autoantibodies to the protein of interest. The biological material may be derived from any biological source but preferably is a biological fluid likely to contain the protein of interest. Examples of biological materials include, but are not limited to, stool, whole blood, serum, plasma, red blood cells, platelets, interstitial fluid, saliva, ocular lens fluid, cerebral spinal fluid, sweat, urine, ascites fluid, mucous, nasal fluid, sputum, synovial fluid, peritoneal fluid, vaginal fluid, menses, amniotic fluid, semen, soil, etc. The test sample may be used directly as obtained from the biological source or following a pretreatment to modify the character of the sample. For example, such pretreatment may include preparing plasma from blood, diluting viscous fluids and so forth. Methods of pretreatment may also involve filtration, precipitation, dilution, distillation, mixing, concentration, inactivation of interfering components, the addition of reagents, lysing, etc. If such methods of pretreatment are employed with respect to the test sample, such pretreatment methods are such that the protein of interest remains in the test sample at a concentration proportional to that in an untreated test sample (e.g., namely, a test sample that is not subjected to any such pretreatment method(s)).

B. Peptide Reagents

[0108] Self-antigens include a number of proteins that are known to be endogenously produced in relation to a particular disease state or injury in a subject. Self-antigens for which autoantibodies have been identified include the troponins, namely cardiac troponin I (SEQ ID NO:1), and cardiac troponin T (SEQ ID NO:2); thyroid stimulating hormone (TSH) (SEQ ID NO:3); the beta subunit of human chorionic gonadotropin (beta-HCG) (SEQ ID NO:4); myeloperoxidase (MPO) (SEQ ID NO:5); prostate specific antigen (PSA) (SEQ ID NO:6); human B-type natriuretic peptide (hBNP) (SEQ ID NO:7); myosin light chain 2 (SEQ ID NO:8); myosin-6 (SEQ ID NO:9) and myosin-7 (SEQ ID NO:10).

[0109] The peptide reagents of the present disclosure are derived from the amino acid sequence of the target self-antigen, and can be used in an immunoassay format to prevent interference by autoantibodies against the self-antigen. More specifically, the peptide reagent is used to block the interaction between the self-antigen and any autoantibodies against the self-antigen that may be present in a test sample. Each peptide reagent may be used alone, or in combination with one or more other peptide reagents derived from the target protein. A synergistic blocking effect is believed to result from a combination of different peptide reagents derived from the same target protein.

[0110] The peptide reagent includes at least five (5) consecutive amino acid residues from the amino acid sequence of the target self-antigen. In one embodiment, the peptide reagent includes five (5) to fifteen (15) consecutive amino acid residues from the amino acid sequence of the target self-antigen. For example, given cardiac troponin I as the target self-antigen, the peptide reagent comprises any sequence of 5 to 15 consecutive amino acid residues from anywhere in the amino acid sequence of cardiac troponin I (FIG. **1**; SEQ ID NO: 1). For example, the peptide reagent can comprise any of the following amino acid sequences: ADGSS (residues 1-5), KFFES (residues 205-209), or KKKSKISASRKLQLK (residues 35-49), or any other sequence of 5 to 15 consecutive amino acid residues from anywhere in the amino acid sequence of cardiac troponin I (SEQ ID NO: 1). Table 2 lists amino acid sequences for exemplary peptide reagents consisting of 5 consecutive amino acid residues from cardiac troponin I (SEQ ID NO: 1). Additional peptide reagents may have a length of up to 15 amino acid residues, comprising any one of the listed 5-amino acid long sequences in Table 2, plus up to a total of 10 additional consecutive amino acid residues from SEQ ID NO:1, that are continuous (from either side within the protein amino sequence) with the 5-amino acid long sequence.

TABLE 2

Ala	Asp	Gly	Ser	Ser	Leu	Leu	Leu	Gln	Ile	Ala	Arg	Val	Asp	Lys
Asp	Gly	Ser	Ser	Asp	Leu	Leu	Gln	Ile	Ala	Arg	Val	Asp	Lys	Val
Gly	Ser	Ser	Asp	Ala	Leu	Gln	Ile	Ala	Lys	Val	Asp	Lys	Val	Asp
Ser	Ser	Asp	Ala	Ala	Gln	Ile	Ala	Lys	Gln	Asp	Lys	Val	Asp	Glu
Ser	Asp	Ala	Ala	Arg	Ile	Ala	Lys	Gln	Glu	Lys	Val	Asp	Glu	Glu
Asp	Ala	Ala	Arg	Glu	Ala	Lys	Gln	Glu	Leu	Val	Asp	Glu	Glu	Arg
Ala	Ala	Arg	Glu	Pro	Lys	Gln	Glu	Leu	Glu	Asp	Glu	Glu	Arg	Tyr
Ala	Arg	Glu	Pro	Arg	Gln	Glu	Leu	Glu	Arg	Glu	Glu	Arg	Tyr	Asp
Arg	Glu	Pro	Arg	Pro	Glu	Leu	Glu	Arg	Glu	Glu	Arg	Tyr	Asp	Ile

TABLE 2-continued

Glu Pro Arg Pro Ala Leu Glu Arg Glu Ala	Arg Tyr Asp Ile Glu
Pro Arg Pro Ala Pro Glu Arg Glu Ala Glu	Tyr Asp Ile Glu Ala
Arg Pro Ala Pro Ala Arg Glu Ala Glu Glu	Asp Ile Glu Ala Lys
Pro Ala Pro Ala Pro Glu Ala Glu Glu Arg	Ile Glu Ala Lys Val
Ala Pro Ala Pro Ile Ala Glu Glu Arg Arg	Glu Ala Lys Val Thr
Pro Ala Pro Ile Arg Glu Glu Arg Arg Gly	Ala Lys Val Thr Lys
Ala Pro Ile Arg Arg Glu Arg Arg Gly Glu	Lys Val Thr Lys Asn
Pro Ile Arg Arg Arg Arg Arg Gly Glu Lys	Val Thr Lys Asn Ile
Ile Arg Arg Arg Ser Arg Gly Glu Lys Gly	Thr Lys Asn Ile Thr
Arg Arg Arg Ser Ser Gly Glu Lys Gly Arg	Lys Asn Ile Thr Glu
Arg Arg Ser Ser Asn Glu Lys Gly Arg Ala	Asn Ile Thr Glu Ile
Arg Ser Ser Asn Tyr Lys Gly Arg Ala Leu	Ile Thr Glu Ile Ala
Ser Ser Asn Tyr Arg Gly Arg Ala Leu Ser	Thr Glu Ile Ala Asp
Ser Asn Tyr Arg Ala Arg Ala Leu Ser Thr	Glu Ile Ala Asp Leu
Asn Tyr Arg Ala Tyr Ala Leu Ser Thr Arg	Ile Ala Asp Leu Thr
Tyr Arg Ala Tyr Ala Leu Ser Thr Arg Cys	Ala Asp Leu Thr Gln
Arg Ala Tyr Ala Thr Ser Thr Arg Cys Gln	Asp Leu Thr Gln Lys
Ala Tyr Ala Thr Glu Thr Arg Cys Gln Pro	Leu Thr Gln Lys Ile
Tyr Ala Thr Glu Pro Arg Cys Gln Pro Leu	Thr Gln Lys Ile Phe
Ala Thr Glu Pro His Cys Gln Pro Leu Glu	Gln Lys Ile Phe Asp
Thr Glu Pro His Ala Gln Pro Leu Glu Leu	Lys Ile Phe Asp Leu
Glu Pro His Ala Lys Pro Leu Glu Leu Ala	Ile Phe Asp Leu Arg
Pro His Ala Lys Lys Leu Glu Leu Ala Gly	Phe Asp Leu Arg Gly
His Ala Lys Lys Lys Glu Leu Ala Gly Leu	Asp Leu Arg Gly Lys
Ala Lys Lys Lys Ser Leu Ala Gly Leu Gly	Leu Arg Gly Lys Phe
Lys Lys Lys Ser Lys Ala Gly Leu Gly Phe	Arg Gly Lys Phe Lys
Lys Lys Ser Lys Ile Gly Leu Gly Phe Ala	Gly Lys Phe Lys Arg
Lys Ser Lys Ile Ser Leu Gly Phe Ala Glu	Lys Phe Lys Arg Pro
Ser Lys Ile Ser Ala Gly Phe Ala Glu Leu	Phe Lys Arg Pro Thr
Lys Ile Ser Ala Ser Phe Ala Glu Leu Gln	Lys Arg Pro Thr Leu
Ile Ser Ala Ser Arg Ala Glu Leu Gln Asp	Arg Pro Thr Leu Arg
Ser Ala Ser Arg Lys Glu Leu Gln Asp Leu	
Ala Ser Arg Lys Leu Leu Gln Asp Leu Cys	
Ser Arg Lys Leu Gln Gln Asp Leu Cys Arg	
Arg Lys Leu Gln Leu Asp Leu Cys Arg Gln	
Lys Leu Gln Leu Lys Leu Cys Arg Gln Leu	
Leu Gln Leu Lys Thr Cys Arg Gln Leu His	
Gln Leu Lys Thr Leu Arg Gln Leu His Ala	

TABLE 2-continued

Leu Lys Thr Leu Leu Gln Leu His Ala Arg
Lys Thr Leu Leu Leu Leu His Ala Arg Val
Thr Leu Leu Leu Gln His Ala Arg Val Asp

[0111] When cardiac troponin T (SEQ ID NO:2) is the target self-antigen, the peptide reagent comprises any sequence of 5 to 15 consecutive amino acid residues from anywhere in the amino acid sequence of cardiac troponin T (SEQ ID NO: 2). Table 3 lists amino acid sequences for exemplary peptide reagents consisting of 5 consecutive amino acid residues from cardiac troponin T (SEQ ID NO: 2). Additional peptide reagents may have a length of up to 15 amino acid residues, comprising any one of the listed 5-amino acid long sequences in Table 3, plus up to a total of 10 additional consecutive amino acid residues from SEQ ID NO:2, that are continuous (from either side within the protein amino sequence) with the 5-amino acid long sequence.

TABLE 3

Ser Asp Ile Glu Glu	Arg Ala Glu Glu Asp
Asp Ile Glu Glu Val	Ala Glu Glu Asp Glu
Ile Glu Glu Val Val	Glu Glu Asp Glu Glu
Glu Glu Val Val Glu	Glu Asp Glu Glu Glu
Glu Val Val Glu Glu	Asp Glu Glu Glu Glu
Val Val Glu Glu Tyr	Glu Glu Glu Glu Glu
Val Glu Glu Tyr Glu	Glu Glu Glu Glu Ala
Glu Glu Tyr Glu Glu	Glu Glu Glu Ala Lys
Glu Tyr Glu Glu Glu	Glu Glu Ala Lys Glu
Tyr Glu Glu Glu Glu	Glu Ala Lys Glu Ala
Glu Glu Glu Glu Gln	Ala Lys Glu Ala Glu
Glu Glu Glu Gln Glu	Lys Glu Ala Glu Asp
Glu Glu Gln Glu Glu	Glu Ala Glu Asp Gly
Glu Gln Glu Glu Ala	Ala Glu Asp Gly Pro
Gln Glu Glu Ala Ala	Glu Asp Gly Pro Met
Glu Glu Ala Ala Val	Asp Gly Pro Met Glu
Glu Ala Ala Val Glu	Gly Pro Met Glu Glu
Ala Ala Val Glu Glu	Pro Met Glu Glu Ser
Ala Val Glu Glu Glu	Met Glu Glu Ser Lys
Val Glu Glu Glu Glu	Glu Glu Ser Lys Pro
Glu Glu Glu Glu Asp	Glu Ser Lys Pro Lys
Glu Glu Glu Asp Trp	Ser Lys Pro Lys Pro
Glu Glu Asp Trp Arg	Lys Pro Lys Pro Arg
Glu Asp Trp Arg Glu	Pro Lys Pro Arg Ser
Asp Trp Arg Glu Asp	Lys Pro Arg Ser Phe

TABLE 3-continued

Trp Arg Glu Asp Glu	Pro Arg Ser Phe Met
Arg Glu Asp Glu Asp	
Glu Asp Glu Asp Glu	
Asp Glu Asp Glu Gln	
Glu Asp Glu Gln Glu	
Asp Glu Gln Glu Glu	
Glu Gln Glu Glu Ala	
Gln Glu Glu Ala Ala	
Glu Glu Ala Ala Glu	
Glu Ala Ala Glu Glu	
Ala Ala Glu Glu Asp	
Ala Glu Glu Asp Ala	
Glu Glu Asp Ala Glu	
Glu Asp Ala Glu Ala	
Asp Ala Glu Ala Glu	
Ala Glu Ala Glu Ala	
Glu Ala Glu Ala Glu	
Ala Glu Ala Glu Thr	
Glu Ala Glu Thr Glu	
Ala Glu Thr Glu Glu	
Glu Thr Glu Glu Thr	
Thr Glu Glu Thr Arg	
Glu Glu Thr Arg Ala	
Glu Thr Arg Ala Glu	
Thr Arg Ala Glu Glu	

[0112] When thyroid stimulating hormone (TSH) (SEQ ID NO:3) is the target self-antigen, the peptide reagent comprises any sequence of 5 to 15 consecutive amino acid residues from anywhere in the amino acid sequence of (TSH) (SEQ ID NO:3). Table 3 lists amino acid sequences for exemplary peptide reagents consisting of 5 consecutive amino acid residues from TSH (SEQ ID NO: 3). Additional peptide reagents may have a length of up to 15 amino acid residues, comprising any one of the listed 5-amino acid long sequences in Table 4, plus up to a total of 10 additional consecutive amino acid residues from SEQ ID NO:3, that are continuous (from either side within the protein amino sequence) with the 5-amino acid long sequence.

TABLE 4

Thr Ala Leu Phe Leu Met Thr Arg Asp Ile	Ser Cys Lys Cys Gly
Ala Leu Phe Leu Met Thr Arg Asp Ile Asn	Cys Lys Cys Gly Lys
Leu Phe Leu Met Ser Arg Asp Ile Asn Gly	Lys Cys Gly Lys Cys
Phe Leu Met Ser Met Asp Ile Asn Gly Lys	Cys Gly Lys Cys Asn
Leu Met Ser Met Leu Ile Asn Gly Lys Leu	Gly Lys Cys Asn Thr
Met Ser Met Leu Phe Asn Gly Lys Leu Phe	Lys Cys Asn Thr Asp
Ser Met Leu Phe Gly Gly Lys Leu Phe Leu	Cys Asn Thr Asp Tyr
Met Leu Phe Gly Leu Lys Leu Phe Leu Pro	Asn Thr Asp Tyr Ser
Leu Phe Gly Leu Ala Leu Phe Leu Pro Lys	Thr Asp Tyr Ser Asp
Phe Gly Leu Ala Cys Phe Leu Pro Lys Tyr	Asp Tyr Ser Asp Cys
Gly Leu Ala Cys Gly Leu Pro Lys Tyr Ala	Tyr Ser Asp Cys Ile
Leu Ala Cys Gly Gln Pro Lys Tyr Ala Leu	Ser Asp Cys Ile His
Ala Cys Gly Gln Ala Lys Tyr Ala Leu Ser	Asp Cys Ile His Glu
Cys Gly Gln Ala Met Tyr Ala Leu Ser Gln	Cys Ile His Glu Ala
Gly Gln Ala Met Ser Ala Leu Ser Gln Asp	Ile His Glu Ala Ile
Gln Ala Met Ser Phe Leu Ser Gln Asp Val	His Glu Ala Ile Lys
Ala Met Ser Phe Cys Ser Gln Asp Val Cys	Glu Ala Ile Lys Thr
Met Ser Phe Cys Ile Gln Asp Val Cys Thr	Ala Ile Lys Thr Asn
Ser Phe Cys Ile Pro Asp Val Cys Thr Tyr	Ile Lys Thr Asn Tyr
Phe Cys Ile Pro Thr Val Cys Thr Tyr Arg	Lys Thr Asn Tyr Cys
Cys Ile Pro Thr Glu Cys Thr Tyr Arg Asp	Thr Asn Tyr Cys Thr
Ile Pro Thr Glu Tyr Thr Tyr Arg Asp Phe	Asn Tyr Cys Thr Lys
Pro Thr Glu Tyr Thr Tyr Arg Asp Phe Ile	Tyr Cys Thr Lys Pro
Thr Glu Tyr Thr Met Arg Asp Phe Ile Tyr	Cys Thr Lys Pro Gln
Glu Tyr Thr Met His Asp Phe Ile Tyr Arg	Thr Lys Pro Gln Lys
Tyr Thr Met His Ile Phe Ile Tyr Arg Thr	Lys Pro Gln Lys Ser
Thr Met His Ile Glu Ile Tyr Arg Thr Val	Pro Gln Lys Ser Tyr
Met His Ile Glu Arg Tyr Arg Thr Val Glu	Gln Lys Ser Tyr Leu
His Ile Glu Arg Arg Arg Thr Val Glu Ile	Lys Ser Tyr Leu Val
Ile Glu Arg Arg Glu Thr Val Glu Ile Pro	Ser Tyr Leu Val Gly
Glu Arg Arg Glu Cys Val Glu Ile Pro Gly	Tyr Leu Val Gly Phe
Arg Arg Glu Cys Ala Glu Ile Pro Gly Cys	Leu Val Gly Phe Ser
Arg Glu Cys Ala Tyr Ile Pro Gly Cys Pro	Val Gly Phe Ser Val
Glu Cys Ala Tyr Cys Pro Gly Cys Pro Leu	
Cys Ala Tyr Cys Leu Gly Cys Pro Leu His	
Ala Tyr Cys Leu Thr Cys Pro Leu His Val	
Tyr Cys Leu Thr Ile Pro Leu His Val Ala	
Cys Leu Thr Ile Asn Leu His Val Ala Pro	

TABLE 4-continued

Leu Thr Ile Asn Thr His Val Ala Pro Tyr
Thr Ile Asn Thr Thr Val Ala Pro Tyr Phe
Ile Asn Thr Thr Ile Ala Pro Tyr Phe Ser
Asn Thr Thr Ile Cys Pro Tyr Phe Ser Tyr
Thr Thr Ile Cys Ala Tyr Phe Ser Tyr Pro
Thr Ile Cys Ala Gly Phe Ser Tyr Pro Val
Ile Cys Ala Gly Tyr Ser Tyr Pro Val Ala
Cys Ala Gly Tyr Cys Tyr Pro Val Ala Leu
Ala Gly Tyr Cys Met Pro Val Ala Leu Ser
Gly Tyr Cys Met Thr Val Ala Leu Ser Cys
Tyr Cys Met Thr Arg Ala Leu Ser Cys Lys
Cys Met Thr Arg Asp Leu Ser Cys Lys Cys

[0113] When the beta subunit of human chorionic gonadotropin (beta-HCG) (SEQ ID NO:4) is the target self-antigen, the peptide reagent comprises any sequence of 5 to 15 consecutive amino acid residues from anywhere in the amino acid sequence of beta-HCG (SEQ ID NO:4). Table 5 lists amino acid sequences for exemplary peptide reagents consisting of 5 consecutive amino acid residues from beta-HCG (SEQ ID NO: 4). Additional peptide reagents may have a length of up to 15 amino acid residues, comprising any one of the listed 5-amino acid long sequences in Table 5, plus up to a total of 10 additional consecutive amino acid residues from SEQ ID NO:4, that are continuous (from either side within the protein amino sequence) with the 5-amino acid long sequence.

TABLE 5

Glu Met Phe Gln Gly Thr Ile Cys Ala Gly Tyr Ala Val Ala Leu
Met Phe Gln Gly Leu Ile Cys Ala Gly Tyr Ala Val Ala Leu Ser
Phe Gln Gly Leu Leu Cys Ala Gly Tyr Cys Val Ala Leu Ser Cys
Gln Gly Leu Leu Leu Ala Gly Tyr Cys Pro Ala Leu Ser Cys Gln
Gly Leu Leu Leu Leu Gly Tyr Cys Pro Thr Leu Ser Cys Gln Cys
Leu Leu Leu Leu Leu Tyr Cys Pro Thr Met Ser Cys Gln Cys Ala
Leu Leu Leu Leu Leu Cys Pro Thr Met Thr Cys Gln Cys Ala Leu
Leu Leu Leu Leu Leu Pro Thr Met Thr Arg Gln Cys Ala Leu Cys
Leu Leu Leu Leu Ser Thr Met Thr Arg Val Cys Ala Leu Cys Arg
Leu Leu Leu Ser Met Met Thr Arg Val Leu Ala Leu Cys Arg Arg
Leu Leu Ser Met Gly Thr Arg Val Leu Gln Leu Cys Arg Arg Ser
Leu Ser Met Gly Gly Arg Val Leu Gln Gly Cys Arg Arg Ser Thr
Ser Met Gly Gly Thr Val Leu Gln Gly Val Arg Arg Ser Thr Thr
Met Gly Gly Thr Trp Leu Gln Gly Val Leu Arg Ser Thr Thr Asp
Gly Gly Thr Trp Ala Gln Gly Val Leu Pro Ser Thr Thr Asp Cys
Gly Thr Trp Ala Ser Gly Val Leu Pro Ala Thr Thr Asp Cys Gly
Thr Trp Ala Ser Lys Val Leu Pro Ala Leu Thr Asp Cys Gly Gly

TABLE 5-continued

Trp Ala Ser Lys Glu Leu Pro Ala Leu Pro	Asp Cys Gly Gly Pro
Ala Ser Lys Glu Pro Pro Ala Leu Pro Gln	Cys Gly Gly Pro Lys
Ser Lys Glu Pro Leu Ala Leu Pro Gln Val	Gly Gly Pro Lys Asp
Lys Glu Pro Leu Arg Leu Pro Gln Val Val	Gly Pro Lys Asp His
Glu Pro Leu Arg Pro Pro Gln Val Val Cys	Pro Lys Asp His Pro
Pro Leu Arg Pro Arg Gln Val Val Cys Asn	Lys Asp His Pro Leu
Leu Arg Pro Arg Cys Val Val Cys Asn Tyr	Asp His Pro Leu Thr
Arg Pro Arg Cys Arg Val Cys Asn Tyr Arg	His Pro Leu Thr Cys
Pro Arg Cys Arg Pro Cys Asn Tyr Arg Asp	Pro Leu Thr Cys Asp
Arg Cys Arg Pro Ile Asn Tyr Arg Asp Val	Leu Thr Cys Asp Asp
Cys Arg Pro Ile Asn Tyr Arg Asp Val Arg	Thr Cys Asp Asp Pro
Arg Pro Ile Asn Ala Arg Asp Val Arg Phe	Cys Asp Asp Pro Arg
Pro Ile Asn Ala Thr Asp Val Arg Phe Glu	Asp Asp Pro Arg Phe
Ile Asn Ala Thr Leu Val Arg Phe Glu Ser	Asp Pro Arg Phe Gln
Asn Ala Thr Leu Ala Arg Phe Glu Ser Ile	Pro Arg Phe Gln Asp
Ala Thr Leu Ala Val Phe Glu Ser Ile Arg	Arg Phe Gln Asp Ser
Thr Leu Ala Val Glu Glu Ser Ile Arg Leu	Phe Gln Asp Ser Ser
Leu Ala Val Glu Lys Ser Ile Arg Leu Pro	Gln Asp Ser Ser Ser
Ala Val Glu Lys Glu Ile Arg Leu Pro Gly	Asp Ser Ser Ser Ser
Val Glu Lys Glu Gly Arg Leu Pro Gly Cys	Ser Ser Ser Ser Lys
Glu Lys Glu Gly Cys Leu Pro Gly Cys Pro	Ser Ser Ser Lys Ala
Lys Glu Gly Cys Pro Pro Gly Cys Pro Arg	Ser Ser Lys Ala Pro
Glu Gly Cys Pro Val Gly Cys Pro Arg Gly	Ser Lys Ala Pro Pro
Gly Cys Pro Val Cys Cys Pro Arg Gly Val	
Cys Pro Val Cys Ile Pro Arg Gly Val Asn	
Pro Val Cys Ile Thr Arg Gly Val Asn Pro	
Val Cys Ile Thr Val Gly Val Asn Pro Val	
Cys Ile Thr Val Asn Val Asn Pro Val Val	
Ile Thr Val Asn Thr Asn Pro Val Val Ser	
Thr Val Asn Thr Thr Pro Val Val Ser Tyr	
Val Asn Thr Thr Ile Val Val Ser Tyr Ala	
Asn Thr Thr Ile Cys Val Ser Tyr Ala Val	
Thr Thr Ile Cys Ala Ser Tyr Ala Val Ala	

[0114] When myeloperoxidase (MPO) (SEQ ID NO:5) is the target self-antigen, the peptide reagent comprises any sequence of 5 to 15 consecutive amino acid residues from anywhere in the amino acid sequence of MPO (SEQ ID NO:5). Table 6 lists amino acid sequences for exemplary peptide reagents consisting of 5 consecutive amino acid residues from MPO (SEQ ID NO: 5). Additional peptide reagents may have a length of up to 15 amino acid residues, comprising any one of the listed 5-amino acid long sequences in Table 6, plus up to a total of 10 additional consecutive amino acid residues from SEQ ID NO:5, that are continuous (from either side within the protein amino sequence) with the 5-amino acid long sequence.

TABLE 6

Gly	Val	Pro	Phe	Phe	Ala	Val	Leu	Gly	Glu	Phe	Lys	Gln	Pro	Val
Val	Pro	Phe	Phe	Ser	Val	Leu	Gly	Glu	Val	Lys	Gln	Pro	Val	Ala
Pro	Phe	Phe	Ser	Ser	Leu	Gly	Glu	Val	Asp	Gln	Pro	Val	Ala	Ala
Phe	Phe	Ser	Ser	Leu	Gly	Glu	Val	Asp	Thr	Pro	Val	Ala	Ala	Thr
Phe	Ser	Ser	Leu	Arg	Glu	Val	Asp	Thr	Ser	Val	Ala	Ala	Thr	Arg
Ser	Ser	Leu	Arg	Cys	Val	Asp	Thr	Ser	Leu	Ala	Ala	Thr	Arg	Thr
Ser	Leu	Arg	Cys	Met	Asp	Thr	Ser	Leu	Val	Ala	Thr	Arg	Thr	Ala
Leu	Arg	Cys	Met	Val	Thr	Ser	Leu	Val	Leu	Thr	Arg	Thr	Ala	Val
Arg	Cys	Met	Val	Asp	Ser	Leu	Val	Leu	Ser	Arg	Thr	Ala	Val	Arg
Cys	Met	Val	Asp	Leu	Leu	Val	Leu	Ser	Ser	Thr	Ala	Val	Arg	Ala
Met	Val	Asp	Leu	Gly	Val	Leu	Ser	Ser	Met	Ala	Val	Arg	Ala	Ala
Val	Asp	Leu	Gly	Pro	Leu	Ser	Ser	Met	Glu	Val	Arg	Ala	Ala	Asp
Asp	Leu	Gly	Pro	Cys	Ser	Ser	Met	Glu	Glu	Arg	Ala	Ala	Asp	Tyr
Leu	Gly	Pro	Cys	Trp	Ser	Met	Glu	Glu	Ala	Ala	Ala	Asp	Tyr	Leu
Gly	Pro	Cys	Trp	Ala	Met	Glu	Glu	Ala	Lys	Ala	Asp	Tyr	Leu	His
Pro	Cys	Trp	Ala	Gly	Glu	Glu	Ala	Lys	Gln	Asp	Tyr	Leu	His	Val
Cys	Trp	Ala	Gly	Gly	Glu	Ala	Lys	Gln	Leu	Tyr	Leu	His	Val	Ala
Trp	Ala	Gly	Gly	Leu	Ala	Lys	Gln	Leu	Val	Leu	His	Val	Ala	Leu
Ala	Gly	Gly	Leu	Thr	Lys	Gln	Leu	Val	Asp	His	Val	Ala	Leu	Asp
Gly	Gly	Leu	Thr	Ala	Gln	Leu	Val	Asp	Lys	Val	Ala	Leu	Asp	Leu
Gly	Leu	Thr	Ala	Glu	Leu	Val	Asp	Lys	Ala	Ala	Leu	Asp	Leu	Leu
Leu	Thr	Ala	Glu	Met	Val	Asp	Lys	Ala	Tyr	Leu	Asp	Leu	Leu	Glu
Thr	Ala	Glu	Met	Lys	Asp	Lys	Ala	Tyr	Lys	Asp	Leu	Leu	Glu	Arg
Ala	Glu	Met	Lys	Leu	Lys	Ala	Tyr	Lys	Glu	Leu	Leu	Glu	Arg	Lys
Glu	Met	Lys	Leu	Leu	Ala	Tyr	Lys	Glu	Arg	Leu	Glu	Arg	Lys	Leu
Met	Lys	Leu	Leu	Leu	Tyr	Lys	Glu	Arg	Arg	Glu	Arg	Lys	Leu	Arg
Lys	Leu	Leu	Leu	Ala	Lys	Glu	Arg	Arg	Glu	Arg	Lys	Leu	Arg	Ser
Leu	Leu	Leu	Ala	Leu	Glu	Arg	Arg	Glu	Ser	Lys	Leu	Arg	Ser	Leu
Leu	Leu	Ala	Leu	Ala	Arg	Arg	Glu	Ser	Ile	Leu	Arg	Ser	Leu	Trp
Leu	Ala	Leu	Ala	Gly	Arg	Glu	Ser	Ile	Lys	Arg	Ser	Leu	Trp	Arg
Ala	Leu	Ala	Gly	Leu	Glu	Ser	Ile	Lys	Gln	Ser	Leu	Trp	Arg	Arg
Leu	Ala	Gly	Leu	Leu	Ser	Ile	Lys	Gln	Arg	Leu	Trp	Arg	Arg	Pro
Ala	Gly	Leu	Leu	Ala	Ile	Lys	Gln	Arg	Leu	Trp	Arg	Arg	Pro	Phe
Gly	Leu	Leu	Ala	Ile	Lys	Gln	Arg	Leu	Arg	Arg	Arg	Pro	Phe	Asn
Leu	Leu	Ala	Ile	Leu	Gln	Arg	Leu	Arg	Ser	Arg	Pro	Phe	Asn	Val
Leu	Ala	Ile	Leu	Ala	Arg	Leu	Arg	Ser	Gly	Pro	Phe	Asn	Val	Thr
Ala	Ile	Leu	Ala	Thr	Leu	Arg	Ser	Gly	Ser	Phe	Asn	Val	Thr	Asp
Ile	Leu	Ala	Thr	Pro	Arg	Ser	Gly	Ser	Ala	Asn	Val	Thr	Asp	Val

TABLE 6-continued

Leu Ala Thr Pro Gln Ser Gly Ser Ala Ser	Val Thr Asp Val Leu
Ala Thr Pro Gln Pro Gly Ser Ala Ser Pro	Thr Asp Val Leu Thr
Thr Pro Gln Pro Ser Ser Ala Ser Pro Met	Asp Val Leu Thr Pro
Pro Gln Pro Ser Glu Ala Ser Pro Met Glu	Val Leu Thr Pro Ala
Gln Pro Ser Glu Gly Ser Pro Met Glu Leu	Leu Thr Pro Ala Gln
Pro Ser Glu Gly Ala Pro Met Glu Leu Leu	Thr Pro Ala Gln Leu
Ser Glu Gly Ala Ala Met Glu Leu Leu Ser	Pro Ala Gln Leu Asn
Glu Gly Ala Ala Pro Glu Leu Leu Ser Tyr	Ala Gln Leu Asn Val
Gly Ala Ala Pro Ala Leu Leu Ser Tyr Phe	Gln Leu Asn Val Leu
Ala Ala Pro Ala Val Leu Ser Tyr Phe Lys	Leu Asn Val Leu Ser
Ala Pro Ala Val Leu Ser Tyr Phe Lys Gln	Asn Val Leu Ser Lys
Pro Ala Val Leu Gly Tyr Phe Lys Gln Pro	Val Leu Ser Lys Ser
Leu Ser Lys Ser Ser Glu Asp Gly Phe Ser	
Ser Lys Ser Ser Gly Asp Gly Phe Ser Leu	
Lys Ser Ser Gly Cys Gly Phe Ser Leu Pro	
Ser Ser Gly Cys Ala Phe Ser Leu Pro Tyr	
Ser Gly Cys Ala Tyr Ser Leu Pro Tyr Gly	
Gly Cys Ala Tyr Gln Leu Pro Tyr Gly Trp	
Cys Ala Tyr Gln Asp Pro Tyr Gly Trp Thr	
Ala Tyr Gln Asp Val Tyr Gly Trp Thr Pro	
Tyr Gln Asp Val Gly Gly Trp Thr Pro Gly	
Gln Asp Val Gly Val Trp Thr Pro Gly Val	
Asp Val Gly Val Thr Thr Pro Gly Val Lys	
Val Gly Val Thr Cys Pro Gly Val Lys Arg	
Gly Val Thr Cys Pro Gly Val Lys Arg Asn	
Val Thr Cys Pro Glu Val Lys Arg Asn Gly	
Thr Cys Pro Glu Gln Lys Arg Asn Gly Phe	
Cys Pro Glu Gln Asp Arg Asn Gly Phe Pro	
Pro Glu Gln Asp Lys Asn Gly Phe Pro Val	
Glu Gln Asp Lys Tyr Gly Phe Pro Val Ala	
Gln Asp Lys Tyr Arg	
Asp Lys Tyr Arg Thr	
Lys Tyr Arg Thr Ile	
Tyr Arg Thr Ile Thr	
Arg Thr Ile Thr Gly	
Thr Ile Thr Gly Met	
Ile Thr Gly Met Cys	
Thr Gly Met Cys Asn	

TABLE 6-continued

Gly Met Cys Asn Asn
Met Cys Asn Asn Arg
Cys Asn Asn Arg Arg
Asn Asn Arg Arg Ser
Asn Arg Arg Ser Pro
Arg Arg Ser Pro Thr
Arg Ser Pro Thr Leu
Ser Pro Thr Leu Gly
Pro Thr Leu Gly Ala
Thr Leu Gly Ala Ser
Leu Gly Ala Ser Asn
Gly Ala Ser Asn Arg
Ala Ser Asn Arg Ala
Ser Asn Arg Ala Phe
Asn Arg Ala Phe Val
Arg Ala Phe Val Arg
Ala Phe Val Arg Trp
Phe Val Arg Trp Leu
Val Arg Trp Leu Pro
Arg Trp Leu Pro Ala
Trp Leu Pro Ala Glu
Leu Pro Ala Glu Tyr
Pro Ala Glu Tyr Glu
Ala Glu Tyr Glu Asp
Glu Tyr Glu Asp Gly
Tyr Glu Asp Gly Phe

[0115] When prostate specific antigen (PSA) (SEQ ID NO:6) is the target self-antigen, the peptide reagent comprises any sequence of 5 to 15 consecutive amino acid residues from anywhere in the amino acid sequence of PSA (SEQ ID NO: 6). Table 6 lists amino acid sequences for exemplary peptide reagents consisting of 5 consecutive amino acid residues from PSA (SEQ ID NO: 6). Additional peptide reagents may have a length of up to 15 amino acid residues, comprising any one of the listed 5-amino acid long sequences in Table 7, plus up to a total of 10 additional consecutive amino acid residues from SEQ ID NO:6, that are continuous (from either side within the protein amino sequence) with the 5-amino acid long sequence.

TABLE 7

Trp	Val	Pro	Val	Val	Gly	Val	Leu	Val	His	Asp Met Ser Leu Leu
Val	Pro	Val	Val	Phe	Val	Leu	Val	His	Pro	Met Ser Leu Leu Lys
Pro	Val	Val	Phe	Leu	Leu	Val	His	Pro	Gln	Ser Leu Leu Lys Asn
Val	Val	Phe	Leu	Thr	Val	His	Pro	Gln	Trp	Leu Leu Lys Asn Arg
Val	Phe	Leu	Thr	Leu	His	Pro	Gln	Trp	Val	Leu Lys Asn Arg Phe

TABLE 7-continued

Phe	Leu	Thr	Leu	Ser	Pro	Gln	Trp	Val	Leu	Lys	Asn	Arg	Phe	Leu
Leu	Thr	Leu	Ser	Val	Gln	Trp	Val	Leu	Thr	Asn	Arg	Phe	Leu	Arg
Thr	Leu	Ser	Val	Thr	Trp	Val	Leu	Thr	Ala	Arg	Phe	Leu	Arg	Pro
Leu	Ser	Val	Thr	Trp	Val	Leu	Thr	Ala	Ala	Phe	Leu	Arg	Pro	Gly
Ser	Val	Thr	Trp	Ile	Leu	Thr	Ala	Ala	His	Leu	Arg	Pro	Gly	Asp
Val	Thr	Trp	Ile	Gly	Thr	Ala	Ala	His	Cys	Arg	Pro	Gly	Asp	Asp
Thr	Trp	Ile	Gly	Ala	Ala	Ala	His	Cys	Ile	Pro	Gly	Asp	Asp	Ser
Trp	Ile	Gly	Ala	Ala	Ala	His	Cys	Ile	Arg	Gly	Asp	Asp	Ser	Ser
Ile	Gly	Ala	Ala	Pro	His	Cys	Ile	Arg	Asn	Asp	Asp	Ser	Ser	His
Gly	Ala	Ala	Pro	Leu	Cys	Ile	Arg	Asn	Lys	Asp	Ser	Ser	His	Asp
Ala	Ala	Pro	Leu	Ile	Ile	Arg	Asn	Lys	Ser	Ser	Ser	His	Asp	Leu
Ala	Pro	Leu	Ile	Leu	Arg	Asn	Lys	Ser	Val	Ser	His	Asp	Leu	Met
Pro	Leu	Ile	Leu	Ser	Asn	Lys	Ser	Val	Ile	His	Asp	Leu	Met	Leu
Leu	Ile	Leu	Ser	Arg	Lys	Ser	Val	Ile	Leu	Asp	Leu	Met	Leu	Leu
Ile	Leu	Ser	Arg	Ile	Ser	Val	Ile	Leu	Leu	Leu	Met	Leu	Leu	Arg
Leu	Ser	Arg	Ile	Val	Val	Ile	Leu	Leu	Gly	Met	Leu	Leu	Arg	Leu
Ser	Arg	Ile	Val	Gly	Ile	Leu	Leu	Gly	Arg	Leu	Leu	Arg	Leu	Ser
Arg	Ile	Val	Gly	Gly	Leu	Leu	Gly	Arg	His	Leu	Arg	Leu	Ser	Glu
Ile	Val	Gly	Gly	Trp	Leu	Gly	Arg	His	Ser	Arg	Leu	Ser	Glu	Pro
Val	Gly	Gly	Trp	Glu	Gly	Arg	His	Ser	Leu	Leu	Ser	Glu	Pro	Ala
Gly	Gly	Trp	Glu	Cys	Arg	His	Ser	Leu	Phe	Ser	Glu	Pro	Ala	Glu
Gly	Trp	Glu	Cys	Glu	His	Ser	Leu	Phe	His	Glu	Pro	Ala	Glu	Leu
Trp	Glu	Cys	Glu	Lys	Ser	Leu	Phe	His	Pro	Pro	Ala	Glu	Leu	Thr
Glu	Cys	Glu	Lys	His	Leu	Phe	His	Pro	Glu	Ala	Glu	Leu	Thr	Asp
Cys	Glu	Lys	His	Ser	Phe	His	Pro	Glu	Asp	Glu	Leu	Thr	Asp	Ala
Glu	Lys	His	Ser	Gln	His	Pro	Glu	Asp	Thr	Leu	Thr	Asp	Ala	Val
Lys	His	Ser	Gln	Pro	Pro	Glu	Asp	Thr	Gly	Thr	Asp	Ala	Val	Lys
His	Ser	Gln	Pro	Trp	Glu	Asp	Thr	Gly	Gln	Asp	Ala	Val	Lys	Val
Ser	Gln	Pro	Trp	Gln	Asp	Thr	Gly	Gln	Val	Ala	Val	Lys	Val	Met
Gln	Pro	Trp	Gln	Val	Thr	Gly	Gln	Val	Phe	Val	Lys	Val	Met	Asp
Pro	Trp	Gln	Val	Leu	Gly	Gln	Val	Phe	Gln	Lys	Val	Met	Asp	Leu
Trp	Gln	Val	Leu	Val	Gln	Val	Phe	Gln	Val	Val	Met	Asp	Leu	Pro
Gln	Val	Leu	Val	Ala	Val	Phe	Gln	Val	Ser	Met	Asp	Leu	Pro	Thr
Val	Leu	Val	Ala	Ser	Phe	Gln	Val	Ser	His	Asp	Leu	Pro	Thr	Gln
Leu	Val	Ala	Ser	Arg	Gln	Val	Ser	His	Ser	Leu	Pro	Thr	Gln	Glu
Val	Ala	Ser	Arg	Gly	Val	Ser	His	Ser	Phe	Pro	Thr	Gln	Glu	Pro
Ala	Ser	Arg	Gly	Arg	Ser	His	Ser	Phe	Pro	Thr	Gln	Glu	Pro	Ala
Ser	Arg	Gly	Arg	Ala	His	Ser	Phe	Pro	His	Gln	Glu	Pro	Ala	Leu

TABLE 7-continued

Arg Gly Arg Ala Val Ser Phe Pro His Pro	Glu Pro Ala Leu Gly
Gly Arg Ala Val Cys Phe Pro His Pro Leu	Pro Ala Leu Gly Thr
Arg Ala Val Cys Gly Pro His Pro Leu Tyr	Ala Leu Gly Thr Thr
Ala Val Cys Gly Gly His Pro Leu Tyr Asp	Leu Gly Thr Thr Cys
Val Cys Gly Gly Val Pro Leu Tyr Asp Met	Gly Thr Thr Cys Tyr
Cys Gly Gly Val Leu Leu Tyr Asp Met Ser	Thr Thr Cys Tyr Ala
Gly Gly Val Leu Val Tyr Asp Met Ser Leu	Thr Cys Tyr Ala Ser
Cys Tyr Ala Ser Gly Gly Gly Lys Ser Thr	Thr Ile Val Ala Asn
Tyr Ala Ser Gly Trp Gly Lys Ser Thr Cys	Ile Val Ala Asn Pro
Ala Ser Gly Trp Gly Lys Ser Thr Cys Ser	
Ser Gly Trp Gly Ser Ser Thr Cys Ser Gly	
Gly Trp Gly Ser Ile Thr Cys Ser Gly Asp	
Trp Gly Ser Ile Glu Cys Ser Gly Asp Ser	
Gly Ser Ile Glu Pro Ser Gly Asp Ser Gly	
Ser Ile Glu Pro Glu Gly Asp Ser Gly Gly	
Ile Glu Pro Glu Glu Asp Ser Gly Gly Pro	
Glu Pro Glu Glu Phe Ser Gly Gly Pro Leu	
Pro Glu Glu Phe Leu Gly Gly Pro Leu Val	
Glu Glu Phe Leu Thr Gly Pro Leu Val Cys	
Glu Phe Leu Thr Pro Pro Leu Val Cys Asn	
Phe Leu Thr Pro Lys Leu Val Cys Asn Gly	
Leu Thr Pro Lys Lys Val Cys Asn Gly Val	
Thr Pro Lys Lys Leu Cys Asn Gly Val Leu	
Pro Lys Lys Leu Gln Asn Gly Val Leu Gln	
Lys Lys Leu Gln Cys Gly Val Leu Gln Gly	
Lys Leu Gln Cys Val Val Leu Gln Gly Ile	
Leu Gln Cys Val Asp Leu Gln Gly Ile Thr	
Gln Cys Val Asp Leu Gln Gly Ile Thr Ser	
Cys Val Asp Leu His Gly Ile Thr Ser Trp	
Val Asp Leu His Val Ile Thr Ser Trp Gly	
Asp Leu His Val Ile Thr Ser Trp Gly Ser	
Leu His Val Ile Ser Ser Trp Gly Ser Glu	
His Val Ile Ser Asn Trp Gly Ser Glu Pro	
Val Ile Ser Asn Asp Gly Ser Glu Pro Cys	
Ile Ser Asn Asp Val Ser Glu Pro Cys Ala	
Ser Asn Asp Val Cys Glu Pro Cys Ala Leu	
Asn Asp Val Cys Ala Pro Cys Ala Leu Pro	
Asp Val Cys Ala Gln Cys Ala Leu Pro Glu	

TABLE 7-continued

Val Cys Ala Gln Val Ala Leu Pro Glu Arg
Cys Ala Gln Val His Leu Pro Glu Arg Pro
Ala Gln Val His Pro Pro Glu Arg Pro Ser
Gln Val His Pro Gln Glu Arg Pro Ser Leu
Val His Pro Gln Lys Arg Pro Ser Leu Tyr
His Pro Gln Lys Val Pro Ser Leu Tyr Thr
Pro Gln Lys Val Thr Ser Leu Tyr Thr Lys
Gln Lys Val Thr Lys Leu Tyr Thr Lys Val
Lys Val Thr Lys Phe Tyr Thr Lys Val Val
Val Thr Lys Phe Met Thr Lys Val Val His
Thr Lys Phe Met Leu Lys Val Val His Tyr
Lys Phe Met Leu Cys Val Val His Tyr Arg
Phe Met Leu Cys Ala Val His Tyr Arg Lys
Met Leu Cys Ala Gly His Tyr Arg Lys Trp
Leu Cys Ala Gly Arg Tyr Arg Lys Trp Ile
Cys Ala Gly Arg Trp Arg Lys Trp Ile Lys
Ala Gly Arg Trp Thr Lys Trp Ile Lys Asp
Gly Arg Trp Thr Gly Trp Ile Lys Asp Thr
Arg Trp Thr Gly Gly Ile Lys Asp Thr Ile
Trp Thr Gly Gly Lys Lys Asp Thr Ile Val
Thr Gly Gly Lys Ser Asp Thr Ile Val Ala

[0116] When human B-type natriuretic peptide (hBNP) (SEQ ID NO:7) is the target self-antigen, the peptide reagent comprises any sequence of 5 to 15 consecutive amino acid residues from anywhere in the amino acid sequence of hBNP (SEQ ID NO:7). Table 8 lists amino acid sequences for exemplary peptide reagents consisting of 5 consecutive amino acid residues from hBNP (SEQ ID NO: 7). Additional peptide reagents may have a length of up to 15 amino acid residues, comprising any one of the listed 5-amino acid long sequences in Table 8, plus up to a total of 10 additional consecutive amino acid residues from SEQ ID NO:7, that are continuous (from either side within the protein amino sequence) with the 5-amino acid long sequence.

TABLE 8

Asp Pro Gln Thr Ala	Gly Lys Leu Ser Glu Arg Ser Pro Lys Met
Pro Gln Thr Ala Pro	Lys Leu Ser Glu Leu Ser Pro Lys Met Val
Gln Thr Ala Pro Ser	Leu Ser Glu Leu Gln Pro Lys Met Val Gln
Thr Ala Pro Ser Arg	Ser Glu Leu Gln Val Lys Met Val Gln Gly
Ala Pro Ser Arg Ala	Glu Leu Gln Val Glu Met Val Gln Gly Ser
Pro Ser Arg Ala Leu	Leu Gln Val Glu Gln Val Gln Gly Ser Gly
Ser Arg Ala Leu Leu	Gln Val Glu Gln Thr Gln Gly Ser Gly Cys
Arg Ala Leu Leu Leu	Val Glu Gln Thr Ser Gly Ser Gly Cys Phe
Ala Leu Leu Leu Leu	Glu Gln Thr Ser Leu Ser Gly Cys Phe Gly

TABLE 8-continued

Leu Leu Leu Leu Leu Gln Thr Ser Leu Glu	Gly Cys Phe Gly Arg
Leu Leu Leu Leu Phe Thr Ser Leu Glu Pro	Cys Phe Gly Arg Lys
Leu Leu Leu Phe Leu Ser Leu Glu Pro Leu	Phe Gly Arg Lys Met
Leu Leu Phe Leu His Leu Glu Pro Leu Gln	Gly Arg Lys Met Asp
Leu Phe Leu His Leu Glu Pro Leu Gln Glu	Arg Lys Met Asp Arg
Phe Leu His Leu Ala Pro Leu Gln Glu Ser	Lys Met Asp Arg Ile
Leu His Leu Ala Phe Leu Gln Glu Ser Pro	Met Asp Arg Ile Ser
His Leu Ala Phe Leu Gln Glu Ser Pro Arg	Asp Arg Ile Ser Ser
Leu Ala Phe Leu Gly Glu Ser Pro Arg Pro	Arg Ile Ser Ser Ser
Ala Phe Leu Gly Gly Ser Pro Arg Pro Thr	Ile Ser Ser Ser Ser
Phe Leu Gly Gly Arg Pro Arg Pro Thr Gly	Ser Ser Ser Ser Gly
Leu Gly Gly Arg Ser Arg Pro Thr Gly Val	Ser Ser Ser Gly Leu
Gly Gly Arg Ser His Pro Thr Gly Val Trp	Ser Ser Gly Leu Gly
Gly Arg Ser His Pro Thr Gly Val Trp Lys	Ser Gly Leu Gly Cys
Arg Ser His Pro Leu Gly Val Trp Lys Ser	Gly Leu Gly Cys Lys
Ser His Pro Leu Gly Val Trp Lys Ser Arg	Leu Gly Cys Lys Val
His Pro Leu Gly Ser Trp Lys Ser Arg Glu	Gly Cys Lys Val Leu
Pro Leu Gly Ser Pro Lys Ser Arg Glu Val	Cys Lys Val Leu Arg
Leu Gly Ser Pro Gly Ser Arg Glu Val Ala	Lys Val Leu Arg Arg
Gly Ser Pro Gly Ser Arg Glu Val Ala Thr	Val Leu Arg Arg His
Ser Pro Gly Ser Ala Glu Val Ala Thr Glu	
Pro Gly Ser Ala Ser Val Ala Thr Glu Gly	
Gly Ser Ala Ser Asp Ala Thr Glu Gly Ile	
Ser Ala Ser Asp Leu Thr Glu Gly Ile Arg	
Ala Ser Asp Leu Glu Glu Gly Ile Arg Gly	
Ser Asp Leu Glu Thr Gly Ile Arg Gly His	
Asp Leu Glu Thr Ser Ile Arg Gly His Arg	
Leu Glu Thr Ser Gly Arg Gly His Arg Lys	
Glu Thr Ser Gly Leu Gly His Arg Lys Met	
Thr Ser Gly Leu Gln His Arg Lys Met Val	
Ser Gly Leu Gln Glu Arg Lys Met Val Leu	
Gly Leu Gln Glu Gln Lys Met Val Leu Tyr	
Leu Gln Glu Gln Arg Met Val Leu Tyr Thr	
Gln Glu Gln Arg Asn Val Leu Tyr Thr Leu	
Glu Gln Arg Asn His Leu Tyr Thr Leu Arg	
Gln Arg Asn His Leu Tyr Thr Leu Arg Ala	
Arg Asn His Leu Gln Thr Leu Arg Ala Pro	
Asn His Leu Gln Gly Leu Arg Ala Pro Arg	

TABLE 8-continued

His Leu Gln Gly Lys Arg Ala Pro Arg Ser
Leu Gln Gly Lys Leu Ala Pro Arg Ser Pro
Gln Gly Lys Leu Ser Pro Arg Ser Pro Lys

[0117] When myosin light chain 2 (SEQ ID NO:8) is the target self-antigen, the peptide reagent comprises any sequence of 5 to 15 consecutive amino acid residues from anywhere in the amino acid sequence of myosin light chain 2 (SEQ ID NO:8). Table 9 lists amino acid sequences for exemplary peptide reagents consisting of 5 consecutive amino acid residues from myosin light chain 2 (SEQ ID NO: 8). Additional peptide reagents may have a length of up to 15 amino acid residues, comprising any one of the listed 5-amino acid long sequences in Table 9, plus up to a total of 10 additional consecutive amino acid residues from SEQ ID NO:8, that are continuous (from either side within the protein amino sequence) with the 5-amino acid long sequence.

TABLE 9

Ala Pro Lys Lys Ala Thr Phe Ala Ala Leu	Ala Phe Lys Val Phe
Pro Lys Lys Ala Lys Phe Ala Ala Leu Gly	Phe Lys Val Phe Asp
Lys Lys Ala Lys Lys Ala Ala Leu Gly Arg	Lys Val Phe Asp Pro
Lys Ala Lys Lys Arg Ala Leu Gly Arg Val	Val Phe Asp Pro Glu
Ala Lys Lys Arg Ala Leu Gly Arg Val Asn	Phe Asp Pro Glu Gly
Lys Lys Arg Ala Gly Gly Arg Val Asn Val	Asp Pro Glu Gly Lys
Lys Arg Ala Gly Gly Arg Val Asn Val Lys	Pro Glu Gly Lys Gly
Arg Ala Gly Gly Ala Val Asn Val Lys Asn	Glu Gly Lys Gly Val
Ala Gly Gly Ala Asn Asn Val Lys Asn Glu	Gly Lys Gly Val Leu
Gly Gly Ala Asn Ser Val Lys Asn Glu Glu	Lys Gly Val Leu Lys
Gly Ala Asn Ser Asn Lys Asn Glu Glu Ile	Gly Val Leu Lys Ala
Ala Asn Ser Asn Val Asn Glu Glu Ile Asp	Val Leu Lys Ala Asp
Asn Ser Asn Val Phe Glu Glu Ile Asp Glu	Leu Lys Ala Asp Tyr
Ser Asn Val Phe Ser Glu Ile Asp Glu Met	Lys Ala Asp Tyr Val
Asn Val Phe Ser Met Ile Asp Glu Met Ile	Ala Asp Tyr Val Arg
Val Phe Ser Met Phe Asp Glu Met Ile Lys	Asp Tyr Val Arg Glu
Phe Ser Met Phe Glu Glu Met Ile Lys Glu	Tyr Val Arg Glu Met
Ser Met Phe Glu Gln Met Ile Lys Glu Ala	Val Arg Glu Met Leu
Met Phe Glu Gln Thr Ile Lys Glu Ala Pro	Arg Glu Met Leu Thr
Phe Glu Gln Thr Gln Lys Glu Ala Pro Gly	Glu Met Leu Thr Thr
Glu Gln Thr Gln Ile Glu Ala Pro Gly Pro	Met Leu Thr Thr Gln
Gln Thr Gln Ile Gln Ala Pro Gly Pro Ile	Leu Thr Thr Gln Ala
Thr Gln Ile Gln Glu Pro Gly Pro Ile Asn	Thr Thr Gln Ala Glu
Gln Ile Gln Glu Phe Gly Pro Ile Asn Phe	Thr Gln Ala Glu Arg
Ile Gln Glu Phe Lys Pro Ile Asn Phe Thr	Gln Ala Glu Arg Phe
Gln Glu Phe Lys Glu Ile Asn Phe Thr Val	Ala Glu Arg Phe Ser
Glu Phe Lys Glu Ala Asn Phe Thr Val Phe	Glu Arg Phe Ser Lys
Phe Lys Glu Ala Phe Phe Thr Val Phe Leu	Arg Phe Ser Lys Glu

TABLE 9-continued

Lys	Glu	Ala	Phe	Thr	Thr	Val	Phe	Leu	Thr	Phe	Ser	Lys	Glu	Glu					
Glu	Ala	Phe	Thr	Ile	Val	Phe	Leu	Thr	Met	Ser	Lys	Glu	Glu	Val					
Ala	Phe	Thr	Ile	Met	Phe	Leu	Thr	Met	Phe	Lys	Glu	Glu	Val	Asp					
Phe	Thr	Ile	Met	Asp	Leu	Thr	Met	Phe	Gly	Glu	Glu	Val	Asp	Gln					
Thr	Ile	Met	Asp	Gln	Thr	Met	Phe	Gly	Glu	Glu	Val	Asp	Gln	Met					
Ile	Met	Asp	Gln	Asn	Met	Phe	Gly	Glu	Lys	Val	Asp	Gln	Met	Phe					
Met	Asp	Gln	Asn	Arg	Phe	Gly	Glu	Lys	Leu	Asp	Gln	Met	Phe	Ala					
Asp	Gln	Asn	Arg	Asp	Gly	Glu	Lys	Leu	Lys	Gln	Met	Phe	Ala	Ala					
Gln	Asn	Arg	Asp	Gly	Glu	Lys	Leu	Lys	Gly	Met	Phe	Ala	Ala	Phe					
Asn	Arg	Asp	Gly	Phe	Lys	Leu	Lys	Gly	Ala	Phe	Ala	Ala	Phe	Pro					
Arg	Asp	Gly	Phe	Ile	Leu	Lys	Gly	Ala	Asp	Ala	Ala	Phe	Pro	Pro					
Asp	Gly	Phe	Ile	Asp	Lys	Gly	Ala	Asp	Pro	Ala	Phe	Pro	Pro	Asp					
Gly	Phe	Ile	Asp	Lys	Gly	Ala	Asp	Pro	Glu	Phe	Pro	Pro	Asp	Val					
Phe	Ile	Asp	Lys	Asn	Ala	Asp	Pro	Glu	Glu	Pro	Pro	Asp	Val	Thr					
Ile	Asp	Lys	Asn	Asp	Asp	Pro	Glu	Glu	Thr	Pro	Asp	Val	Thr	Gly					
Asp	Lys	Asn	Asp	Leu	Pro	Glu	Glu	Thr	Ile	Asp	Val	Thr	Gly	Asn					
Lys	Asn	Asp	Leu	Arg	Glu	Glu	Thr	Ile	Leu	Val	Thr	Gly	Asn	Leu					
Asn	Asp	Leu	Arg	Asp	Glu	Thr	Ile	Leu	Asn	Thr	Gly	Asn	Leu	Asp					
Asp	Leu	Arg	Asp	Thr	Thr	Ile	Leu	Asn	Ala	Gly	Asn	Leu	Asp	Tyr					
Leu	Arg	Asp	Thr	Phe	Ile	Leu	Asn	Ala	Phe	Asn	Leu	Asp	Tyr	Lys					
Arg	Asp	Thr	Phe	Ala	Leu	Asn	Ala	Phe	Lys	Leu	Asp	Tyr	Lys	Asn					
Asp	Thr	Phe	Ala	Ala	Asn	Ala	Phe	Lys	Val	Asp	Tyr	Lys	Asn	Leu					
Tyr	Lys	Asn	Leu	Val															
Lys	Asn	Leu	Val	His															
Asn	Leu	Val	His	Ile															
Leu	Val	His	Ile	Ile															
Val	His	Ile	Ile	Thr															
His	Ile	Ile	Thr	His															
Ile	Ile	Thr	His	Gly															
Ile	Thr	His	Gly	Glu															
Thr	His	Gly	Glu	Glu															
His	Gly	Glu	Glu	Lys															
Gly	Glu	Glu	Lys	Asp															

[0118] When myosin-6 (SEQ ID NO:9) is the target self-antigen, the peptide reagent comprises any sequence of 5 to 15 consecutive amino acid residues from anywhere in the amino acid sequence of myosin-6 (SEQ ID NO:9). Table 10 lists amino acid sequences for exemplary peptide reagents consisting of 5 consecutive amino acid residues from myosin-6 (SEQ ID NO: 9). Additional peptide reagents may have a length of up to 15 amino acid residues, comprising any one of the listed 5-amino acid long sequences in Table 10, plus up to a total of 10 additional consecutive amino acid residues from SEQ ID NO:9, that are continuous (from either side within the protein amino sequence) with the 5-amino acid long sequence.

TABLE 10

Thr Asp Ala Gln Met Leu Ser Arg Glu Gly	Leu Phe Asn Leu Lys
Asp Ala Gln Met Ala Ser Arg Glu Gly Gly	Phe Asn Leu Lys Glu
Ala Gln Met Ala Asp Arg Glu Gly Gly Lys	Asn Leu Lys Glu Arg
Gln Met Ala Asp Phe Glu Gly Gly Lys Val	Leu Lys Glu Arg Tyr
Met Ala Asp Phe Gly Gly Gly Lys Val Ile	Lys Glu Arg Tyr Ala
Ala Asp Phe Gly Ala Gly Lys Val Ile Ala	Glu Arg Tyr Ala Ala
Asp Phe Gly Ala Ala Lys Val Ile Ala Glu	Arg Tyr Ala Ala Trp
Phe Gly Ala Ala Ala Val Ile Ala Glu Thr	Tyr Ala Ala Trp Met
Gly Ala Ala Ala Gln Ile Ala Glu Thr Glu	Ala Ala Trp Met Ile
Ala Ala Ala Gln Tyr Ala Glu Thr Glu Asn	Ala Trp Met Ile Tyr
Ala Ala Gln Tyr Leu Glu Thr Glu Asn Gly	Trp Met Ile Tyr Thr
Ala Gln Tyr Leu Arg Thr Glu Asn Gly Lys	Met Ile Tyr Thr Tyr
Gln Tyr Leu Arg Lys Glu Asn Gly Lys Thr	Ile Tyr Thr Tyr Ser
Tyr Leu Arg Lys Ser Asn Gly Lys Thr Val	Tyr Thr Tyr Ser Gly
Leu Arg Lys Ser Glu Gly Lys Thr Val Thr	Thr Tyr Ser Gly Leu
Arg Lys Ser Glu Lys Lys Thr Val Thr Val	Tyr Ser Gly Leu Phe
Lys Ser Glu Lys Glu Thr Val Thr Val Lys	Ser Gly Leu Phe Cys
Ser Glu Lys Glu Arg Val Thr Val Lys Glu	Gly Leu Phe Cys Val
Glu Lys Glu Arg Leu Thr Val Lys Glu Asp	Leu Phe Cys Val Thr
Lys Glu Arg Leu Glu Val Lys Glu Asp Gln	Phe Cys Val Thr Val
Glu Arg Leu Glu Ala Lys Glu Asp Gln Val	Cys Val Thr Val Asn
Arg Leu Glu Ala Gln Glu Asp Gln Val Leu	Val Thr Val Asn Pro
Leu Glu Ala Gln Thr Asp Gln Val Leu Gln	Thr Val Asn Pro Tyr
Glu Ala Gln Thr Arg Gln Val Leu Gln Gln	Val Asn Pro Tyr Lys
Ala Gln Thr Arg Pro Val Leu Gln Gln Asn	Asn Pro Tyr Lys Trp
Gln Thr Arg Pro Phe Leu Gln Gln Asn Pro	Pro Tyr Lys Trp Leu
Thr Arg Pro Phe Asp Gln Gln Asn Pro Pro	Tyr Lys Trp Leu Pro
Arg Pro Phe Asp Ile Gln Asn Pro Pro Lys	Lys Trp Leu Pro Val
Pro Phe Asp Ile Arg Asn Pro Pro Lys Phe	Trp Leu Pro Val Tyr
Phe Asp Ile Arg Thr Pro Pro Lys Phe Asp	Leu Pro Val Tyr Asn
Asp Ile Arg Thr Glu Pro Lys Phe Asp Lys	Pro Val Tyr Asn Ala
Ile Arg Thr Glu Cys Lys Phe Asp Lys Ile	Val Tyr Asn Ala Glu
Arg Thr Glu Cys Phe Phe Asp Lys Ile Gln	Tyr Asn Ala Glu Val
Thr Glu Cys Phe Val Asp Lys Ile Gln Asp	Asn Ala Glu Val Val
Glu Cys Phe Val Pro Lys Ile Gln Asp Met	Ala Glu Val Val Ala
Cys Phe Val Pro Asp Ile Gln Asp Met Ala	Glu Val Val Ala Ala
Phe Val Pro Asp Asp Gln Asp Met Ala Met	Val Val Ala Ala Tyr
Val Pro Asp Asp Lys Asp Met Ala Met Leu	Val Ala Ala Tyr Arg

TABLE 10-continued

Pro	Asp	Asp	Lys	Glu	Met	Ala	Met	Leu	Thr	Ala	Ala	Tyr	Arg	Gly
Asp	Asp	Lys	Glu	Glu	Ala	Met	Leu	Thr	Phe	Ala	Tyr	Arg	Gly	Lys
Asp	Lys	Glu	Glu	Phe	Met	Leu	Thr	Phe	Leu	Tyr	Arg	Gly	Lys	Lys
Lys	Glu	Glu	Phe	Val	Leu	Thr	Phe	Leu	His	Arg	Gly	Lys	Lys	Arg
Glu	Glu	Phe	Val	Lys	Thr	Phe	Leu	His	Glu	Gly	Lys	Lys	Arg	Ser
Glu	Phe	Val	Lys	Ala	Phe	Leu	His	Glu	Pro	Lys	Lys	Arg	Ser	Glu
Phe	Val	Lys	Ala	Lys	Leu	His	Glu	Pro	Ala	Lys	Arg	Ser	Glu	Ala
Val	Lys	Ala	Lys	Ile	His	Glu	Pro	Ala	Val	Arg	Ser	Glu	Ala	Pro
Lys	Ala	Lys	Ile	Leu	Glu	Pro	Ala	Val	Leu	Ser	Glu	Ala	Pro	Pro
Ala	Lys	Ile	Leu	Ser	Pro	Ala	Val	Leu	Phe	Glu	Ala	Pro	Pro	His
Lys	Ile	Leu	Ser	Arg	Ala	Val	Leu	Phe	Asn	Ala	Pro	Pro	His	Ile
Ile	Leu	Ser	Arg	Glu	Val	Leu	Phe	Asn	Leu	Pro	Pro	His	Ile	Phe
Pro	His	Ile	Phe	Ser	Arg	Gly	Lys	Lys	Asp	Thr	Gly	Lys	Leu	Ala
His	Ile	Phe	Ser	Ile	Gly	Lys	Lys	Asp	Asn	Gly	Lys	Leu	Ala	Ser
Ile	Phe	Ser	Ile	Ser	Lys	Lys	Asp	Asn	Ala	Lys	Leu	Ala	Ser	Ala
Phe	Ser	Ile	Ser	Asp	Lys	Asp	Asn	Ala	Asn	Leu	Ala	Ser	Ala	Asp
Ser	Ile	Ser	Asp	Asn	Asp	Asn	Ala	Asn	Ala	Ala	Ser	Ala	Asp	Ile
Ile	Ser	Asp	Asn	Ala	Asn	Ala	Asn	Ala	Asn	Ser	Ala	Asp	Ile	Glu
Ser	Asp	Asn	Ala	Tyr	Ala	Asn	Ala	Asn	Lys	Ala	Asp	Ile	Glu	Thr
Asp	Asn	Ala	Tyr	Gln	Asn	Ala	Asn	Lys	Gly	Asp	Ile	Glu	Thr	Tyr
Asn	Ala	Tyr	Gln	Tyr	Ala	Asn	Lys	Gly	Thr	Ile	Glu	Thr	Tyr	Leu
Ala	Tyr	Gln	Tyr	Met	Asn	Lys	Gly	Thr	Leu	Glu	Thr	Tyr	Leu	Leu
Tyr	Gln	Tyr	Met	Leu	Lys	Gly	Thr	Leu	Glu	Thr	Tyr	Leu	Leu	Glu
Gln	Tyr	Met	Leu	Thr	Gly	Thr	Leu	Glu	Asp	Tyr	Leu	Leu	Glu	Lys
Tyr	Met	Leu	Thr	Asp	Thr	Leu	Glu	Asp	Gln	Leu	Leu	Glu	Lys	Ser
Met	Leu	Thr	Asp	Arg	Leu	Glu	Asp	Gln	Ile	Leu	Glu	Lys	Ser	Arg
Leu	Thr	Asp	Arg	Glu	Glu	Asp	Gln	Ile	Ile	Glu	Lys	Ser	Arg	Val
Thr	Asp	Arg	Glu	Asn	Asp	Gln	Ile	Ile	Gln	Lys	Ser	Arg	Val	Ile
Asp	Arg	Glu	Asn	Gln	Gln	Ile	Ile	Gln	Ala	Ser	Arg	Val	Ile	Phe
Arg	Glu	Asn	Gln	Ser	Ile	Ile	Gln	Ala	Asn	Arg	Val	Ile	Phe	Gln
Glu	Asn	Gln	Ser	Ile	Ile	Gln	Ala	Asn	Pro	Val	Ile	Phe	Gln	Leu
Asn	Gln	Ser	Ile	Leu	Gln	Ala	Asn	Pro	Ala	Ile	Phe	Gln	Leu	Lys
Gln	Ser	Ile	Leu	Ile	Ala	Asn	Pro	Ala	Leu	Phe	Gln	Leu	Lys	Ala
Ser	Ile	Leu	Ile	Thr	Asn	Pro	Ala	Leu	Glu	Gln	Leu	Lys	Ala	Glu
Ile	Leu	Ile	Thr	Gly	Pro	Ala	Leu	Glu	Ala	Leu	Lys	Ala	Glu	Arg
Leu	Ile	Thr	Gly	Glu	Ala	Leu	Glu	Ala	Phe	Lys	Ala	Glu	Arg	Asn
Ile	Thr	Gly	Glu	Ser	Leu	Glu	Ala	Phe	Gly	Ala	Glu	Arg	Asn	Tyr
Thr	Gly	Glu	Ser	Gly	Glu	Ala	Phe	Gly	Asn	Glu	Arg	Asn	Tyr	His

TABLE 10-continued

Gly Glu Ser Gly Ala Ala Phe Gly Asn Ala	Arg Asn Tyr His Ile
Glu Ser Gly Ala Gly Phe Gly Asn Ala Lys	Asn Tyr His Ile Phe
Ser Gly Ala Gly Lys Gly Asn Ala Lys Thr	Tyr His Ile Phe Tyr
Gly Ala Gly Lys Thr Asn Ala Lys Thr Val	His Ile Phe Tyr Gln
Ala Gly Lys Thr Val Ala Lys Thr Val Arg	Ile Phe Tyr Gln Ile
Gly Lys Thr Val Asn Lys Thr Val Arg Asn	Phe Tyr Gln Ile Leu
Lys Thr Val Asn Thr Thr Val Arg Asn Asp	Tyr Gln Ile Leu Ser
Thr Val Asn Thr Lys Val Arg Asn Asp Asn	Gln Ile Leu Ser Asn
Val Asn Thr Lys Arg Arg Asn Asp Asn Ser	Ile Leu Ser Asn Lys
Asn Thr Lys Arg Val Asn Asp Asn Ser Ser	Leu Ser Asn Lys Lys
Thr Lys Arg Val Ile Asp Asn Ser Ser Arg	Ser Asn Lys Lys Pro
Lys Arg Val Ile Gln Asn Ser Ser Arg Phe	Asn Lys Lys Pro Glu
Arg Val Ile Gln Tyr Ser Ser Arg Phe Gly	Lys Lys Pro Glu Leu
Val Ile Gln Tyr Phe Ser Arg Phe Gly Lys	Lys Pro Glu Leu Leu
Ile Gln Tyr Phe Ala Arg Phe Gly Lys Phe	Pro Glu Leu Leu Asp
Gln Tyr Phe Ala Ser Phe Gly Lys Phe Ile	Glu Leu Leu Asp Met
Tyr Phe Ala Ser Ile Gly Lys Phe Ile Arg	Leu Leu Asp Met Leu
Phe Ala Ser Ile Ala Lys Phe Ile Arg Ile	Leu Asp Met Leu Leu
Ala Ser Ile Ala Ala Phe Ile Arg Ile His	Asp Met Leu Leu Val
Ser Ile Ala Ala Ile Ile Arg Ile His Phe	Met Leu Leu Val Thr
Ile Ala Ala Ile Gly Arg Ile His Phe Gly	Leu Leu Val Thr Asn
Ala Ala Ile Gly Asp Ile His Phe Gly Ala	Leu Val Thr Asn Asn
Ala Ile Gly Asp Arg His Phe Gly Ala Thr	Val Thr Asn Asn Pro
Ile Gly Asp Arg Gly Phe Gly Ala Thr Gly	Thr Asn Asn Pro Tyr
Gly Asp Arg Gly Lys Gly Ala Thr Gly Lys	Asn Asn Pro Tyr Asp
Asp Arg Gly Lys Lys Ala Thr Gly Lys Leu	Asn Pro Tyr Asp Tyr
Pro Tyr Asp Tyr Ala Tyr Gly Asn Met Lys	Val Thr Lys Gly Gln
Tyr Asp Tyr Ala Phe Gly Asn Met Lys Phe	Thr Lys Gly Gln Ser
Asp Tyr Ala Phe Val Asn Met Lys Phe Lys	Lys Gly Gln Ser Val
Tyr Ala Phe Val Ser Met Lys Phe Lys Gln	Gly Gln Ser Val Gln
Ala Phe Val Ser Gln Lys Phe Lys Gln Lys	Gln Ser Val Gln Gln
Phe Val Ser Gln Gly Phe Lys Gln Lys Gln	Ser Val Gln Gln Val
Val Ser Gln Gly Glu Lys Gln Lys Gln Arg	Val Gln Gln Val Tyr
Ser Gln Gly Glu Val Gln Lys Gln Arg Glu	Gln Gln Val Tyr Tyr
Gln Gly Glu Val Ser Lys Gln Arg Glu Glu	Gln Val Tyr Tyr Ser
Gly Glu Val Ser Val Gln Arg Glu Glu Gln	Val Tyr Tyr Ser Ile
Glu Val Ser Val Ala Arg Glu Glu Gln Ala	Tyr Tyr Ser Ile Gly
Val Ser Val Ala Ser Glu Glu Gln Ala Glu	Tyr Ser Ile Gly Ala

TABLE 10-continued

Ser Val Ala Ser Ile Glu Gln Ala Glu Pro	Ser Ile Gly Ala Leu
Val Ala Ser Ile Asp Gln Ala Glu Pro Asp	Ile Gly Ala Leu Ala
Ala Ser Ile Asp Asp Ala Glu Pro Asp Gly	Gly Ala Leu Ala Lys
Ser Ile Asp Asp Ser Glu Pro Asp Gly Thr	Ala Leu Ala Lys Ala
Ile Asp Asp Ser Glu Pro Asp Gly Thr Glu	Leu Ala Lys Ala Val
Asp Asp Ser Glu Glu Asp Gly Thr Glu Asp	Ala Lys Ala Val Tyr
Asp Ser Glu Glu Leu Gly Thr Glu Asp Ala	
Ser Glu Glu Leu Met Thr Glu Asp Ala Asp	
Glu Glu Leu Met Ala Glu Asp Ala Asp Lys	
Glu Leu Met Ala Thr Asp Ala Asp Lys Ser	
Leu Met Ala Thr Asp Ala Asp Lys Ser Ala	
Met Ala Thr Asp Ser Asp Lys Ser Ala Tyr	
Ala Thr Asp Ser Ala Lys Ser Ala Tyr Leu	
Thr Asp Ser Ala Phe Ser Ala Tyr Leu Met	
Asp Ser Ala Phe Asp Ala Tyr Leu Met Gly	
Ser Ala Phe Asp Val Tyr Leu Met Gly Leu	
Ala Phe Asp Val Leu Leu Met Gly Leu Asn	
Phe Asp Val Leu Gly Met Gly Leu Asn Ser	
Asp Val Leu Gly Phe Gly Leu Asn Ser Ala	
Val Leu Gly Phe Thr Leu Asn Ser Ala Asp	
Leu Gly Phe Thr Ser Asn Ser Ala Asp Leu	
Gly Phe Thr Ser Glu Ser Ala Asp Leu Leu	
Phe Thr Ser Glu Glu Ala Asp Leu Leu Lys	
Thr Ser Glu Glu Lys Asp Leu Leu Lys Gly	
Ser Glu Glu Lys Ala Leu Leu Lys Gly Leu	
Glu Glu Lys Ala Gly Leu Lys Gly Leu Cys	
Glu Lys Ala Gly Val Lys Gly Leu Cys His	
Lys Ala Gly Val Tyr Gly Leu Cys His Pro	
Ala Gly Val Tyr Lys Leu Cys His Pro Arg	
Gly Val Tyr Lys Leu Cys His Pro Arg Val	
Val Tyr Lys Leu Thr His Pro Arg Val Lys	
Tyr Lys Leu Thr Gly Pro Arg Val Lys Val	
Lys Leu Thr Gly Ala Arg Val Lys Val Gly	
Leu Thr Gly Ala Ile Val Lys Val Gly Asn	
Thr Gly Ala Ile Met Lys Val Gly Asn Glu	
Gly Ala Ile Met His Val Gly Asn Glu Tyr	
Ala Ile Met His Tyr Gly Asn Glu Tyr Val	
Ile Met His Tyr Gly Asn Glu Tyr Val Thr	

TABLE 10-continued

Met His Tyr Gly Asn Glu Tyr Val Thr Lys
His Tyr Gly Asn Met Tyr Val Thr Lys Gly

[0119] When myosin-7 (SEQ ID NO:10) is the target self-antigen, the peptide reagent comprises any sequence of 5 to 15 consecutive amino acid residues from anywhere in the amino acid sequence of myosin-7 (SEQ ID NO:10). Table 11 lists amino acid sequences for exemplary peptide reagents consisting of 5 consecutive amino acid residues from myosin-7 (SEQ ID NO: 10). Additional peptide reagents may have a length of up to 15 amino acid residues, comprising any one of the listed 5-amino acid long sequences in Table 11, plus up to a total of 10 additional consecutive amino acid residues from SEQ ID NO:10, that are continuous (from either side within the protein amino sequence) with the 5-amino acid long sequence.

TABLE 11

Gly Asp Ser Glu Met Val Ser Arg Glu Gly
Asp Ser Glu Met Ala Ser Arg Glu Gly Gly
Ser Glu Met Ala Val Arg Glu Gly Gly Lys
Glu Met Ala Val Phe Glu Gly Gly Lys Val
Met Ala Val Phe Gly Gly Gly Lys Val Thr
Ala Val Phe Gly Ala Gly Lys Val Thr Ala
Val Phe Gly Ala Ala Lys Val Thr Ala Glu
Phe Gly Ala Ala Ala Val Thr Ala Glu Thr
Gly Ala Ala Ala Pro Thr Ala Glu Thr Glu
Ala Ala Ala Pro Tyr Ala Glu Thr Glu Tyr
Ala Ala Pro Tyr Leu Glu Thr Glu Tyr Gly
Ala Pro Tyr Leu Arg Thr Glu Tyr Gly Lys
Pro Tyr Leu Arg Lys Glu Tyr Gly Lys Thr
Tyr Leu Arg Lys Ser Tyr Gly Lys Thr Val
Leu Arg Lys Ser Glu Gly Lys Thr Val Thr
Arg Lys Ser Glu Lys Lys Thr Val Thr Val
Lys Ser Glu Lys Glu Thr Val Thr Val Lys
Ser Glu Lys Glu Arg Val Thr Val Lys Glu
Glu Lys Glu Arg Leu Thr Val Lys Glu Asp
Lys Glu Arg Leu Glu Val Lys Glu Asp Gln
Glu Arg Leu Glu Ala Lys Glu Asp Gln Val
Arg Leu Glu Ala Gln Glu Asp Gln Val Met
Leu Glu Ala Gln Thr Asp Gln Val Met Gln
Glu Ala Gln Thr Arg Gln Val Met Gln Gln
Ala Gln Thr Arg Pro Val Met Gln Gln Asn
Gln Thr Arg Pro Phe Met Gln Gln Asn Pro
Thr Arg Pro Phe Asp Gln Gln Asn Pro Pro
Arg Pro Phe Asp Leu Gln Asn Pro Pro Lys
Pro Phe Asp Leu Lys Asn Pro Pro Lys Phe
Leu Tyr Asn Leu Lys
Tyr Asn Leu Lys Asp
Asn Leu Lys Asp Arg
Leu Lys Asp Arg Tyr
Lys Asp Arg Tyr Gly
Asp Arg Tyr Gly Ser
Arg Tyr Gly Ser Trp
Tyr Gly Ser Trp Met
Gly Ser Trp Met Ile
Ser Trp Met Ile Tyr
Trp Met Ile Tyr Thr
Met Ile Tyr Thr Tyr
Ile Tyr Thr Tyr Ser
Tyr Thr Tyr Ser Gly
Thr Tyr Ser Gly Leu
Tyr Ser Gly Leu Phe
Ser Gly Leu Phe Cys
Gly Leu Phe Cys Val
Leu Phe Cys Val Thr
Phe Cys Val Thr Val
Cys Val Thr Val Asn
Val Thr Val Asn Pro
Thr Val Asn Pro Tyr
Val Asn Pro Tyr Lys
Asn Pro Tyr Lys Trp
Pro Tyr Lys Trp Leu
Tyr Lys Trp Leu Pro
Lys Trp Leu Pro Val
Trp Leu Pro Val Tyr

TABLE 11-continued

Phe Asp Leu Lys Lys Pro Pro Lys Phe Asp	Leu Pro Val Tyr Thr
Asp Leu Lys Lys Asp Pro Lys Phe Asp Lys	Pro Val Tyr Thr Pro
Leu Lys Lys Asp Val Lys Phe Asp Lys Ile	Val Tyr Thr Pro Glu
Lys Lys Asp Val Phe Phe Asp Lys Ile Glu	Tyr Thr Pro Glu Val
Lys Asp Val Phe Val Asp Lys Ile Glu Asp	Thr Pro Glu Val Val
Asp Val Phe Val Pro Lys Ile Glu Asp Met	Pro Glu Val Val Ala
Val Phe Val Pro Asp Ile Glu Asp Met Ala	Glu Val Val Ala Ala
Phe Val Pro Asp Asp Glu Asp Met Ala Met	Val Val Ala Ala Tyr
Val Pro Asp Asp Lys Asp Met Ala Met Leu	Val Ala Ala Tyr Arg
Pro Asp Asp Lys Gln Met Ala Met Leu Thr	Ala Ala Tyr Arg Gly
Asp Asp Lys Gln Glu Ala Met Leu Thr Phe	Ala Tyr Arg Gly Lys
Asp Lys Gln Glu Phe Met Leu Thr Phe Leu	Tyr Arg Gly Lys Lys
Lys Gln Glu Phe Val Leu Thr Phe Leu His	Arg Gly Lys Lys Arg
Gln Glu Phe Val Lys Thr Phe Leu His Glu	Gly Lys Lys Arg Ser
Glu Phe Val Lys Ala Phe Leu His Glu Pro	Lys Lys Arg Ser Glu
Phe Val Lys Ala Lys Leu His Glu Pro Ala	Lys Arg Ser Glu Ala
Val Lys Ala Lys Ile His Glu Pro Ala Val	Arg Ser Glu Ala Pro
Lys Ala Lys Ile Val Glu Pro Ala Val Leu	Ser Glu Ala Pro Pro
Ala Lys Ile Val Ser Pro Ala Val Leu Tyr	Glu Ala Pro Pro His
Lys Ile Val Ser Arg Ala Val Leu Tyr Asn	Ala Pro Pro His Ile
Ile Val Ser Arg Glu Val Leu Tyr Asn Leu	Pro Pro His Ile Phe
Pro His Ile Phe Ser Arg Ser Lys Lys Asp	Gly Lys Leu Ala Ser
His Ile Phe Ser Ile Ser Lys Lys Asp Gln	Lys Leu Ala Ser Ala
Ile Phe Ser Ile Ser Lys Lys Asp Gln Ser	Leu Ala Ser Ala Asp
Phe Ser Ile Ser Asp Lys Asp Gln Ser Pro	Ala Ser Ala Asp Ile
Ser Ile Ser Asp Asn Asp Gln Ser Pro Gly	Ser Ala Asp Ile Glu
Ile Ser Asp Asn Ala Gln Ser Pro Gly Lys	Ala Asp Ile Glu Thr
Ser Asp Asn Ala Tyr Ser Pro Gly Lys Gly	Asp Ile Glu Thr Tyr
Asp Asn Ala Tyr Gln Pro Gly Lys Gly Thr	Ile Glu Thr Tyr Leu
Asn Ala Tyr Gln Tyr Gly Lys Gly Thr Leu	Glu Thr Tyr Leu Leu
Ala Tyr Gln Tyr Met Lys Gly Thr Leu Glu	Thr Tyr Leu Leu Glu
Tyr Gln Tyr Met Leu Gly Thr Leu Glu Asp	Tyr Leu Leu Glu Lys
Gln Tyr Met Leu Thr Thr Leu Glu Asp Gln	Leu Leu Glu Lys Ser
Tyr Met Leu Thr Asp Leu Glu Asp Gln Ile	Leu Glu Lys Ser Arg
Met Leu Thr Asp Arg Glu Asp Gln Ile Ile	Glu Lys Ser Arg Val
Leu Thr Asp Arg Glu Asp Gln Ile Ile Gln	Lys Ser Arg Val Ile
Thr Asp Arg Glu Asn Gln Ile Ile Gln Ala	Ser Arg Val Ile Phe
Asp Arg Glu Asn Gln Ile Ile Gln Ala Asn	Arg Val Ile Phe Gln

TABLE 11-continued

Arg	Glu	Asn	Gln	Ser	Ile	Gln	Ala	Asn	Pro	Val	Ile	Phe	Gln	Leu
Glu	Asn	Gln	Ser	Ile	Gln	Ala	Asn	Pro	Ala	Ile	Phe	Gln	Leu	Lys
Asn	Gln	Ser	Ile	Leu	Ala	Asn	Pro	Ala	Leu	Phe	Gln	Leu	Lys	Ala
Gln	Ser	Ile	Leu	Ile	Asn	Pro	Ala	Leu	Glu	Gln	Leu	Lys	Ala	Glu
Ser	Ile	Leu	Ile	Thr	Pro	Ala	Leu	Glu	Ala	Leu	Lys	Ala	Glu	Arg
Ile	Leu	Ile	Thr	Gly	Ala	Leu	Glu	Ala	Phe	Lys	Ala	Glu	Arg	Asp
Leu	Ile	Thr	Gly	Glu	Leu	Glu	Ala	Phe	Gly	Ala	Glu	Arg	Asp	Tyr
Ile	Thr	Gly	Glu	Ser	Glu	Ala	Phe	Gly	Asn	Glu	Arg	Asp	Tyr	His
Thr	Gly	Glu	Ser	Gly	Ala	Phe	Gly	Asn	Ala	Arg	Asp	Tyr	His	Ile
Gly	Glu	Ser	Gly	Ala	Phe	Gly	Asn	Ala	Lys	Asp	Tyr	His	Ile	Phe
Glu	Ser	Gly	Ala	Gly	Gly	Asn	Ala	Lys	Thr	Tyr	His	Ile	Phe	Tyr
Ser	Gly	Ala	Gly	Lys	Asn	Ala	Lys	Thr	Val	His	Ile	Phe	Tyr	Gln
Gly	Ala	Gly	Lys	Thr	Ala	Lys	Thr	Val	Arg	Ile	Phe	Tyr	Gln	Ile
Ala	Gly	Lys	Thr	Val	Lys	Thr	Val	Arg	Asn					
Gly	Lys	Thr	Val	Asn	Thr	Val	Arg	Asn	Asp					
Lys	Thr	Val	Asn	Thr	Val	Arg	Asn	Asp	Asn					
Thr	Val	Asn	Thr	Lys	Arg	Asn	Asp	Asn	Ser					
Val	Asn	Thr	Lys	Arg	Asn	Asp	Asn	Ser	Ser					
Asn	Thr	Lys	Arg	Val	Asp	Asn	Ser	Ser	Arg					
Thr	Lys	Arg	Val	Ile	Asn	Ser	Ser	Arg	Phe					
Lys	Arg	Val	Ile	Gln	Ser	Ser	Arg	Phe	Gly					
Arg	Val	Ile	Gln	Tyr	Ser	Arg	Phe	Gly	Lys					
Val	Ile	Gln	Tyr	Phe	Arg	Phe	Gly	Lys	Phe					
Ile	Gln	Tyr	Phe	Ala	Phe	Gly	Lys	Phe	Ile					
Gln	Tyr	Phe	Ala	Val	Gly	Lys	Phe	Ile	Arg					
Tyr	Phe	Ala	Val	Ile	Lys	Phe	Ile	Arg	Ile					
Phe	Ala	Val	Ile	Ala	Phe	Ile	Arg	Ile	His					
Ala	Val	Ile	Ala	Ala	Ile	Arg	Ile	His	Phe					
Val	Ile	Ala	Ala	Ile	Arg	Ile	His	Phe	Gly					
Ile	Ala	Ala	Ile	Gly	Ile	His	Phe	Gly	Ala					
Ala	Ala	Ile	Gly	Asp	His	Phe	Gly	Ala	Thr					
Ala	Ile	Gly	Asp	Arg	Phe	Gly	Ala	Thr	Gly					
Ile	Gly	Asp	Arg	Ser	Gly	Ala	Thr	Gly	Lys					
Gly	Asp	Arg	Ser	Lys	Ala	Thr	Gly	Lys	Leu					
Asp	Arg	Ser	Lys	Lys	Thr	Gly	Lys	Leu	Ala					

[0120] Any one of the peptide reagents optionally can be modified at either or both of the N-terminal and C-terminal ends. N-terminal modifications include for example: acetylation [Ac], benzyloxycarbonyl [Cbz], biotin [Btn], cinnamoylation [Cinn], dabcyl [Dabc], dabsyl [Dabs], innamoylation [Cinn], dabcyl [Dabc], dabsyl [Dabs], dansyl [Dans], dinitrophenyl [Dnp], fluorescein [Flc], FMOC [Fmoc], formylation [Form], lissamine rhodamine [Liss], myristoylation [Mgrs], N-methyl [Nme], palmitoylation [Palm], steroylation [Ster], and 7-methoxycoumarin acetic acid [Mca]. C-terminal modifications include for example: amide [NH2], 4-Branch MAP resin [MAPC], and hydroxyl [OH].

[0121] Given a protein and thus a starting amino acid sequence from which a peptide reagent is to be derived, the peptide, or a library of multiple peptides, including peptides with modifications to either or both terminal ends, can be prepared by readily commercially accessible custom peptide synthesis services. Such services are now routinely available from, for example Sigma-Genosys (as PEPscreen®), Invitrogen and GeneTel Laboratories.

[0122] Peptide reagents according to the present disclosure can be tested for inhibition of autoantibody binding to the target protein by any of several detection methods as will be recognized by those of skill in the art. Typically a peptide reagent is prepared in a diluent to produce several solutions of varying concentrations. Each solution is combined with a selected amount of a test sample containing a known amount of autoantibody and target protein. A detection conjugate that includes a detectable label and a specific binding partner, i.e. antibody, against the target protein is also added. A signal generated by the detection conjugate can be used to quantify the relative inhibitory activity of each dilution of the peptide reagent with respect to autoantibody binding to the target protein.

[0123] For example, equimolar starting solutions of each peptide reagent, each having a different amino acid sequence derived from the target protein, can be obtained and then diluted in a suitable pre-incubation diluent to give solutions of pre-selected, varying concentrations, typically in the nmol/mL range. The target protein, typically a recombinant protein, can be coated in a suitable buffer solution on a microplate and maintained under conditions sufficient to obtain binding of the target protein to the plate, for example at 38° C., for about 1 h. The protein can then be overcoated sequentially with bovine serum albumin and a solution of sucrose in PBS. A detection conjugate can be prepared by labeling a murine anti-human IgG with a detectable label according to labeling methods well-known in the art. For example, the detectable label can be but is not limited to a chemiluminescent compound, such s an acridinium compound.

[0124] Each dilution of the inhibitor peptide reagent is then mixed, preferably at about a 1:1 ratio by volume, with a test sample that contains a known amount of endogenous autoantibodies to the target self-antigen. The resulting solutions are arrayed in microplates, sealed and maintained under conditions sufficient to obtain binding of the peptide reagent to the autoantibodies, for example for a period of about 6 to 24 hours at ambient temperature. Test samples that are positive and low controls are diluted with a suitable preincubation diluent and arrayed, for example in triplicate, on the microplate. The plates are incubated under conditions sufficient to obtain binding, for example at 37° C. for at least about 2 hours, and the plate is washed with a suitable buffer such as ARCHITECT® Wash Buffer. A detection conjugate is then added to the plate. For example, a detection conjugate can be a murine anti-human IgG specific monoclonal antibody conjugated to a detectable label. The plate is incubated again under conditions sufficient to achieve binding of the detection conjugate to the target self-antigen, for example at 37° C. for about 1 hour, before a final wash with the wash buffer.

[0125] For detection, the microplate is processed according to methods appropriate for the particular label and detection method selected. For example, when using a detection conjugate in which an acridinium compound is the detectable label, the microplate is loaded into a microplate reader (e.g. a Mithras microplate reader, Berthold Technologies Inc, Oak Ridge, Tenn.), and then equilibrated at a suitable temperature, for example at 28° C. A chemiluminescence signal from each well is recorded for a period of seconds following sequential addition of a pre-trigger solution and a trigger solution. The resulting chemiluminescent signals are then recorded. Data analysis of the signals can include a comparison of the signals as a plot of the ratio of signal to the low control (S/LC) against concentration of each peptide reagent to reveal the relative strength of inhibition by each peptide reagent.

C. Immunoassay for Detecting a Protein of Interest in a Test Sample

[0126] The present disclosure also relates methods of using the peptide reagents as disclosed herein in immunoassays for detecting protein analytes of interest in a test sample in which autoantibodies against the target protein may or may not be present. The protein analytes of interest are typically self-antigens. As set forth elsewhere herein, examples of self-antigens which are proteins for which autoantibodies have been described include but are not limited to cardiac troponin, myeloperoxidase (MPO), prostate specific antigen (PSA), and thyroid stimulating hormone (TSH). It will be understood that the peptide reagents and related methods described herein are also applicable to the detection of any other protein of diagnostic interest for which autoantibodies not yet described may interfere with immunodetection of the protein.

[0127] The methods of the present disclosure involves obtaining a test sample from a subject and then detecting the presence of a protein of interest, especially a self-antigen of clinical interest, using immunodetection, while compensating for the presence of any autoantibodies against the analyte that may be present in the sample. This is achieved in part by providing a peptide reagent derived from the protein, which inhibits binding to the protein of the autoantibody that may be present in the sample.

Immunoassay Methods

[0128] It will be recognized that methods of the present disclosure can be applied to immunoassays carried out in any of a wide variety of formats. The various immunoassay formats can be applied both to detection per se of a protein of interest, and also to testing of peptide reagents as disclosed herein to evaluate the inhibitory strength of a peptide reagent. A general review of immunoassays is available in METHODS IN CELL BIOLOGY VOLUME 37: ANTIBODIES IN CELL BIOLOGY, Asai, ed. Academic Press, Inc. New York (1993), and BASIC AND CLINICAL IMMUNOLOGY 7TH EDITION, Stites & Terr, eds. (1991), which are herein incorporated by reference in their entirety.

[0129] A peptide reagent according to the present disclosure assists in immunodetection of at least one protein (anti-

gen) of interest in a test sample in which autoantibodies to the protein may be present. As described elsewhere herein, the protein from which the peptide reagent is derived can be, for example, selected from the group consisting of: cardiac troponin I, cardiac troponin T, thyroid stimulating hormone (TSH), beta-human chorionic gonadotropin (beta-HCG), myeloperoxidase (MPO), prostate specific antigen (PSA), human B-type natriuretic peptide (hBNP), myosin light chain 2, myosin-6 and myosin-7. Typically the test sample is for example whole blood, serum or plasma, but can be any biological material, preferably is a biological fluid, suspected of containing a protein of interest and which may also include autoantibodies to the protein of interest.

[0130] In use, at least one peptide reagent as disclosed herein is combined with the test sample to form a first mixture. Thus the first mixture contains at least the peptide reagent, and may contain an amount of the target protein and any autoantibodies against the target protein. When the target protein and endogenous autoantibodies against the protein are present in the sample, the peptide reagent disrupts, i.e. blocks the interaction between the autoantibody in the test sample and the protein, leaving the target protein free for specific binding with another binding partner. The method then proceeds according to a typical sandwich immunoassay format. For example, a second mixture is then prepared by combining the first mixture and a first specific binding partner, namely an antibody that binds specifically with the protein of interest. The protein and antibody pair form a first specific binding partner-protein complex. A detection conjugate, i.e. an antibody conjugated to a detectable label, is then introduced to the second mixture. The antibody of the detection conjugate is also a specific binding partner of the protein, i.e. a second specific binding partner. The antibody of the detection conjugate binds to the first specific binding partner-protein complex to form an immunodetection complex that includes the first specific binding partner, protein and second specific binding partner. As the peptide reagent prevents binding of any autoantibody present in the sample to the target protein, the peptide reagent thus prevents autoantibodies from interfering with formation of the immunodetection complex. A signal is generated by or emitted from the detectable label on the detection conjugate, and the signal is used to detect presence of the protein of interest in the test sample. The signal generated by the detection conjugate is proportional to the concentration of the protein of interest as determined by the rate of formation (k1) of the immunodetection complex versus the rate of dissociation of the immunodetection complex (k2).

[0131] The method may involve, for example, use of an acridinium compound as the detectable label. When an acridinium compound is used, the method may further include generating or providing a source of hydrogen peroxide to the second mixture, adding a basic solution to the resulting mixture, and measuring the light signal generated or emitted and detecting the protein of interest in the sample. The hydrogen peroxide source may be a buffer, a solution containing hydrogen peroxide, or a hydrogen peroxide generating enzyme. The basic solution is for example a solution having a pH of at least about 10.

[0132] The method can optionally involve use of a solid phase. For example, the first specific binding partner can be immobilized on a solid phase either before or after the formation of the first specific binding partner-protein complex. The second specific binding partner can be immobilized on a solid phase either before or after formation of the first specific binding partner-protein-second specific binding partner complex. The solid phase when used can be any suitable material with sufficient surface affinity to bind the antibodies being used, and can take any of a number of forms, such as a magnetic particle, bead, test tube, microtiter plate, cuvette, membrane, a scaffolding molecule, quartz crystal, film, filter paper, disc or a chip. Useful solid phase materials include: natural polymeric carbohydrates and their synthetically modified, crosslinked, or substituted derivatives, such as agar, agarose, cross-linked alginic acid, substituted and cross-linked guar gums, cellulose esters, especially with nitric acid and carboxylic acids, mixed cellulose esters, and cellulose ethers; natural polymers containing nitrogen, such as proteins and derivatives, including cross-linked or modified gelatins; natural hydrocarbon polymers, such as latex and rubber; synthetic polymers, such as vinyl polymers, including polyethylene, polypropylene, polystyrene, polyvinylchloride, polyvinylacetate and its partially hydrolyzed derivatives, polyacrylamides, polymethacrylates, copolymers and terpolymers of the above polycondensates, such as polyesters, polyamides, and other polymers, such as polyurethanes or polyepoxides; inorganic materials such as sulfates or carbonates of alkaline earth metals and magnesium, including barium sulfate, calcium sulfate, calcium carbonate, silicates of alkali and alkaline earth metals, aluminum and magnesium; and aluminum or silicon oxides or hydrates, such as clays, alumina, talc, kaolin, zeolite, silica gel, or glass (these materials may be used as filters with the above polymeric materials); and mixtures or copolymers of the above classes, such as graft copolymers obtained by initializing polymerization of synthetic polymers on a pre-existing natural polymer. All of these materials may be used in suitable shapes, such as films, sheets, tubes, particulates, or plates, or they may be coated onto, bonded, or laminated to appropriate inert carriers, such as paper, glass, plastic films, fabrics, or the like. Nitrocellulose has excellent absorption and adsorption qualities for a wide variety of reagents including monoclonal antibodies. Nylon also possesses similar characteristics and also is suitable.

[0133] Alternatively, the solid phase can constitute microparticles. Microparticles useful in the present disclosure can be selected by one skilled in the art from any suitable type of particulate material and include those composed of polystyrene, polymethylacrylate, polypropylene, latex, polytetrafluoroethylene, polyacrylonitrile, polycarbonate, or similar materials. Further, the microparticles can be magnetic or paramagnetic microparticles, such as carboxylated magnetic microparticles. The methods of the present disclosure can be adapted for use in systems that utilize microparticle technology including automated and semi-automated systems wherein the solid phase comprises a microparticle. Such systems include those described in pending U.S. Pat. No. 425, 651 and U.S. Pat. No. 5,089,424, which correspond to published EPO App. Nos. EP 0 425 633 and EP 0 424 634, respectively, and U.S. Pat. No. 5,006,309.

[0134] In particular embodiments, the solid phase includes one or more electrodes. Antibodies can be affixed, directly or indirectly, to the electrode(s). In one embodiment, for example, an antibody of the first specific binding partner can be affixed to magnetic or paramagnetic microparticles, which are then positioned in the vicinity of the electrode surface using a magnet. Systems in which one or more electrodes serve as the solid phase are useful where detection is based on

electrochemical interactions. Exemplary systems of this type are described, for example, in U.S. Pat. No. 6,887,714 (issued May 3, 2005). The basic method is described further below with respect to electrochemical detection.

[0135] Other considerations affecting the choice of a solid phase include the ability to minimize non-specific binding of labeled entities and compatibility with the labeling system employed. For, example, solid phases used with fluorescent labels should have sufficiently low background fluorescence to allow signal detection.

[0136] Thus, according to the present disclosure, an immunoassay of the present disclosure to detect the presence of a protein of interest is a heterogeneous assay employing a solid phase which can be a solid support. The immunoassay can be performed for example by immobilizing an exogenous antibody on the solid phase, wherein the exogenous antibody is reactive with at least one epitope on the protein of interest and functions as the first specific binding partner. The peptide reagent is introduced to the test sample. The test sample is then contacted with first specific binding partner, under conditions sufficient for specific binding of the first specific binding partner to the protein of interest, thus forming a first specific binding partner-protein complex bound to the solid phase. In the case of a test sample containing at least one autoantibody against the protein, the peptide reagent blocks the interaction between the protein of interest and the autoantibody. The first specific binding partner-protein complex bound to the solid phase is contacted with the detection conjugate under conditions sufficient for specific binding of the detection conjugate to any of the protein of interest that is present in the test sample. An immunodetection complex is thus formed, which includes the first specific binding partner-protein complex and the detection conjugate.

[0137] Typically the detection conjugate includes a detectable label. Depending on the detection approach used, an optical, electrical, or change-of-state signal of the immunodetection complex is measured. The immunodetection complex is thus typically a configuration of molecules that once formed generates a signal susceptible to physical detection and/or quantification. Although the immunoassay is described above as including a sequence of steps for illustrative purposes, the test sample may be contacted with the first (capture) antibody and the second (detection) antibody simultaneously or sequentially, in any order. Regardless of the order of contact, if autoantibodies are present in the sample, the peptide reagent blocks interaction of the protein of interest with the autoantibodies that are present in the test sample.

[0138] In one format of a sandwich immunoassay according to the present disclosure, detecting comprises detecting a signal from the solid phase-affixed immunodetection complex, which includes the first specific binding partner, protein of interest and second specific binding partner (detection conjugate). In one embodiment, the immunodetection complex is separated from the solid phase, typically by washing, and the signal from the bound label is detected. In another format of a sandwich immunoassay according to the present disclosure, the immunodetection complex remains a solid phase-affixed complex, which is then detected.

Antibodies

[0139] In the immunoassays according to the present disclosure, the first specific binding partner can be an antibody including a polyclonal antibody, a monoclonal antibody, a chimeric antibody, a human antibody, an affinity maturated antibody or an antibody fragment. Similarly, the second antibody can be a polyclonal antibody, a monoclonal antibody, a chimeric antibody, a human antibody, an affinity maturated antibody or an antibody fragment.

[0140] While monoclonal antibodies are highly specific to the protein/antigen, a polyclonal antibody can preferably be used as the capture (first) antibody to immobilize as much of the protein/antigen as possible. A monoclonal antibody with inherently higher binding specificity for the protein/antigen may then preferably be used as the detection (second) antibody. In any case, the antibody serving as the first specific binding partner and that serving as the second specific binding partner preferably recognize two non-overlapping epitopes on the protein to avoid blockage of, or interference by one with the epitope recognized by the other. Preferably the antibodies being used are capable of binding simultaneously to different epitopes on the protein of interest, each without interfering with the binding of the other.

[0141] Polyclonal antibodies are raised by injecting (e.g., subcutaneous or intramuscular injection) an immunogen into a suitable non-human mammal (e.g., a mouse or a rabbit). Generally, the immunogen should induce production of high titers of antibody with relatively high affinity for the target antigen (protein of interest).

[0142] If desired, the antigen may be conjugated to a carrier protein by conjugation techniques that are well known in the art. Commonly used carriers include keyhole limpet hemocyanin (KLH), thyroglobulin, bovine serum albumin (BSA), and tetanus toxoid. The conjugate is then used to immunize the animal.

[0143] The antibodies are then obtained from blood samples taken from the animal. The techniques used to produce polyclonal antibodies are extensively described in the literature (see, e.g., Methods of Enzymology, "Production of Antisera With Small Doses of Immunogen: Multiple Intradermal Injections," Langone, et al. eds. (Acad. Press, 1981)). Polyclonal antibodies produced by the animals can be further purified, for example, by binding to and elution from a matrix to which the target antigen is bound. Those of skill in the art will know of various techniques common in the immunology arts for purification and/or concentration of polyclonal, as well as monoclonal, antibodies (see, e.g., Coligan, et al. (1991) Unit 9, Current Protocols in Immunology, Wiley Interscience).

[0144] For many applications, monoclonal antibodies (mAbs) are preferred. The general method used for production of hybridomas secreting mAbs is well known (Kohler and Milstein (1975) Nature, 256:495). Briefly, as described by Kohler and Milstein, the technique involves isolating lymphocytes from regional draining lymph nodes of five separate cancer patients with either melanoma, teratocarcinoma or cancer of the cervix, glioma or lung, pooling the cells, and fusing the cells with SHFP-1. Hybridomas are screened for production of antibody that binds to cancer cell lines. Confirmation of specificity among mAbs can be accomplished using routine screening techniques such as ELISA to determine the elementary reaction pattern of the mAb of interest.

[0145] As used herein, the term "antibody" encompasses antigen-binding antibody fragments, e.g., single chain antibodies (scFv or others), which can be produced/selected using phage display technology. The ability to express antibody fragments on the surface of viruses that infect bacteria (bacteriophage or phage) makes it possible to isolate a single binding antibody fragment, e.g., from a library of greater than

10^{10} nonbinding clones. To express antibody fragments on the surface of phage (phage display), an antibody fragment gene is inserted into the gene encoding a phage surface protein (e.g., pIII) and the antibody fragment-pIII fusion protein is displayed on the phage surface (McCafferty et al. (1990) Nature, 348: 552-554; Hoogenboom et al. (1991) Nucleic Acids Res. 19: 4133-4137).

[0146] Since the antibody fragments on the surface of the phage are functional, phage-bearing antigen-binding antibody fragments can be separated from non-binding phage by antigen affinity chromatography (McCafferty et al. (1990) Nature, 348: 552-554). Depending on the affinity of the antibody fragment, enrichment factors of 20-fold-1,000,000-fold are obtained for a single round of affinity selection. By infecting bacteria with the eluted phage, however, more phage can be grown and subjected to another round of selection. In this way, an enrichment of 1000-fold in one round can become 1,000,000-fold in two rounds of selection (McCafferty et al. (1990) Nature, 348: 552-554). Thus, even when enrichments are low (Marks et al. (1991) J. Mol. Biol. 222: 581-597), multiple rounds of affinity selection can lead to the isolation of rare phage. Since selection of the phage antibody library on antigen results in enrichment, the majority of clones bind antigen after as few as three to four rounds of selection. Thus only a relatively small number of clones (several hundred) need to be analyzed for binding to antigen.

[0147] Human antibodies can be produced without prior immunization by displaying very large and diverse V-gene repertoires on phage (Marks et al. (1991) J. Mol. Biol. 222: 581-597). In one embodiment, natural VH and VL repertoires present in human peripheral blood lymphocytes are isolated from unimmunized donors by PCR. The V-gene repertoires can be spliced together at random using PCR to create a scFv gene repertoire which can be cloned into a phage vector to create a library of 30 million phage antibodies (Id.). From a single "naive" phage antibody library, binding antibody fragments have been isolated against more than 17 different antigens, including haptens, polysaccharides, and proteins (Marks et al. (1991) J. Mol. Biol. 222: 581-597; Marks et al. (1993). Bio/Technology. 10: 779-783; Griffiths et al. (1993) EMBO J. 12: 725-734; Clackson et al. (1991) Nature. 352: 624-628). Antibodies have been produced against self proteins, including human thyroglobulin, immunoglobulin, tumor necrosis factor, and CEA (Griffiths et al. (1993) EMBO J. 12: 725-734). The antibody fragments are highly specific for the antigen used for selection and have affinities in the 1 nM to 100 nM range (Marks et al. (1991) J. Mol. Biol. 222: 581-597; Griffiths et al. (1993) EMBO J. 12: 725-734). Larger phage antibody libraries result in the isolation of more antibodies of higher binding affinity to a greater proportion of antigens.

[0148] As those of skill in the art readily appreciate, antibodies can be prepared by any of a number of commercial services (e.g., Berkeley Antibody Laboratories, Bethyl Laboratories, Anawa, Eurogenetec, etc.).

Detection Systems in General

[0149] As discussed above, immunoassays according to the present disclosure employ a second specific binding partner that typically includes an antibody specific to the protein of interest. In certain embodiments, the second specific binding partner includes a detectable label conjugated to the antibody, and function as a detection conjugate.

[0150] Detectable labels suitable for use in the detection conjugate include any compound or composition having a moiety that is detectable by spectroscopic, photochemical, biochemical, immunochemical, electrical, optical, or chemical means. Such labels include, for example, a radioactive label, an enzymatic label, a chemiluminescent label, a fluorescence label, a thermometric label, and an immuno-polymerase chain reaction label.

[0151] Thus for example, in an immunoassay employing an optical signal, the optical signal is measured as a protein concentration dependent change in chemiluminescence, fluorescence, phosphorescence, electrochemiluminescence, ultraviolet absorption, visible absorption, infrared absorption, refraction, surface plasmon resonance. In an immunoassay employing an electrical signal, the electrical signal is measured as an protein concentration dependent change in current, resistance, potential, mass to charge ratio, or ion count. In an immunoassay employing a change-of-state signal, the change of state signal is measured as an protein concentration dependent change in size, solubility, mass, or resonance.

[0152] More specifically, the label can be for example an enzyme, oligonucleotide, nanoparticle chemiluminophore, fluorophore, fluorescence quencher, chemiluminescence quencher, or biotin. Useful labels according to the present disclosure include magnetic beads (e.g., Dynabeads™), fluorescent dyes (e.g., fluorescein, Texas Red, rhodamine, green fluorescent protein) and the like (see, e.g., Molecular Probes, Eugene, Oreg., USA), chemiluminescent compounds such as acridinium (e.g., acridinium-9-carboxamide), phenanthridinium, dioxetanes, luminol and the like, radiolabels (e.g., ^{3}H, ^{125}I, ^{35}S, ^{14}C, or ^{32}P), catalysts such as enzymes (e.g., horse radish peroxidase, alkaline phosphatase, beta-galactosidase and others commonly used in an ELISA), and colorimetric labels such as colloidal gold (e.g., gold particles in the 40-80 nm diameter size range scatter green light with high efficiency) or colored glass or plastic (e.g., polystyrene, polypropylene, latex, etc.) beads. Patents teaching the use of such labels include U.S. Pat. Nos. 3,817,837; 3,850,752; 3,939,350; 3,996,345; 4,277,437; 4,275,149; and 4,366,241.

[0153] The label can be attached to the detection antibody to form the detection conjugate prior to, or during, or after contact with the biological sample. So-called "direct labels" are detectable labels that are directly attached to or incorporated into the detection antibody prior to use in the assay. Direct labels can be attached to or incorporated into the detection antibody by any of a number of means well known to those of skill in the art.

[0154] In contrast, so-called "indirect labels" typically bind to the detection antibody at some point during the assay. Often, the indirect label binds to a moiety that is attached to or incorporated into the detection agent prior to use. Thus, for example, a detection antibody can be biotinylated before use in an assay. During the assay, an avidin-conjugated fluorophore can bind the biotin-bearing detection agent, to provide a label that is easily detected.

[0155] In another example of indirect labeling, polypeptides capable of specifically binding immunoglobulin constant regions, such as polypeptide A or polypeptide G, can also be used as labels for detection antibodies. These polypeptides are normal constituents of the cell walls of streptococcal bacteria. They exhibit a strong non-immunogenic reactivity with immunoglobulin constant regions from a variety of species (see, generally Kronval, et al. (1973) J. Immu-

nol., 111: 1401-1406, and Akerstrom (1985) J. Immunol., 135: 2589-2542). Such polypeptides can thus be labeled and added to the assay mixture, where they will bind to the capture and detection antibodies, as well as to the autoantibodies, labeling all and providing a composite signal attributable to protein and autoantibody present in the sample.

[0156] Some labels useful in the present disclosure may require the use of an additional reagent(s) to produce a detectable signal. In an ELISA, for example, an enzyme label (e.g., beta-galactosidase) will require the addition of a substrate (e.g., X-gal) to produce a detectable signal. In immunoassay detection methods using an acridinium compound as a direct label, a basic solution and a source of hydrogen peroxide are added.

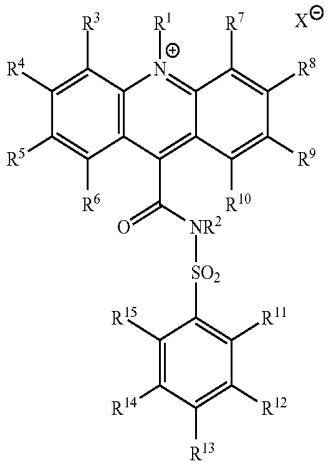
Detection Systems—Exemplary Formats

[0157] Chemiluminescence Immunoassay: In an exemplary embodiment, a chemiluminescent compound is used in the above-described methods as a direct label as part of a detection conjugate. The chemiluminescent compound can be an acridinium compound. When an acridinium compound is used as the detectable label, then the above-described method may further include generating or providing a source of hydrogen peroxide to the mixture resulting from contacting the test sample with the first specific binding partner and the second specific binding partner (detection conjugate) and adding at least one basic solution to the mixture to generate a light signal. The light signal generated or emitted by the mixture is then measured to detect the protein of interest in the test sample.

[0158] The source of hydrogen peroxide may be a buffer solution or a solution containing hydrogen peroxide or an enzyme that generates hydrogen peroxide when added to the test sample. A hydrogen peroxide generating enzyme can be selected for example from the group consisting of: (R)-6-hydroxynicotine oxidase, (S)-2-hydroxy acid oxidase, (S)-6-hydroxynicotine oxidase, 3-aci-nitropropanoate oxidase, 3-hydroxyanthranilate oxidase, 4-hydroxymandelate oxidase, 6-hydroxynicotinate dehydrogenase, abscisic-aldehyde oxidase, acyl-CoA oxidase, alcohol oxidase, aldehyde oxidase, amine oxidase, amine oxidase (copper-containing), amine oxidase (flavin-containing), aryl-alcohol oxidase, aryl-aldehyde oxidase, catechol oxidase, cholesterol oxidase, choline oxidase, columbamine oxidase, cyclohexylamine oxidase, cytochrome c oxidase, D-amino-acid oxidase, D-arabinono-1,4-lactone oxidase, D-arabinono-1,4-lactone oxidase, D-aspartate oxidase, D-glutamate oxidase, D-glutamate(D-aspartate) oxidase, dihydrobenzophenanthridine oxidase, dihydroorotate oxidase, dihydrouracil oxidase, dimethylglycine oxidase, D-mannitol oxidase, ecdysone oxidase, ethanolamine oxidase, galactose oxidase, glucose oxidase, glutathione oxidase, glycerol-3-phosphate oxidase, glycine oxidase, glyoxylate oxidase, hexose oxidase, hydroxyphytanate oxidase, indole-3-acetaldehyde oxidase, lactic acid oxidase, L-amino-acid oxidase, L-aspartate oxidase, L-galactonolactone oxidase, L-glutamate oxidase, L-gulonolactone oxidase, L-lysine 6-oxidase, L-lysine oxidase, long-chain-alcohol oxidase, L-pipecolate oxidase, L-sorbose oxidase, malate oxidase, methanethiol oxidase, monoamino acid oxidase, N6-methyl-lysine oxidase, N-acylhexosamine oxidase, NAD(P)H oxidase, nitroalkane oxidase, N-methyl-L-amino-acid oxidase, nucleoside oxidase, oxalate oxidase, polyamine oxidase, polyphenol oxidase, polyvinylalcohol oxidase, prenylcysteine oxidase, protein-lysine 6-oxidase, putrescine oxidase, pyranose oxidase, pyridoxal 5'-phosphate synthase, pyridoxine 4-oxidase, pyrroloquinoline-quinone synthase, pyruvate oxidase, pyruvate oxidase (CoA-acetylating), reticuline oxidase, retinal oxidase, rifamycin-B oxidase, sarcosine oxidase, secondary-alcohol oxidase, sulfite oxidase, superoxide dismutase, superoxide reductase, tetrahydroberberine oxidase, thiamine oxidase, tryptophan α,β-oxidase, urate oxidase (uricase, uric acid oxidase), vanillyl-alcohol oxidase, xanthine oxidase, xylitol oxidase and combinations thereof.

[0159] The basic solution serves as a trigger solution, and the order in which the at least one basic solution and detectable label are added is not critical. The basic solution used in the method is a solution that contains at least one base and that has a pH greater than or equal to 10, preferably, greater than or equal to 12. Examples of basic solutions include, but are not limited to, sodium hydroxide, potassium hydroxide, calcium hydroxide, ammonium hydroxide, magnesium hydroxide, sodium carbonate, sodium bicarbonate, calcium hydroxide, calcium carbonate and calcium bicarbonate. The amount of basic solution added to the test sample depends on the concentration of the basic solution used in the assay. Based on the concentration of the basic solution used, one skilled in the art could easily determine the amount of basic solution to be used in the method described herein.

[0160] In a chemiluminescence immunoassay according to the present disclosure and using an acridinium compound as the detectable label, preferably the acridinium compound is an acridinium-9-carboxamide. Specifically, the acridinium-9-carboxamide has a structure according to formula I:



I

[0161] wherein R^1 and R^2 are each independently selected from the group consisting of: alkyl, alkenyl, alkynyl, aryl or aralkyl, sulfoalkyl, carboxyalkyl and oxoalkyl, and

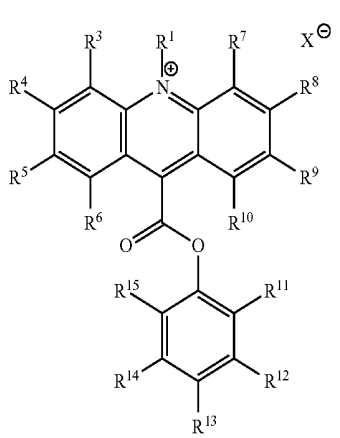
[0162] wherein R^3 through R^{15} are each independently selected from the group consisting of: hydrogen, alkyl, alkenyl, alkynyl, aryl or aralkyl, amino, amido, acyl, alkoxyl, hydroxyl, carboxyl, halogen, halide, nitro, cyano, sulfo, sulfoalkyl, carboxyalkyl and oxoalkyl; and further wherein any of the alkyl, alkenyl, alkynyl, aryl or aralkyl may contain one or more heteroatoms; and

[0163] optionally, if present, $X^{\ominus}$ is an anion.

[0164] Methods for preparing acridinium 9-carboxamides are described in Mattingly, P. G. *J. Biolumin. Chemilumin.*, 6,

107-14; (1991); Adamczyk, M.; Chen, Y.-Y., Mattingly, P. G.; Pan, Y. *J. Org. Chem.,* 63, 5636-5639 (1998); Adamczyk, M.; Chen, Y.-Y.; Mattingly, P. G.; Moore, J. A.; Shreder, K. *Tetrahedron,* 55, 10899-10914 (1999); Adamczyk, M.; Mattingly, P. G.; Moore, J. A.; Pan, Y. *Org. Lett.,* 1, 779-781 (1999); Adamczyk, M.; Chen, Y.-Y.; Fishpaugh, J. R.; Mattingly, P. G.; Pan, Y.; Shreder, K.; Yu, Z. *Bioconjugate Chem.,* 11, 714-724 (2000); Mattingly, P. G.; Adamczyk, M. In *Luminescence Biotechnology: Instruments and Applications*; Dyke, K. V. Ed.; CRC Press: Boca Raton, pp. 77-105 (2002); Adamczyk, M.; Mattingly, P. G.; Moore, J. A.; Pan, Y. *Org. Lett.,* 5, 3779-3782 (2003); and U.S. Pat. Nos. 5,468,646, 5,543,524 and 5,783,699 (each incorporated herein by reference in their entireties for their teachings regarding same).

[0165] Alternatively, the acridinium compound can be an acridinium-9-carboxylate aryl ester; the acridinium-9-carboxylate aryl ester can have a structure according to formula II:



II

[0166] wherein R^1 is an alkyl, alkenyl, alkynyl, aryl or aralkyl, sulfoalkyl, carboxyalkyl and oxoalkyl; and

[0167] wherein R^3 through R^{15} are each independently selected from the group consisting of: hydrogen, alkyl, alkenyl, alkynyl, aryl or aralkyl, amino, amido, acyl, alkoxyl, hydroxyl, carboxyl, halogen, halide, nitro, cyano, sulfo, sulfoalkyl, carboxyalkyl and oxoalkyl; and

[0168] optionally, if present, $X^{\ominus}$ is an anion.

[0169] Examples of acridinium-9-carboxylate aryl esters having the above formula II that can be used in the present disclosure include, but are not limited to, 10-methyl-9-(phenoxycarbonyl)acridinium fluorosulfonate (available from Cayman Chemical, Ann Arbor, Mich.). Methods for preparing acridinium 9-carboxylate aryl esters are described in McCapra, F., et al., *Photochem. Photobiol.,* 4, 1111-21 (1965); Razavi, Z et al., *Luminescence,* 15:245-249 (2000); Razavi, Z et al., *Luminescence,* 15:239-244 (2000); and U.S. Pat. No. 5,241,070 (each incorporated herein by reference in their entireties for their teachings regarding same).

[0170] In addition to the at least one acridinium compound, the indicator solution can also contain at least one surfactant. Any surfactant that when dissolved in water, lowers the surface tension of the water and increases the solubility of organic compounds, can be used in the present invention. Examples of surfactants that can be used is one or more non-ionic or ionic surfactants (e.g., anionic, cationic or zwitterionic surfactants). Examples of non-ionic surfactants that can be used include, but are not limited to, t-octylpheoxypolyethoxyethanol (TRITON X-100, Sigma Aldrich, St. Louis, Mo.), polyoxyethylenesorbitan monolaurate (Tween 20), nonylphenol polyoxyethylene ether (Nonidet P10), decyldimethylphosphine oxide (APO-10), Cyclohexyl-n-ethyl-β-D-Maltoside, Cyclohexyl-n-hexyl-β-D-Maltoside, Cyclohexyl-n-methyl-β-D-Maltoside, n-Decanoylsucrose, n-Decyl-β-D-glucopyranoside, n-Decyl-β-D-maltopyranoside, n-Decyl-β-D-thiomaltoside, Digitonin, n-Dodecanoyl sucrose, n-Dodecyl-β-D-glucopyranoside, n-Dodecyl-β-D-maltoside, polyoxyethylene (10) dodecyl ether (Genapol C-100), isotridecanol polyglycol ether (Genapol X-80), isotridecanol polyglycol ether (Genapol X-100), Heptane-1,2,3-triol, n-Heptyl-β-D-glucopyranoside, n-Heptyl-β-D-thioglucopyranoside and combinations thereof. An example of a ionic surfactant that can be used include, sodium cholate, chenodeoxycholic acid, cholic acid, dehydrocholic acid, docusate sodium, docusate sodium salt, glycocholic acid hydrate, glycodeoxycholic acid monohydrate, glycolithocholic acid ethyl ester, N-lauroylsarcosine sodium salt, N-lauroylsarcosine, lithium dodecyl sulfate, calcium propionate, 1-octanesulfonic acid sodium salt, sodium 1-butanesulfonate, sodium chenodeoxycholate, sodium cholate hydrate, sodium 1-decanesulfonate, sodium 1-decanesulfonate, sodium deoxycholate, sodium deoxycholate monohydrate, sodium dodecylbenzenesulfonate, sodium dodecyl sulfate, sodium glycochenodeoxycholate, sodium glycocholate hydrate, sodium 1-heptanesulfonate, sodium hexanesulfonate, sodium 1-nonanesulfonate, sodium octyle sulfate, sodium pentanesulfonate, sodium 1-propanesulfonate hydrate, sodium taurodeoxycholate hydrate, sodium taurohyodeoxycholate hydrate, sodium tauroursodeoxycholate, taurocholic acid sodium salt hydrate, taurolithocholic acid 3-sulfate disodium salt, Triton® X-200, Triton® QS-15, Triton® QS-44, Triton® XQS-20, Trizma® dodecyl sulfate, ursodeoxycholic acid, alkyltrimethylammonium bromide, amprolium hydrocholoride, benzalkonium chloride, benzethonium hydroxide, benzyldimethylhexadecylammonium chloride, benzyldodecyldimethylammonium bromide, choline p-toluenesulfonate salt, dimethyldioctadecylammonium bromide, dodecylethyldimethylammonium bromide, dodecyltrimethylammonium bromide, ethylhexadecyldimethylammonium bromide, Ggirard's reagent, hexadecylpyridinium bromide, hexadecylpyridinium chloride monohydrate, hexadecylpyridinium chloride monohydrate, hexadecyltrimethylammonium bromide, hexadecyltrimethylammonium p-toluenesulfonate, hexadecyltrimethylammonium bromide, hexadecyltrimethylammonium p-toluenesulfonate, Hyamine® 1622, methylbenzethonium chloride, myristyltrimethylammonium bromide, oxyphenonium bromide, N,N',N'-polyoxyethylene (10)-N-tallow-1,3-diaminopropane, tetraheptylammonium bromide, tetrakis(decyl)ammonium bromide, thonzonium bromide and Luviquat™ FC370, Luviquat™ HM 552, Luviquat™ HOLD, Luviquat™ MS 370, Luviquat™ PQ 11PN and combinations thereof (all available from Sigma Aldrich, St. Louis, Mo.).

[0171] Optionally, the test sample may be treated prior to the addition of any one or more of the at least one basic solution, hydrogen peroxide source and detectable label. Such treatment may include dilution, ultrafiltration, extraction, precipitation, dialysis, chromatography and digestion. Such treatment may be in addition to and separate from any pretreatment that the test sample may receive or be subjected to as discussed previously herein. Moreover, if such treatment

methods are employed with respect to the test sample, such treatment methods are such that the protein of interest remains in the test sample at a concentration proportional to that in an untreated test sample (e.g., namely, a test sample that is not subjected to any such treatment method(s)).

[0172] As mentioned briefly previously herein, the time and order in which the test sample, the at least one basic solution, source of hydrogen peroxide and the detectable label are added to form a mixture is not critical. Additionally, the mixture formed by the at least one basic solution, hydrogen peroxide source and the detectable label, can optionally be allowed to incubate for a period of time. For example, the mixture can be allowed to incubate for a period of time of from about 1 second to about 60 minutes. Specifically, the mixture can be allowed to incubate for a period of from about 1 second to about 18 minutes.

[0173] When a chemiluminescent detectable label is used, after the addition of the at least one basic solution, hydrogen peroxide source, and the detectable label to the test sample, a detectable signal, namely, a chemiluminescent signal, is generated. The signal generated by the mixture is detected for a fixed duration of time. Preferably, the mixture is formed and the signal is detected concurrently. The duration of the detection may range from about 0.01 to about 360 seconds, more preferably from about 0.1 to about 30 seconds, and most preferably from about 0.5 to about 5 seconds. Chemiluminescent signals generated can be detected using routine techniques known to those skilled in the art.

[0174] Thus, in a chemiluminescent immunoassay according to the present disclosure, a chemiluminescent detectable label is used and added to the test sample, the chemiluminescent signal generated after the addition of the basic solution and the detectable label indicates the presence of the protein of interest in the test sample, which signal can be detected. The amount or concentration of the protein of interest in the test sample can be quantified based on the intensity of the signal generated. Specifically, the amount of the protein of interest contained in a test sample is proportional to the intensity of the signal generated. Specifically, the amount of the protein of interest present can be quantified based on comparing the amount of light generated to a standard curve for the protein of interest or by comparison to a reference standard. The standard curve can be generated using serial dilutions or solutions to the protein of interest of known concentration, by mass spectroscopy, gravimetrically and by other techniques known in the art.

[0175] Fluorescence Polarization Immunoassay (FPIA): In an exemplary embodiment, a fluorescent label is employed in a fluorescence polarization immunoassay (FPIA) according to the invention. Generally, fluorescent polarization techniques are based on the principle that a fluorescent label, when excited by plane-polarized light of a characteristic wavelength, will emit light at another characteristic wavelength (i.e., fluorescence) that retains a degree of the polarization relative to the incident light that is inversely related to the rate of rotation of the label in a given medium. As a consequence of this property, a label with constrained rotation, such as one bound to another solution component with a relatively lower rate of rotation, will retain a relatively greater degree of polarization of emitted light than when free in solution.

[0176] This technique can be employed in an immunoassay according to the present disclosure, for example, by selecting reagents such that binding of the fluorescently labeled entities forms a complex sufficiently different in size such that a change in the intensity light emitted in a given plane can be detected. For example, when a labeled cardiac troponin antibody, i.e. a second specific binding partner is bound by one or more cardiac troponin antigens bound to the first specific binding partner, the resulting complex is sufficiently larger, and its rotation is sufficiently constrained, relative to any free labeled cardiac troponin antibody that binding is easily detected.

[0177] Fluorophores useful in FPIA include fluorescein, aminofluorescein, carboxyfluorescein, and the like, preferably 5 and 6-aminomethylfluorescein, 5 and 6-aminofluorescein, 6-carboxyfluorescein, 5-carboxyfluorescein, thioureafluorescein, and methoxytriazinolyl-aminofluorescein, and similar fluorescent derivatives. Examples of commercially available automated instruments with which fluorescence polarization assays can be conducted include: the IMx system, the TDx system, and TDxFLx system (all available from Abbott Laboratories, Abbott Park, Ill.).

[0178] Scanning Probe Microscopy (SPM): The use of scanning probe microscopy (SPM) for immunoassays also is a technology to which the immunoassay methods of the present disclosure are easily adaptable. In SPM, in particular in atomic force microscopy, the capture antibody is affixed to the solid phase that in addition to being capable of binding autoantibodies, has a surface suitable for scanning. The capture antibody can, for example, be adsorbed to a plastic or metal surface. Alternatively, the capture antibody can be covalently attached to, e.g., derivatized plastic, metal, silicon, or glass according to methods known to those of ordinary skill in the art. Following attachment of the capture antibody, the test sample is contacted with the solid phase, and a scanning probe microscope is used to detect and quantify solid phase-affixed complexes. The use of SPM eliminates the need for labels that are typically employed in immunoassay systems. Such a system is described in U.S. Pat. No. 662,147, which is incorporated herein by reference.

[0179] MicroElectroMechanical Systems (MEMS): Immunoassays according to the present disclosure can also be carried out using a MicroElectroMechanical System (MEMS). MEMS are microscopic structures integrated onto silicon that combine mechanical, optical, and fluidic elements with electronics, allowing convenient detection of an protein of interest. An exemplary MEMS device suitable for use in the present disclosure is the Protiveris' multicantilever array. This array is based on chemo-mechanical actuation of specially designed silicon microcantilevers and subsequent optical detection of the microcantilever deflections. When coated on one side with a binding partner, a microcantilever will bend when it is exposed to a solution containing the complementary molecule. This bending is caused by the change in the surface energy due to the binding event. Optical detection of the degree of bending (deflection) allows measurement of the amount of complementary molecule bound to the microcantilever.

[0180] Electrochemical Detection Systems: In other embodiments, immunoassays according to the present disclosure are carried out using electrochemical detection, the techniques for which are well known to those skilled in the art. Such electrochemical detection often employs one or more electrodes connected to a device that measures and records an electrical current. Such techniques can be realized in a number of commercially available devices, such as the I-STAT® (Abbott Laboratories, Abbott Park, Ill.) system, which comprises a hand-held electrochemical detection instrument and self-contained assay-specific reagent cartridges. For example, in the present invention, the basic trigger solution could be contained in the self-contained hemoglobin reagent

cartridge and upon addition of the test sample, a current would be generated at least one electrode that is proportional to the amount of hemoglobin in the test sample. A basic procedure for electrochemical detection has been described for example by Heineman and coworkers. This entailed immobilization of a primary antibody (Ab, rat-anti mouse IgG), followed by exposure to a sequence of solutions containing the antigen (Ag, mouse IgG), the secondary antibody conjugated to an enzyme label (AP-Ab, rat anti mouse IgG and alkaline phosphatase), and p-aminophenyl phosphate (PAPP). The AP converts PAPP to p-aminophenol (PAP_R, the "R" is intended to distinguish the reduced form from the oxidized form, PAP_O, the quinoneimine), which is electrochemically reversible at potentials that do not interfere with reduction of oxygen and water at pH 9.0, where AP exhibits optimum activity. PAP_R does not cause electrode fouling, unlike phenol whose precursor, phenylphosphate, is often used as the enzyme substrate. Although PAP_R undergoes air and light oxidation, these are easily prevented on small scales and short time frames. Picomole detection limits for PAP_R and femtogram detection limits for IgG achieved in microelectrochemical immunoassays using PAPP volumes ranging from 20 μl to 360 μL have been reported previously. In capillary immunoassays with electrochemical detection, the lowest detection limit reported thus far is 3000 molecules of mouse IgG using a volume of 70 μL and a 30 min or 25 min assay time.

[0181] In an exemplary embodiment employing electrochemical detection according to the present disclosure, an antibody serving as the first specific binding partner, which is reactive with the protein of interest, can be immobilized on the surface of an electrode, which is the solid phase. The electrode is then contacted with a test sample from, e.g., a human. Any protein in the sample binds to the first specific binding partner, e.g. antibody to form a solid phase-affixed complex. Autoantibodies present in the sample are blocked by the peptide reagent from interacting with the target protein and thus from interfering with binding of the target protein to the first specific binding partner. The solid phase-affixed complexes are contacted with the detection conjugate including a detectable label. Formation of an immunodetection complex that includes the first specific binding partner, protein, and detection conjugate results in generation of a signal by the detectable label, which is then detected.

[0182] Various electrochemical detection systems are described in U.S. Pat. No. 7,045,364 (issued May 16, 2006; incorporated herein by reference), U.S. Pat. No. 7,045,310 (issued May 16, 2006; incorporated herein by reference), U.S. Pat. No. 6,887,714 (issued May 3, 2005; incorporated herein by reference), U.S. Pat. No. 6,682,648 (issued Jan. 27, 2004; incorporated herein by reference); U.S. Pat. No. 6,670,115 (issued Dec. 30, 2003; incorporated herein by reference).

D. Kits

[0183] The present disclosure also provides kits for assaying test samples for presence of an protein of interest wherein the test sample may contain autoantibodies. Kits according to the present disclosure include one or more reagents useful for practicing one or more immunoassays according to the present disclosure. A kit generally includes a package with one or more containers holding the reagents, as one or more separate compositions or, optionally, as admixture where the compatibility of the reagents will allow. The test kit can also include other material(s), which may be desirable from a user standpoint, such as a buffer(s), a diluent(s), a standard(s), and/or any other material useful in sample processing, washing, or conducting any other step of the assay.

[0184] In certain embodiments, a test kit for detecting and/or quantifying at least one protein of interest in a test sample includes a capture reagent comprising an antibody that binds to the protein of interest; and instructions for detecting and/or quantifying at least one protein of interest in a test sample. The kit may further include a conjugate which includes an antibody conjugated to a detectable label.

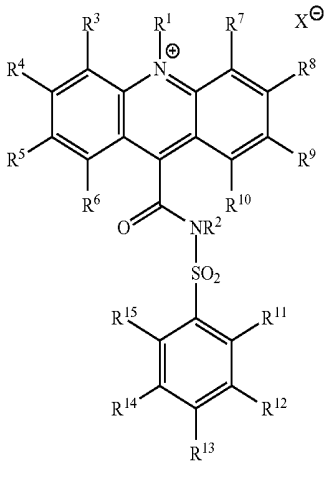
[0185] In certain embodiments, a test kit may include a humanized monoclonal antibody, wherein the humanized monoclonal antibody is specific for the protein of interest. This component can be used as a positive control in immunoassays according to the invention. If desired, this component can be included in the test kit in multiple concentrations to facilitate the generation of a standard curve to which the signal detected in the test sample can be compared. Alternatively, a standard curve can be generated by preparing dilutions of a single humanized monoclonal antibody solution provided in the kit.

[0186] Kits according to the present disclosure can include one or more peptide reagents having a sequence derived from the protein of interest, an antibody (first specific binding partner) that binds to at least one epitope on the protein of interest, a solid phase capable of binding the first specific binding partner, a second antibody that binds to at least one epitope on the protein of interest, and instructions for detecting or quantifying the protein of interest. In certain embodiments test kits according to the present disclosure may include the solid phase as a material such as a magnetic particle, a bead, a test tube, a microtiter plate, a cuvette, a membrane, a scaffolding molecule, a quartz crystal, a film, a filter paper, a disc or a chip.

[0187] Test kits according to the present disclosure can include for example non-human monoclonal antibodies against the protein of interest, as the first and second specific binding partners. The kit may also include a detectable label that can be or is conjugated to an antibody to provide a detection conjugate as the second specific binding partner.

[0188] In certain embodiments, the test kit includes the detectable label as at least one direct label, which may be an enzyme, oligonucleotide, nanoparticle chemiluminophore, fluorophore, fluorescence quencher, chemiluminescence quencher, or biotin. In some embodiments, the direct label is an acridinium compound such as an acridinium-9-carboxamide according to formula I:

I



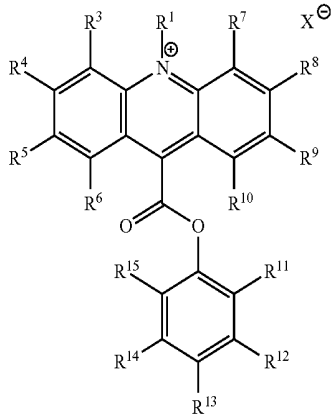
[0189] wherein R1 and R2 are each independently selected from the group consisting of: alkyl, alkenyl, alkynyl, aryl or aralkyl, sulfoalkyl, carboxyalkyl and oxoalkyl, and

[0190] wherein R3 through R15 are each independently selected from the group consisting of: hydrogen, alkyl, alkenyl, alkynyl, aryl or aralkyl, amino, amido, acyl, alkoxyl, hydroxyl, carboxyl, halogen, halide, nitro, cyano, sulfo, sulfoalkyl, carboxyalkyl and oxoalkyl; and

[0191] optionally, if present, X® is an anion.

[0192] Alternatively, the acridinium compound can be an acridinium-9-carboxylate aryl ester having a structure according to formula II:

II



[0193] wherein R1 is an alkyl, alkenyl, alkynyl, aryl or aralkyl, sulfoalkyl, carboxyalkyl and oxoalkyl; and

[0194] wherein R3 through R15 are each independently selected from the group consisting of: hydrogen, alkyl, alkenyl, alkynyl, aryl or aralkyl, amino, amido, acyl, alkoxyl, hydroxyl, carboxyl, halogen, halide, nitro, cyano, sulfo, sulfoalkyl, carboxyalkyl and oxoalkyl; and

[0195] optionally, if present, $X^{\ominus}$ is an anion.

[0196] Test kits according to the present disclosure and which include an acridinium compound can also include a basic solution. For example, the basic solution can be a solution having a pH of at least about 10. In certain embodiments, test kits according to the present disclosure may further include a hydrogen peroxide source, such as a buffer solution, a solution containing hydrogen peroxide, or a hydrogen peroxide generating enzyme. For example, test kits may include an amount of a hydrogen peroxide generating enzymes selected from the following: (R)-6-hydroxynicotine oxidase, (S)-2-hydroxy acid oxidase, (S)-6-hydroxynicotine oxidase, 3-aci-nitropropanoate oxidase, 3-hydroxyanthranilate oxidase, 4-hydroxymandelate oxidase, 6-hydroxynicotinate dehydrogenase, abscisic-aldehyde oxidase, acyl-CoA oxidase, alcohol oxidase, aldehyde oxidase, amine oxidase, amine oxidase (copper-containing), amine oxidase (flavin-containing), aryl-alcohol oxidase, aryl-aldehyde oxidase, catechol oxidase, cholesterol oxidase, choline oxidase, columbamine oxidase, cyclohexylamine oxidase, cytochrome c oxidase, D-amino-acid oxidase, D-arabinono-1,4-lactone oxidase, D-arabinono-1,4-lactone oxidase, D-aspartate oxidase, D-glutamate oxidase, D-glutamate(D-aspartate) oxidase, dihydrobenzophenanthridine oxidase, dihydroorotate oxidase, dihydrouracil oxidase, dimethylglycine oxidase, D-mannitol oxidase, ecdysone oxidase, ethanolamine oxidase, galactose oxidase, glucose oxidase, glutathione oxidase, glycerol-3-phosphate oxidase, glycine oxidase, glyoxylate oxidase, hexose oxidase, hydroxyphytanate oxidase, indole-3-acetaldehyde oxidase, lactic acid oxidase, L-amino-acid oxidase, L-aspartate oxidase, L-galactonolactone oxidase, L-glutamate oxidase, L-gulonolactone oxidase, L-lysine 6-oxidase, L-lysine oxidase, long-chain-alcohol oxidase, L-pipecolate oxidase, L-sorbose oxidase, malate oxidase, methanethiol oxidase, monoamino acid oxidase, N6-methyl-lysine oxidase, N-acylhexosamine oxidase, NAD(P)H oxidase, nitroalkane oxidase, N-methyl-L-amino-acid oxidase, nucleoside oxidase, oxalate oxidase, polyamine oxidase, polyphenol oxidase, polyvinyl-alcohol oxidase, prenylcysteine oxidase, protein-lysine 6-oxidase, putrescine oxidase, pyranose oxidase, pyridoxal 5'-phosphate synthase, pyridoxine 4-oxidase, pyrroloquinoline-quinone synthase, pyruvate oxidase, pyruvate oxidase (CoA-acetylating), reticuline oxidase, retinal oxidase, rifamycin-B oxidase, sarcosine oxidase, secondary-alcohol oxidase, sulfite oxidase, superoxide dismutase, superoxide reductase, tetrahydroberberine oxidase, thiamine oxidase, tryptophan α,β-oxidase, urate oxidase (uricase, uric acid oxidase), vanillyl-alcohol oxidase, xanthine oxidase, xylitol oxidase and combinations thereof.

[0197] In certain embodiments, test kits according to the present disclosure are configured for detection or quantification of one of the following specific analytes of interest cardiac troponin, thyroid stimulating hormone (TSH), beta human chorionic gonadotropin (beta-HCG); myeloperoxidase (MPO), prostate specific antigen (PSA), human B-type natriuretic peptide (BNP), myosin light chain 2, myosin-6 and myosin-7. In such embodiments, the test kits include at least one peptide reagent having a sequence derived from the protein of interest, a first antibody and a second antibody that each bind to an epitope on the selected protein of interest, i.e. a first antibody and a second antibody and second antibody that each bind to an epitope on one of the following: cardiac troponin, thyroid stimulating hormone (TSH), beta human chorionic gonadotropin (beta-HCG); myeloperoxidase (MPO), prostate specific antigen (PSA), human B-type natriuretic peptide (BNP), myosin light chain 2, myosin-6 and myosin-7.

[0198] Test kits according to the present disclosure preferably include instructions for carrying out one or more of the immunoassays of the invention. Instructions included in kits of the present disclosure can be affixed to packaging material or can be included as a package insert. While the instructions are typically written or printed materials they are not limited to such. Any medium capable of storing such instructions and communicating them to an end user is contemplated by this disclosure. Such media include, but are not limited to, electronic storage media (e.g., magnetic discs, tapes, cartridges, chips), optical media (e.g., CD ROM), and the like. As used herein, the term "instructions" can include the address of an internet site that provides the instructions.

E. Adaptations of the Methods of the Present Disclosure

[0199] The present disclosure is for example applicable to the jointly owned commercial Abbott Point of Care (i-STAT™) electrochemical immunoassay system which performs sandwich immunoassays for several cardiac markers, including TnI, CKMB and BNP. Immunosensors and ways of

operating them in single-use test devices are described in jointly owned Publication Nos. US 20030170881, US 20040018577, US 20050054078, and US 20060160164, each of which is incorporated herein by reference. Additional background on the manufacture of electrochemical and other types of immunosensors is found in jointly owned U.S. Pat. No. 5,063,081 which is also incorporated by reference.

[0200] By way of example, and not of limitation, examples of the present disclosures shall now be given.

Example 1

Inhibition of Anti-cTnI Autoantibody Binding to Cardiac Troponin-I (ELN Ref E000777-253)

[0201] Inhibitor working solutions: The peptides listed in Table 12 (obtained from Sigma-Genosys, PEPscreen custom library) were diluted in AxSYM® Troponin-I ADV Preincubation Diluent to give solutions ranging from 240 nmol/mL to 0 nmol/mL. An equimolar mixture of the peptides listed in Table 12 was prepared and diluted to give solutions ranging from 240 nmol/mL to 0 nmol/mL/.

TABLE 12

Peptide inhibitors of anti-cTnI autoantibody binding to cardiac troponin-I

Peptide#	Amino-terminus	Sequence	Carboxy-terminus
1	[Btn]	SSDAAREPRPAPAPI	[NH2]
2	[Btn]	VDEERYDIEAKVTKN	[NH2]
3	[Btn]	DIEAKVTKNITEIAD	[NH2]
4	[Btn]	LDLRAHLKQVKKEDT	[NH2]
5	[Btn]	ALSGMEGRKKKFES	[NH2]

[0202] Microplate preparation: Recombinant human cardiac troponin-I (cTnI, BiosPacific, Emeryville, Calif.) was coated on white high-binding flat-bottom 96-well polystyrene microplates (Costar) in phosphate buffer (100 μL, 0.2 M, pH 8, 4 μg/mL) at 38° C., for 1 h, then overcoated sequentially with bovine serum albumin and 2% wt/v sucrose in PBS.

[0203] Chemiluminescent detection conjugate: A murine anti-human IgG (subtype IgG2b, kappa;) was labeled with a chemiluminescent acridinium-9-carboxamide. This antibody recognized all human IgG subtypes while having no significant reactivity toward human IgM or IgA, or rabbit, sheep or goat IgG.

[0204] Samples: A human serum sample containing a high level of endogenous antibodies to cardiac troponin-I was mixed 1:1 with each inhibitor dilution. The solutions were arrayed in a black polypropylene microplate, sealed and stored overnight at ambient temperature.

[0205] Assay protocol: The samples, positive and low controls (10 μL) were diluted with AxSYM® Troponin-I ADV Preincubation Diluent (90 μL) and arrayed in triplicate on the microplate. After incubating at 37° C. for 2 h, the plate was washed with ARCHITECT® Wash Buffer (6×, 350 μL). The murine anti-human IgG specific monoclonal-acridinium conjugate (100 μL) was then added and the plate incubated at 37° C. for 1 h, before a final wash with ARCHITECT® Wash Buffer (6×, 350 μL).

[0206] Chemiluminescent detection: The microplate was loaded into a Mithras microplate reader (Berthold Technologies Inc, Oak Ridge, Tenn.) equilibrated at 28° C. The chemiluminescence signal from each well was recorded for 2 s after the sequential addition of ARCHITECT® Pre-Trigger solution (100 μL) and ARCHITECT® Trigger solution (100 μL).

[0207] A plot of the ratio of signal to the low control (S/LC) (FIG. **11**) showed that peptide #5 has the greatest inhibition of the binding of endogenous antibodies to the cTnI antigen on the microplate while the mixture of peptides gave a synergistic inhibitory effect.

Example 2

Inhibition of Anti-cTnI Autoantibody Binding to Cardiac Troponin-I (ELN Ref E000777-272)

[0208] The procedure of Example 1 was repeated using the peptides listed in Table 13.

TABLE 13

Peptide inhibitors of anti-cTnI autoantibody binding to cardiac troponin-I

Peptide#	Amino-terminus	Sequence	Carboxy-terminus
1	[Ac]	SSDAAREPRPAPAPI	[NH2]
2	[Ac]	VDEERYDIEAKVTKN	[NH2]
3	[[Ac]	DIEAKVTKNITEIAD	[NH2]
4	[Ac]	LDLRAHLKQVKKEDT	[NH2]
5	[[Ac]	ALSGMEGRKKKFES	[OH]

[0209] A plot of the ratio of signal to the low control (S/LC) (FIG. **12**) showed that peptide #5 has the greatest inhibition of the binding of endogenous antibodies to the cTnI antigen on the microplate in this experiment, while the mixture of peptides again gave a synergistic inhibitory effect.

[0210] One skilled in the art would readily appreciate that the peptide reagents and related methods are well adapted to carry out the objects and obtain the ends and advantages mentioned, as well as those inherent therein. The molecular complexes and the methods, procedures, treatments, molecules, specific compounds described herein are presently representative of preferred embodiments, are exemplary, and are not intended as limitations on the scope of the invention. It will be readily apparent to one skilled in the art that varying substitutions and modifications may be made to the present disclosure disclosed herein without departing from the scope and spirit of the invention.

[0211] All patents and publications mentioned in the specification are indicative of the levels of those skilled in the art to which the present disclosure pertains. All patents and publications are herein incorporated by reference to the same extent as if each individual publication was specifically and individually indicated to be incorporated by reference.

[0212] The present disclosure illustratively described herein suitably may be practiced in the absence of any element or elements, limitation or limitations which are not specifically disclosed herein. Thus, for example, in each instance herein any of the terms "comprising," "consisting essentially of" and "consisting of" may be replaced with either of the other two terms. The terms and expressions which have been employed are used as terms of description

and not of limitation, and there is no intention that in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the present disclosure claimed. Thus, it should be understood that although the present disclosure has been specifically disclosed by preferred embodiments and optional features, modification and variation of the concepts herein disclosed may be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope of this invention as defined by the appended claims.

SEQUENCE LISTING

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<210> SEQ ID NO 1
<211> LENGTH: 209
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 1

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Pro Ile Arg Arg Arg Ser Ser Asn Tyr Arg Ala Tyr Ala Thr Glu Pro
20 25 30

His Ala Lys Lys Lys Ser Lys Ile Ser Ala Ser Arg Lys Leu Gln Leu
35 40 45

Lys Thr Leu Leu Leu Gln Ile Ala Lys Gln Glu Leu Glu Arg Glu Ala
50 55 60

Glu Glu Arg Arg Gly Glu Lys Gly Arg Ala Leu Ser Thr Arg Cys Gln
65 70 75 80

Pro Leu Glu Leu Ala Gly Leu Gly Phe Ala Glu Leu Gln Asp Leu Cys
85 90 95

Arg Gln Leu His Ala Arg Val Asp Lys Val Asp Glu Glu Arg Tyr Asp
100 105 110

Ile Glu Ala Lys Val Thr Lys Asn Ile Thr Glu Ile Ala Asp Leu Thr
115 120 125

Gln Lys Ile Phe Asp Leu Arg Gly Lys Phe Lys Arg Pro Thr Leu Arg
130 135 140

Arg Val Arg Ile Ser Ala Asp Ala Met Met Gln Ala Leu Leu Gly Ala
145 150 155 160

Arg Ala Lys Glu Ser Leu Asp Leu Arg Ala His Leu Lys Gln Val Lys
165 170 175

Lys Glu Asp Thr Glu Lys Glu Asn Arg Glu Val Gly Asp Trp Arg Lys
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Asn Ile Asp Ala Leu Ser Gly Met Glu Gly Arg Lys Lys Lys Phe Glu
195 200 205

Ser

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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 2

Ser Asp Ile Glu Glu Val Val Glu Glu Tyr Glu Glu Glu Glu Gln Glu
1 5 10 15

Glu Ala Ala Val Glu Glu Glu Glu Asp Trp Arg Glu Asp Glu Asp Glu
20 25 30

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Gln Glu Glu Ala Ala Glu Glu Asp Ala Glu Ala Glu Ala Glu Thr Glu
        35                  40                  45

Glu Thr Arg Ala Glu Glu Asp Glu Glu Glu Glu Glu Ala Lys Glu Ala
    50                  55                  60

Glu Asp Gly Pro Met Glu Glu Ser Lys Pro Lys Pro Arg Ser Phe Met
65                  70                  75                  80

Pro Asn Leu Val Pro Pro Lys Ile Pro Asp Gly Glu Arg Val Asp Phe
                85                  90                  95

Asp Asp Ile His Arg Lys Arg Met Glu Lys Asp Leu Asn Glu Leu Gln
            100                 105                 110

Ala Leu Ile Glu Ala His Phe Glu Asn Arg Lys Lys Glu Glu Glu Glu
        115                 120                 125

Leu Val Ser Leu Lys Asp Arg Ile Glu Arg Arg Arg Ala Glu Arg Ala
    130                 135                 140

Glu Gln Gln Arg Ile Arg Asn Glu Arg Glu Lys Glu Arg Gln Asn Arg
145                 150                 155                 160

Leu Ala Glu Glu Arg Ala Arg Arg Glu Glu Glu Glu Asn Arg Arg Lys
                165                 170                 175

Ala Glu Asp Glu Ala Arg Lys Lys Lys Ala Leu Ser Asn Met Met His
            180                 185                 190

Phe Gly Gly Tyr Ile Gln Lys Gln Ala Gln Thr Glu Arg Lys Ser Gly
        195                 200                 205

Lys Arg Gln Thr Glu Arg Glu Lys Lys Lys Lys Ile Leu Ala Glu Arg
    210                 215                 220

Arg Lys Val Leu Ala Ile Asp His Leu Asn Glu Asp Gln Leu Arg Glu
225                 230                 235                 240

Lys Ala Lys Glu Leu Trp Gln Ser Ile Tyr Asn Leu Glu Ala Glu Lys
                245                 250                 255

Phe Asp Leu Gln Glu Lys Phe Lys Gln Gln Lys Tyr Glu Ile Asn Val
            260                 265                 270

Leu Arg Asn Arg Ile Asn Asp Asn Gln Lys Val Ser Lys Thr Arg Gly
        275                 280                 285

Lys Ala Lys Val Thr Gly Arg Trp Lys
    290                 295


<210> SEQ ID NO 3
<211> LENGTH: 137
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3

Thr Ala Leu Phe Leu Met Ser Met Leu Phe Gly Leu Ala Cys Gly Gln
1               5                   10                  15

Ala Met Ser Phe Cys Ile Pro Thr Glu Tyr Thr Met His Ile Glu Arg
            20                  25                  30

Arg Glu Cys Ala Tyr Cys Leu Thr Ile Asn Thr Thr Ile Cys Ala Gly
        35                  40                  45

Tyr Cys Met Thr Arg Asp Ile Asn Gly Lys Leu Phe Leu Pro Lys Tyr
    50                  55                  60

Ala Leu Ser Gln Asp Val Cys Thr Tyr Arg Asp Phe Ile Tyr Arg Thr
65                  70                  75                  80

Val Glu Ile Pro Gly Cys Pro Leu His Val Ala Pro Tyr Phe Ser Tyr
                85                  90                  95
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Pro Val Ala Leu Ser Cys Lys Cys Gly Lys Cys Asn Thr Asp Tyr Ser
            100                 105                 110

Asp Cys Ile His Glu Ala Ile Lys Thr Asn Tyr Cys Thr Lys Pro Gln
        115                 120                 125

Lys Ser Tyr Leu Val Gly Phe Ser Val
    130                 135


<210> SEQ ID NO 4
<211> LENGTH: 164
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 4

Glu Met Phe Gln Gly Leu Leu Leu Leu Leu Leu Leu Ser Met Gly Gly
1               5                   10                  15

Thr Trp Ala Ser Lys Glu Pro Leu Arg Pro Arg Cys Arg Pro Ile Asn
            20                  25                  30

Ala Thr Leu Ala Val Glu Lys Glu Gly Cys Pro Val Cys Ile Thr Val
        35                  40                  45

Asn Thr Thr Ile Cys Ala Gly Tyr Cys Pro Thr Met Thr Arg Val Leu
    50                  55                  60

Gln Gly Val Leu Pro Ala Leu Pro Gln Val Val Cys Asn Tyr Arg Asp
65                  70                  75                  80

Val Arg Phe Glu Ser Ile Arg Leu Pro Gly Cys Pro Arg Gly Val Asn
                85                  90                  95

Pro Val Val Ser Tyr Ala Val Ala Leu Ser Cys Gln Cys Ala Leu Cys
            100                 105                 110

Arg Arg Ser Thr Thr Asp Cys Gly Gly Pro Lys Asp His Pro Leu Thr
        115                 120                 125

Cys Asp Asp Pro Arg Phe Gln Asp Ser Ser Ser Ser Lys Ala Pro Pro
    130                 135                 140

Pro Ser Leu Pro Ser Pro Ser Arg Leu Pro Gly Pro Ser Asp Thr Pro
145                 150                 155                 160

Ile Leu Pro Gln


<210> SEQ ID NO 5
<211> LENGTH: 744
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 5

Gly Val Pro Phe Phe Ser Ser Leu Arg Cys Met Val Asp Leu Gly Pro
1               5                   10                  15

Cys Trp Ala Gly Gly Leu Thr Ala Glu Met Lys Leu Leu Leu Ala Leu
            20                  25                  30

Ala Gly Leu Leu Ala Ile Leu Ala Thr Pro Gln Pro Ser Glu Gly Ala
        35                  40                  45

Ala Pro Ala Val Leu Gly Glu Val Asp Thr Ser Leu Val Leu Ser Ser
    50                  55                  60

Met Glu Glu Ala Lys Gln Leu Val Asp Lys Ala Tyr Lys Glu Arg Arg
65                  70                  75                  80

Glu Ser Ile Lys Gln Arg Leu Arg Ser Gly Ser Ala Ser Pro Met Glu
                85                  90                  95
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Leu Leu Ser Tyr Phe Lys Gln Pro Val Ala Ala Thr Arg Thr Ala Val
            100                 105                 110

Arg Ala Ala Asp Tyr Leu His Val Ala Leu Asp Leu Leu Glu Arg Lys
        115                 120                 125

Leu Arg Ser Leu Trp Arg Arg Pro Phe Asn Val Thr Asp Val Leu Thr
    130                 135                 140

Pro Ala Gln Leu Asn Val Leu Ser Lys Ser Ser Gly Cys Ala Tyr Gln
145                 150                 155                 160

Asp Val Gly Val Thr Cys Pro Glu Gln Asp Lys Tyr Arg Thr Ile Thr
                165                 170                 175

Gly Met Cys Asn Asn Arg Arg Ser Pro Thr Leu Gly Ala Ser Asn Arg
            180                 185                 190

Ala Phe Val Arg Trp Leu Pro Ala Glu Tyr Glu Asp Gly Phe Ser Leu
        195                 200                 205

Pro Tyr Gly Trp Thr Pro Gly Val Lys Arg Asn Gly Phe Pro Val Ala
    210                 215                 220

Leu Ala Arg Ala Val Ser Asn Glu Ile Val Arg Phe Pro Thr Asp Gln
225                 230                 235                 240

Leu Thr Pro Asp Gln Glu Arg Ser Leu Met Phe Met Gln Trp Gly Gln
                245                 250                 255

Leu Leu Asp His Asp Leu Asp Phe Thr Pro Glu Pro Ala Ala Arg Ala
            260                 265                 270

Ser Phe Val Thr Gly Val Asn Cys Glu Thr Ser Cys Val Gln Gln Pro
        275                 280                 285

Pro Cys Phe Pro Leu Lys Ile Pro Pro Asn Asp Pro Arg Ile Lys Asn
    290                 295                 300

Gln Ala Asp Cys Ile Pro Phe Phe Arg Ser Cys Pro Ala Cys Pro Gly
305                 310                 315                 320

Ser Asn Ile Thr Ile Arg Asn Gln Ile Asn Ala Leu Thr Ser Phe Val
                325                 330                 335

Asp Ala Ser Met Val Tyr Gly Ser Glu Glu Pro Leu Ala Arg Asn Leu
            340                 345                 350

Arg Asn Met Ser Asn Gln Leu Gly Leu Leu Ala Val Asn Gln Arg Phe
        355                 360                 365

Gln Asp Asn Gly Arg Ala Leu Leu Pro Phe Asp Asn Leu His Asp Asp
    370                 375                 380

Pro Cys Leu Leu Thr Asn Arg Ser Ala Arg Ile Pro Cys Phe Leu Ala
385                 390                 395                 400

Gly Asp Thr Arg Ser Ser Glu Met Pro Glu Leu Thr Ser Met His Thr
                405                 410                 415

Leu Leu Leu Arg Glu His Asn Arg Leu Ala Thr Glu Leu Lys Ser Leu
            420                 425                 430

Asn Pro Arg Trp Asp Gly Glu Arg Leu Tyr Gln Glu Ala Arg Lys Ile
        435                 440                 445

Val Gly Ala Met Val Gln Ile Ile Thr Tyr Arg Asp Tyr Leu Pro Leu
    450                 455                 460

Val Leu Gly Pro Thr Ala Met Arg Lys Tyr Leu Pro Thr Tyr Arg Ser
465                 470                 475                 480

Tyr Asn Asp Ser Val Asp Pro Arg Ile Ala Asn Val Phe Thr Asn Ala
                485                 490                 495

Phe Arg Tyr Gly His Thr Leu Ile Gln Pro Phe Met Phe Arg Leu Asp
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           500                 505                 510

Asn Arg Tyr Gln Pro Met Glu Pro Asn Pro Arg Val Pro Leu Ser Arg
        515                 520                 525

Val Phe Phe Ala Ser Trp Arg Val Val Leu Glu Gly Gly Ile Asp Pro
    530                 535                 540

Ile Leu Arg Gly Leu Met Ala Thr Pro Ala Lys Leu Asn Arg Gln Asn
545                 550                 555                 560

Gln Ile Ala Val Asp Glu Ile Arg Glu Arg Leu Phe Glu Gln Val Met
                565                 570                 575

Arg Ile Gly Leu Asp Leu Pro Ala Leu Asn Met Gln Arg Ser Arg Asp
            580                 585                 590

His Gly Leu Pro Gly Tyr Asn Ala Trp Arg Arg Phe Cys Gly Leu Pro
        595                 600                 605

Gln Pro Glu Thr Val Gly Gln Leu Gly Thr Val Leu Arg Asn Leu Lys
    610                 615                 620

Leu Ala Arg Lys Leu Met Glu Gln Tyr Gly Thr Pro Asn Asn Ile Asp
625                 630                 635                 640

Ile Trp Met Gly Gly Val Ser Glu Pro Leu Lys Arg Lys Gly Arg Val
                645                 650                 655

Gly Pro Leu Leu Ala Cys Ile Ile Gly Thr Gln Phe Arg Lys Leu Arg
            660                 665                 670

Asp Gly Asp Arg Phe Trp Trp Glu Asn Glu Gly Val Phe Ser Met Gln
        675                 680                 685

Gln Arg Gln Ala Leu Ala Gln Ile Ser Leu Pro Arg Ile Ile Cys Asp
    690                 695                 700

Asn Thr Gly Ile Thr Thr Val Ser Lys Asn Asn Ile Phe Met Ser Asn
705                 710                 715                 720

Ser Tyr Pro Arg Asp Phe Val Asn Cys Ser Thr Leu Pro Ala Leu Asn
                725                 730                 735

Leu Ala Ser Trp Arg Glu Ala Ser
            740


<210> SEQ ID NO 6
<211> LENGTH: 260
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 6

Trp Val Pro Val Val Phe Leu Thr Leu Ser Val Thr Trp Ile Gly Ala
1               5                   10                  15

Ala Pro Leu Ile Leu Ser Arg Ile Val Gly Gly Trp Glu Cys Glu Lys
            20                  25                  30

His Ser Gln Pro Trp Gln Val Leu Val Ala Ser Arg Gly Arg Ala Val
        35                  40                  45

Cys Gly Gly Val Leu Val His Pro Gln Trp Val Leu Thr Ala Ala His
    50                  55                  60

Cys Ile Arg Asn Lys Ser Val Ile Leu Leu Gly Arg His Ser Leu Phe
65                  70                  75                  80

His Pro Glu Asp Thr Gly Gln Val Phe Gln Val Ser His Ser Phe Pro
                85                  90                  95

His Pro Leu Tyr Asp Met Ser Leu Leu Lys Asn Arg Phe Leu Arg Pro
            100                 105                 110
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```
Gly Asp Asp Ser Ser His Asp Leu Met Leu Leu Arg Leu Ser Glu Pro
        115                 120                 125

Ala Glu Leu Thr Asp Ala Val Lys Val Met Asp Leu Pro Thr Gln Glu
    130                 135                 140

Pro Ala Leu Gly Thr Thr Cys Tyr Ala Ser Gly Trp Gly Ser Ile Glu
145                 150                 155                 160

Pro Glu Glu Phe Leu Thr Pro Lys Lys Leu Gln Cys Val Asp Leu His
                165                 170                 175

Val Ile Ser Asn Asp Val Cys Ala Gln Val His Pro Gln Lys Val Thr
            180                 185                 190

Lys Phe Met Leu Cys Ala Gly Arg Trp Thr Gly Gly Lys Ser Thr Cys
        195                 200                 205

Ser Gly Asp Ser Gly Gly Pro Leu Val Cys Asn Gly Val Leu Gln Gly
    210                 215                 220

Ile Thr Ser Trp Gly Ser Glu Pro Cys Ala Leu Pro Glu Arg Pro Ser
225                 230                 235                 240

Leu Tyr Thr Lys Val Val His Tyr Arg Lys Trp Ile Lys Asp Thr Ile
                245                 250                 255

Val Ala Asn Pro
            260


<210> SEQ ID NO 7
<211> LENGTH: 133
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 7

Asp Pro Gln Thr Ala Pro Ser Arg Ala Leu Leu Leu Leu Leu Phe Leu
1               5                   10                  15

His Leu Ala Phe Leu Gly Gly Arg Ser His Pro Leu Gly Ser Pro Gly
            20                  25                  30

Ser Ala Ser Asp Leu Glu Thr Ser Gly Leu Gln Glu Gln Arg Asn His
        35                  40                  45

Leu Gln Gly Lys Leu Ser Glu Leu Gln Val Glu Gln Thr Ser Leu Glu
    50                  55                  60

Pro Leu Gln Glu Ser Pro Arg Pro Thr Gly Val Trp Lys Ser Arg Glu
65                  70                  75                  80

Val Ala Thr Glu Gly Ile Arg Gly His Arg Lys Met Val Leu Tyr Thr
                85                  90                  95

Leu Arg Ala Pro Arg Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe
            100                 105                 110

Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys
        115                 120                 125

Val Leu Arg Arg His
    130


<210> SEQ ID NO 8
<211> LENGTH: 165
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 8

Ala Pro Lys Lys Ala Lys Lys Arg Ala Gly Gly Ala Asn Ser Asn Val
1               5                   10                  15
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Phe Ser Met Phe Glu Gln Thr Gln Ile Gln Glu Phe Lys Glu Ala Phe
            20                  25                  30

Thr Ile Met Asp Gln Asn Arg Asp Gly Phe Ile Asp Lys Asn Asp Leu
        35                  40                  45

Arg Asp Thr Phe Ala Ala Leu Gly Arg Val Asn Val Lys Asn Glu Glu
    50                  55                  60

Ile Asp Glu Met Ile Lys Glu Ala Pro Gly Pro Ile Asn Phe Thr Val
65                  70                  75                  80

Phe Leu Thr Met Phe Gly Glu Lys Leu Lys Gly Ala Asp Pro Glu Glu
                85                  90                  95

Thr Ile Leu Asn Ala Phe Lys Val Phe Asp Pro Glu Gly Lys Gly Val
            100                 105                 110

Leu Lys Ala Asp Tyr Val Arg Glu Met Leu Thr Thr Gln Ala Glu Arg
        115                 120                 125

Phe Ser Lys Glu Glu Val Asp Gln Met Phe Ala Ala Phe Pro Pro Asp
    130                 135                 140

Val Thr Gly Asn Leu Asp Tyr Lys Asn Leu Val His Ile Ile Thr His
145                 150                 155                 160

Gly Glu Glu Lys Asp
                165


<210> SEQ ID NO 9
<211> LENGTH: 1938
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 9

Thr Asp Ala Gln Met Ala Asp Phe Gly Ala Ala Ala Gln Tyr Leu Arg
1               5                   10                  15

Lys Ser Glu Lys Glu Arg Leu Glu Ala Gln Thr Arg Pro Phe Asp Ile
            20                  25                  30

Arg Thr Glu Cys Phe Val Pro Asp Asp Lys Glu Glu Phe Val Lys Ala
        35                  40                  45

Lys Ile Leu Ser Arg Glu Gly Gly Lys Val Ile Ala Glu Thr Glu Asn
    50                  55                  60

Gly Lys Thr Val Thr Val Lys Glu Asp Gln Val Leu Gln Gln Asn Pro
65                  70                  75                  80

Pro Lys Phe Asp Lys Ile Gln Asp Met Ala Met Leu Thr Phe Leu His
                85                  90                  95

Glu Pro Ala Val Leu Phe Asn Leu Lys Glu Arg Tyr Ala Ala Trp Met
            100                 105                 110

Ile Tyr Thr Tyr Ser Gly Leu Phe Cys Val Thr Val Asn Pro Tyr Lys
        115                 120                 125

Trp Leu Pro Val Tyr Asn Ala Glu Val Val Ala Ala Tyr Arg Gly Lys
    130                 135                 140

Lys Arg Ser Glu Ala Pro Pro His Ile Phe Ser Ile Ser Asp Asn Ala
145                 150                 155                 160

Tyr Gln Tyr Met Leu Thr Asp Arg Glu Asn Gln Ser Ile Leu Ile Thr
                165                 170                 175

Gly Glu Ser Gly Ala Gly Lys Thr Val Asn Thr Lys Arg Val Ile Gln
            180                 185                 190

Tyr Phe Ala Ser Ile Ala Ala Ile Gly Asp Arg Gly Lys Lys Asp Asn
        195                 200                 205
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```
Ala Asn Ala Asn Lys Gly Thr Leu Glu Asp Gln Ile Ile Gln Ala Asn
    210                 215                 220

Pro Ala Leu Glu Ala Phe Gly Asn Ala Lys Thr Val Arg Asn Asp Asn
225                 230                 235                 240

Ser Ser Arg Phe Gly Lys Phe Ile Arg Ile His Phe Gly Ala Thr Gly
                245                 250                 255

Lys Leu Ala Ser Ala Asp Ile Glu Thr Tyr Leu Leu Glu Lys Ser Arg
            260                 265                 270

Val Ile Phe Gln Leu Lys Ala Glu Arg Asn Tyr His Ile Phe Tyr Gln
        275                 280                 285

Ile Leu Ser Asn Lys Lys Pro Glu Leu Leu Asp Met Leu Leu Val Thr
    290                 295                 300

Asn Asn Pro Tyr Asp Tyr Ala Phe Val Ser Gln Gly Glu Val Ser Val
305                 310                 315                 320

Ala Ser Ile Asp Asp Ser Glu Glu Leu Met Ala Thr Asp Ser Ala Phe
                325                 330                 335

Asp Val Leu Gly Phe Thr Ser Glu Glu Lys Ala Gly Val Tyr Lys Leu
            340                 345                 350

Thr Gly Ala Ile Met His Tyr Gly Asn Met Lys Phe Lys Gln Lys Gln
        355                 360                 365

Arg Glu Glu Gln Ala Glu Pro Asp Gly Thr Glu Asp Ala Asp Lys Ser
    370                 375                 380

Ala Tyr Leu Met Gly Leu Asn Ser Ala Asp Leu Leu Lys Gly Leu Cys
385                 390                 395                 400

His Pro Arg Val Lys Val Gly Asn Glu Tyr Val Thr Lys Gly Gln Ser
                405                 410                 415

Val Gln Gln Val Tyr Tyr Ser Ile Gly Ala Leu Ala Lys Ala Val Tyr
            420                 425                 430

Glu Lys Met Phe Asn Trp Met Val Thr Arg Ile Asn Ala Thr Leu Glu
        435                 440                 445

Thr Lys Gln Pro Arg Gln Tyr Phe Ile Gly Val Leu Asp Ile Ala Gly
    450                 455                 460

Phe Glu Ile Phe Asp Phe Asn Ser Phe Glu Gln Leu Cys Ile Asn Phe
465                 470                 475                 480

Thr Asn Glu Lys Leu Gln Gln Phe Phe Asn His His Met Phe Val Leu
                485                 490                 495

Glu Gln Glu Glu Tyr Lys Lys Glu Gly Ile Glu Trp Thr Phe Ile Asp
            500                 505                 510

Phe Gly Met Asp Leu Gln Ala Cys Ile Asp Leu Ile Glu Lys Pro Met
        515                 520                 525

Gly Ile Met Ser Ile Leu Glu Glu Glu Cys Met Phe Pro Lys Ala Thr
    530                 535                 540

Asp Met Thr Phe Lys Ala Lys Leu Tyr Asp Asn His Leu Gly Lys Ser
545                 550                 555                 560

Asn Asn Phe Gln Lys Pro Arg Asn Ile Lys Gly Lys Gln Glu Ala His
                565                 570                 575

Phe Ser Leu Ile His Tyr Ala Gly Thr Val Asp Tyr Asn Ile Leu Gly
            580                 585                 590

Trp Leu Glu Lys Asn Lys Asp Pro Leu Asn Glu Thr Val Val Ala Leu
        595                 600                 605
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Tyr Gln Lys Ser Ser Leu Lys Leu Met Ala Thr Leu Phe Ser Ser Tyr
    610                 615                 620

Ala Thr Ala Asp Thr Gly Asp Ser Gly Lys Ser Lys Gly Gly Lys Lys
625                 630                 635                 640

Lys Gly Ser Ser Phe Gln Thr Val Ser Ala Leu His Arg Glu Asn Leu
                645                 650                 655

Asn Lys Leu Met Thr Asn Leu Arg Thr Thr His Pro His Phe Val Arg
            660                 665                 670

Cys Ile Ile Pro Asn Glu Arg Lys Ala Pro Gly Val Met Asp Asn Pro
        675                 680                 685

Leu Val Met His Gln Leu Arg Cys Asn Gly Val Leu Glu Gly Ile Arg
    690                 695                 700

Ile Cys Arg Lys Gly Phe Pro Asn Arg Ile Leu Tyr Gly Asp Phe Arg
705                 710                 715                 720

Gln Arg Tyr Arg Ile Leu Asn Pro Val Ala Ile Pro Glu Gly Gln Phe
                725                 730                 735

Ile Asp Ser Arg Lys Gly Thr Glu Lys Leu Leu Ser Ser Leu Asp Ile
            740                 745                 750

Asp His Asn Gln Tyr Lys Phe Gly His Thr Lys Val Phe Phe Lys Ala
        755                 760                 765

Gly Leu Leu Gly Leu Leu Glu Glu Met Arg Asp Glu Arg Leu Ser Arg
    770                 775                 780

Ile Ile Thr Arg Met Gln Ala Gln Ala Arg Gly Gln Leu Met Arg Ile
785                 790                 795                 800

Glu Phe Lys Lys Ile Val Glu Arg Arg Asp Ala Leu Leu Val Ile Gln
                805                 810                 815

Trp Asn Ile Arg Ala Phe Met Gly Val Lys Asn Trp Pro Trp Met Lys
            820                 825                 830

Leu Tyr Phe Lys Ile Lys Pro Leu Leu Lys Ser Ala Glu Thr Glu Lys
        835                 840                 845

Glu Met Ala Thr Met Lys Glu Glu Phe Gly Arg Ile Lys Glu Thr Leu
    850                 855                 860

Glu Lys Ser Glu Ala Arg Arg Lys Glu Leu Glu Glu Lys Met Val Ser
865                 870                 875                 880

Leu Leu Gln Glu Lys Asn Asp Leu Gln Leu Gln Val Gln Ala Glu Gln
                885                 890                 895

Asp Asn Leu Asn Asp Ala Glu Glu Arg Cys Asp Gln Leu Ile Lys Asn
            900                 905                 910

Lys Ile Gln Leu Glu Ala Lys Val Lys Glu Met Asn Glu Arg Leu Glu
        915                 920                 925

Asp Glu Glu Glu Met Asn Ala Glu Leu Thr Ala Lys Lys Arg Lys Leu
    930                 935                 940

Glu Asp Glu Cys Ser Glu Leu Lys Lys Asp Ile Asp Asp Leu Glu Leu
945                 950                 955                 960

Thr Leu Ala Lys Val Glu Lys Glu Lys His Ala Thr Glu Asn Lys Val
                965                 970                 975

Lys Asn Leu Thr Glu Glu Met Ala Gly Leu Asp Glu Ile Ile Ala Lys
            980                 985                 990

Leu Thr Lys Glu Lys Lys Ala Leu  Gln Glu Ala His Gln  Gln Ala Leu
        995                 1000                1005

Asp Asp  Leu Gln Val Glu Glu  Asp Lys Val Asn Ser  Leu Ser Lys
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    1010                1015                1020

Ser Lys  Val Lys Leu Glu Gln  Gln Val Asp Asp Leu  Glu Gly Ser
    1025                1030                1035

Leu Glu  Gln Glu Lys Lys Val  Arg Met Asp Leu Glu  Arg Ala Lys
    1040                1045                1050

Arg Lys  Leu Glu Gly Asp Leu  Lys Leu Thr Gln Glu  Ser Ile Met
    1055                1060                1065

Asp Leu  Glu Asn Asp Lys Leu  Gln Leu Glu Glu Lys  Leu Lys Lys
    1070                1075                1080

Lys Glu  Phe Asp Ile Asn Gln  Gln Asn Ser Lys Ile  Glu Asp Glu
    1085                1090                1095

Gln Ala  Leu Ala Leu Gln Leu  Gln Lys Lys Leu Lys  Glu Asn Gln
    1100                1105                1110

Ala Arg  Ile Glu Glu Leu Glu  Glu Glu Leu Glu Ala  Glu Arg Thr
    1115                1120                1125

Ala Arg  Ala Lys Val Glu Lys  Leu Arg Ser Asp Leu  Ser Arg Glu
    1130                1135                1140

Leu Glu  Glu Ile Ser Glu Arg  Leu Glu Glu Ala Gly  Gly Ala Thr
    1145                1150                1155

Ser Val  Gln Ile Glu Met Asn  Lys Lys Arg Glu Ala  Glu Phe Gln
    1160                1165                1170

Lys Met  Arg Arg Asp Leu Glu  Glu Ala Thr Leu Gln  His Glu Ala
    1175                1180                1185

Thr Ala  Ala Ala Leu Arg Lys  Lys His Ala Asp Ser  Val Ala Glu
    1190                1195                1200

Leu Gly  Glu Gln Ile Asp Asn  Leu Gln Arg Val Lys  Gln Lys Leu
    1205                1210                1215

Glu Lys  Glu Lys Ser Glu Phe  Lys Leu Glu Leu Asp  Asp Val Thr
    1220                1225                1230

Ser Asn  Met Glu Gln Ile Ile  Lys Ala Lys Ala Asn  Leu Glu Lys
    1235                1240                1245

Val Ser  Arg Thr Leu Glu Asp  Gln Ala Asn Glu Tyr  Arg Val Lys
    1250                1255                1260

Leu Glu  Glu Ala Gln Arg Ser  Leu Asn Asp Phe Thr  Thr Gln Arg
    1265                1270                1275

Ala Lys  Leu Gln Thr Glu Asn  Gly Glu Leu Ala Arg  Gln Leu Glu
    1280                1285                1290

Glu Lys  Glu Ala Leu Ile Ser  Gln Leu Thr Arg Gly  Lys Leu Ser
    1295                1300                1305

Tyr Thr  Gln Gln Met Glu Asp  Leu Lys Arg Gln Leu  Glu Glu Glu
    1310                1315                1320

Gly Lys  Ala Lys Asn Ala Leu  Ala His Ala Leu Gln  Ser Ala Arg
    1325                1330                1335

His Asp  Cys Asp Leu Leu Arg  Glu Gln Tyr Glu Glu  Glu Thr Glu
    1340                1345                1350

Ala Lys  Ala Glu Leu Gln Arg  Val Leu Ser Lys Ala  Asn Ser Glu
    1355                1360                1365

Val Ala  Gln Trp Arg Thr Lys  Tyr Glu Thr Asp Ala  Ile Gln Arg
    1370                1375                1380

Thr Glu  Glu Leu Glu Glu Ala  Lys Lys Lys Leu Ala  Gln Arg Leu
    1385                1390                1395
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Gln Asp  Ala Glu Glu Ala Val  Glu Ala Val Asn Ala  Lys Cys Ser
    1400                1405                1410

Ser Leu  Glu Lys Thr Lys His  Arg Leu Gln Asn Glu  Ile Glu Asp
    1415                1420                1425

Leu Met  Val Asp Val Glu Arg  Ser Asn Ala Ala Ala  Ala Ala Leu
    1430                1435                1440

Asp Lys  Lys Gln Arg Asn Phe  Asp Lys Ile Leu Ala  Glu Trp Lys
    1445                1450                1455

Gln Lys  Tyr Glu Glu Ser Gln  Ser Glu Leu Glu Ser  Ser Gln Lys
    1460                1465                1470

Glu Ala  Arg Ser Leu Ser Thr  Glu Leu Phe Lys Leu  Lys Asn Ala
    1475                1480                1485

Tyr Glu  Glu Ser Leu Glu His  Leu Glu Thr Phe Lys  Arg Glu Asn
    1490                1495                1500

Lys Asn  Leu Gln Glu Glu Ile  Ser Asp Leu Thr Glu  Gln Leu Gly
    1505                1510                1515

Glu Gly  Gly Lys Asn Val His  Glu Leu Glu Lys Val  Arg Lys Gln
    1520                1525                1530

Leu Glu  Val Glu Lys Leu Glu  Leu Gln Ser Ala Leu  Glu Glu Ala
    1535                1540                1545

Glu Ala  Ser Leu Glu His Glu  Glu Gly Lys Ile Leu  Arg Ala Gln
    1550                1555                1560

Leu Glu  Phe Asn Gln Ile Lys  Ala Glu Ile Glu Arg  Lys Leu Ala
    1565                1570                1575

Glu Lys  Asp Glu Glu Met Glu  Gln Ala Lys Arg Asn  His Gln Arg
    1580                1585                1590

Val Val  Asp Ser Leu Gln Thr  Ser Leu Asp Ala Glu  Thr Arg Ser
    1595                1600                1605

Arg Asn  Glu Val Leu Arg Val  Lys Lys Lys Met Glu  Gly Asp Leu
    1610                1615                1620

Asn Glu  Met Glu Ile Gln Leu  Ser His Ala Asn Arg  Met Ala Ala
    1625                1630                1635

Glu Ala  Gln Lys Gln Val Lys  Ser Leu Gln Ser Leu  Leu Lys Asp
    1640                1645                1650

Thr Gln  Ile Gln Leu Asp Asp  Ala Val Arg Ala Asn  Asp Asp Leu
    1655                1660                1665

Lys Glu  Asn Ile Ala Ile Val  Glu Arg Arg Asn Asn  Leu Leu Gln
    1670                1675                1680

Ala Glu  Leu Glu Glu Leu Arg  Ala Val Val Glu Gln  Thr Glu Arg
    1685                1690                1695

Ser Arg  Lys Leu Ala Glu Gln  Glu Leu Ile Glu Thr  Ser Glu Arg
    1700                1705                1710

Val Gln  Leu Leu His Ser Gln  Asn Thr Ser Leu Ile  Asn Gln Lys
    1715                1720                1725

Lys Lys  Met Glu Ala Asp Leu  Thr Gln Leu Gln Ser  Glu Val Glu
    1730                1735                1740

Glu Ala  Val Gln Glu Cys Arg  Asn Ala Glu Glu Lys  Ala Lys Lys
    1745                1750                1755

Ala Ile  Thr Asp Ala Ala Met  Met Ala Glu Glu Leu  Lys Lys Glu
    1760                1765                1770
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Gln Asp  Thr Ser Ala His Leu  Glu Arg Met Lys Lys  Asn Met Glu
    1775                1780                1785

Gln Thr  Ile Lys Asp Leu Gln  His Arg Leu Asp Glu  Ala Glu Gln
    1790                1795                1800

Ile Ala  Leu Lys Gly Gly Lys  Lys Gln Leu Gln Lys  Leu Glu Ala
    1805                1810                1815

Arg Val  Arg Glu Leu Glu Gly  Glu Leu Glu Ala Glu  Gln Lys Arg
    1820                1825                1830

Asn Ala  Glu Ser Val Lys Gly  Met Arg Lys Ser Glu  Arg Arg Ile
    1835                1840                1845

Lys Glu  Leu Thr Tyr Gln Thr  Glu Glu Asp Lys Lys  Asn Leu Leu
    1850                1855                1860

Arg Leu  Gln Asp Leu Val Asp  Lys Leu Gln Leu Lys  Val Lys Ala
    1865                1870                1875

Tyr Lys  Arg Gln Ala Glu Glu  Ala Glu Glu Gln Ala  Asn Thr Asn
    1880                1885                1890

Leu Ser  Lys Phe Arg Lys Val  Gln His Glu Leu Asp  Glu Ala Glu
    1895                1900                1905

Glu Arg  Ala Asp Ile Ala Glu  Ser Gln Val Asn Lys  Leu Arg Ala
    1910                1915                1920

Lys Ser  Arg Asp Ile Gly Ala  Lys Gln Lys Met His  Asp Glu Glu
    1925                1930                1935


<210> SEQ ID NO 10
<211> LENGTH: 1934
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 10

Gly Asp Ser Glu Met Ala Val Phe Gly Ala Ala Ala Pro Tyr Leu Arg
1               5                  10                  15

Lys Ser Glu Lys Glu Arg Leu Glu Ala Gln Thr Arg Pro Phe Asp Leu
            20                  25                  30

Lys Lys Asp Val Phe Val Pro Asp Asp Lys Gln Glu Phe Val Lys Ala
        35                  40                  45

Lys Ile Val Ser Arg Glu Gly Gly Lys Val Thr Ala Glu Thr Glu Tyr
    50                  55                  60

Gly Lys Thr Val Thr Val Lys Glu Asp Gln Val Met Gln Gln Asn Pro
65                  70                  75                  80

Pro Lys Phe Asp Lys Ile Glu Asp Met Ala Met Leu Thr Phe Leu His
                85                  90                  95

Glu Pro Ala Val Leu Tyr Asn Leu Lys Asp Arg Tyr Gly Ser Trp Met
            100                 105                 110

Ile Tyr Thr Tyr Ser Gly Leu Phe Cys Val Thr Val Asn Pro Tyr Lys
        115                 120                 125

Trp Leu Pro Val Tyr Thr Pro Glu Val Val Ala Ala Tyr Arg Gly Lys
    130                 135                 140

Lys Arg Ser Glu Ala Pro Pro His Ile Phe Ser Ile Ser Asp Asn Ala
145                 150                 155                 160

Tyr Gln Tyr Met Leu Thr Asp Arg Glu Asn Gln Ser Ile Leu Ile Thr
                165                 170                 175

Gly Glu Ser Gly Ala Gly Lys Thr Val Asn Thr Lys Arg Val Ile Gln
            180                 185                 190
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Tyr Phe Ala Val Ile Ala Ala Ile Gly Asp Arg Ser Lys Lys Asp Gln
        195                 200                 205

Ser Pro Gly Lys Gly Thr Leu Glu Asp Gln Ile Ile Gln Ala Asn Pro
    210                 215                 220

Ala Leu Glu Ala Phe Gly Asn Ala Lys Thr Val Arg Asn Asp Asn Ser
225                 230                 235                 240

Ser Arg Phe Gly Lys Phe Ile Arg Ile His Phe Gly Ala Thr Gly Lys
                245                 250                 255

Leu Ala Ser Ala Asp Ile Glu Thr Tyr Leu Leu Glu Lys Ser Arg Val
            260                 265                 270

Ile Phe Gln Leu Lys Ala Glu Arg Asp Tyr His Ile Phe Tyr Gln Ile
        275                 280                 285

Leu Ser Asn Lys Lys Pro Glu Leu Leu Asp Met Leu Leu Ile Thr Asn
    290                 295                 300

Asn Pro Tyr Asp Tyr Ala Phe Ile Ser Gln Gly Glu Thr Thr Val Ala
305                 310                 315                 320

Ser Ile Asp Asp Ala Glu Glu Leu Met Ala Thr Asp Asn Ala Phe Asp
                325                 330                 335

Val Leu Gly Phe Thr Ser Glu Glu Lys Asn Ser Met Tyr Lys Leu Thr
            340                 345                 350

Gly Ala Ile Met His Phe Gly Asn Met Lys Phe Lys Leu Lys Gln Arg
        355                 360                 365

Glu Glu Gln Ala Glu Pro Asp Gly Thr Glu Glu Ala Asp Lys Ser Ala
    370                 375                 380

Tyr Leu Met Gly Leu Asn Ser Ala Asp Leu Leu Lys Gly Leu Cys His
385                 390                 395                 400

Pro Arg Val Lys Val Gly Asn Glu Tyr Val Thr Lys Gly Gln Asn Val
                405                 410                 415

Gln Gln Val Ile Tyr Ala Thr Gly Ala Leu Ala Lys Ala Val Tyr Glu
            420                 425                 430

Arg Met Phe Asn Trp Met Val Thr Arg Ile Asn Ala Thr Leu Glu Thr
        435                 440                 445

Lys Gln Pro Arg Gln Tyr Phe Ile Gly Val Leu Asp Ile Ala Gly Phe
    450                 455                 460

Glu Ile Phe Asp Phe Asn Ser Phe Glu Gln Leu Cys Ile Asn Phe Thr
465                 470                 475                 480

Asn Glu Lys Leu Gln Gln Phe Phe Asn His His Met Phe Val Leu Glu
                485                 490                 495

Gln Glu Glu Tyr Lys Lys Glu Gly Ile Glu Trp Thr Phe Ile Asp Phe
            500                 505                 510

Gly Met Asp Leu Gln Ala Cys Ile Asp Leu Ile Glu Lys Pro Met Gly
        515                 520                 525

Ile Met Ser Ile Leu Glu Glu Glu Cys Met Phe Pro Lys Ala Thr Asp
    530                 535                 540

Met Thr Phe Lys Ala Lys Leu Phe Asp Asn His Leu Gly Lys Ser Ala
545                 550                 555                 560

Asn Phe Gln Lys Pro Arg Asn Ile Lys Gly Lys Pro Glu Ala His Phe
                565                 570                 575

Ser Leu Ile His Tyr Ala Gly Ile Val Asp Tyr Asn Ile Ile Gly Trp
            580                 585                 590
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Leu Gln Lys Asn Lys Asp Pro Leu Asn Glu Thr Val Val Gly Leu Tyr
        595                 600                 605

Gln Lys Ser Ser Leu Lys Leu Leu Ser Thr Leu Phe Ala Asn Tyr Ala
    610                 615                 620

Gly Ala Asp Ala Pro Ile Glu Lys Gly Lys Gly Lys Ala Lys Lys Gly
625                 630                 635                 640

Ser Ser Phe Gln Thr Val Ser Ala Leu His Arg Glu Asn Leu Asn Lys
                645                 650                 655

Leu Met Thr Asn Leu Arg Ser Thr His Pro His Phe Val Arg Cys Ile
            660                 665                 670

Ile Pro Asn Glu Thr Lys Ser Pro Gly Val Met Asp Asn Pro Leu Val
        675                 680                 685

Met His Gln Leu Arg Cys Asn Gly Val Leu Glu Gly Ile Arg Ile Cys
    690                 695                 700

Arg Lys Gly Phe Pro Asn Arg Ile Leu Tyr Gly Asp Phe Arg Gln Arg
705                 710                 715                 720

Tyr Arg Ile Leu Asn Pro Ala Ala Ile Pro Glu Gly Gln Phe Ile Asp
                725                 730                 735

Ser Arg Lys Gly Ala Glu Lys Leu Leu Ser Ser Leu Asp Ile Asp His
            740                 745                 750

Asn Gln Tyr Lys Phe Gly His Thr Lys Val Phe Phe Lys Ala Gly Leu
        755                 760                 765

Leu Gly Leu Leu Glu Glu Met Arg Asp Glu Arg Leu Ser Arg Ile Ile
    770                 775                 780

Thr Arg Ile Gln Ala Gln Ser Arg Gly Val Leu Ala Arg Met Glu Tyr
785                 790                 795                 800

Lys Lys Leu Leu Glu Arg Arg Asp Ser Leu Leu Val Ile Gln Trp Asn
                805                 810                 815

Ile Arg Ala Phe Met Gly Val Lys Asn Trp Pro Trp Met Lys Leu Tyr
            820                 825                 830

Phe Lys Ile Lys Pro Leu Leu Lys Ser Ala Glu Arg Glu Lys Glu Met
        835                 840                 845

Ala Ser Met Lys Glu Glu Phe Thr Arg Leu Lys Glu Ala Leu Glu Lys
    850                 855                 860

Ser Glu Ala Arg Arg Lys Glu Leu Glu Glu Lys Met Val Ser Leu Leu
865                 870                 875                 880

Gln Glu Lys Asn Asp Leu Gln Leu Gln Val Gln Ala Glu Gln Asp Asn
                885                 890                 895

Leu Ala Asp Ala Glu Glu Arg Cys Asp Gln Leu Ile Lys Asn Lys Ile
            900                 905                 910

Gln Leu Glu Ala Lys Val Lys Glu Met Asn Glu Arg Leu Glu Asp Glu
        915                 920                 925

Glu Glu Met Asn Ala Glu Leu Thr Ala Lys Lys Arg Lys Leu Glu Asp
    930                 935                 940

Glu Cys Ser Glu Leu Lys Arg Asp Ile Asp Asp Leu Glu Leu Thr Leu
945                 950                 955                 960

Ala Lys Val Glu Lys Glu Lys His Ala Thr Glu Asn Lys Val Lys Asn
                965                 970                 975

Leu Thr Glu Glu Met Ala Gly Leu Asp Glu Ile Ile Ala Lys Leu Thr
            980                 985                 990

Lys Glu Lys Lys Ala Leu Gln Glu  Ala His Gln Gln Ala  Leu Asp Asp
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       995                1000                1005

Leu Gln  Ala Glu Glu Asp Lys  Val Asn Thr Leu Thr  Lys Ala Lys
    1010                1015                1020

Val Lys  Leu Glu Gln Gln Val  Asp Asp Leu Glu Gly  Ser Leu Glu
    1025                1030                1035

Gln Glu  Lys Lys Val Arg Met  Asp Leu Glu Arg Ala  Lys Arg Lys
    1040                1045                1050

Leu Glu  Gly Asp Leu Lys Leu  Thr Gln Glu Ser Ile  Met Asp Leu
    1055                1060                1065

Glu Asn  Asp Lys Gln Gln Leu  Asp Glu Arg Leu Lys  Lys Lys Asp
    1070                1075                1080

Phe Glu  Leu Asn Ala Leu Asn  Ala Arg Ile Glu Asp  Glu Gln Ala
    1085                1090                1095

Leu Gly  Ser Gln Leu Gln Lys  Lys Leu Lys Glu Leu  Gln Ala Arg
    1100                1105                1110

Ile Glu  Glu Leu Glu Glu Glu  Leu Glu Ala Glu Arg  Thr Ala Arg
    1115                1120                1125

Ala Lys  Val Glu Lys Leu Arg  Ser Asp Leu Ser Arg  Glu Leu Glu
    1130                1135                1140

Glu Ile  Ser Glu Arg Leu Glu  Glu Ala Gly Gly Ala  Thr Ser Val
    1145                1150                1155

Gln Ile  Glu Met Asn Lys Lys  Arg Glu Ala Glu Phe  Gln Lys Met
    1160                1165                1170

Arg Arg  Asp Leu Glu Glu Ala  Thr Leu Gln His Glu  Ala Thr Ala
    1175                1180                1185

Ala Ala  Leu Arg Lys Lys His  Ala Asp Ser Val Ala  Glu Leu Gly
    1190                1195                1200

Glu Gln  Ile Asp Asn Leu Gln  Arg Val Lys Gln Lys  Leu Glu Lys
    1205                1210                1215

Glu Lys  Ser Glu Phe Lys Leu  Glu Leu Asp Asp Val  Thr Ser Asn
    1220                1225                1230

Met Glu  Gln Ile Ile Lys Ala  Lys Ala Asn Leu Glu  Lys Met Cys
    1235                1240                1245

Arg Thr  Leu Glu Asp Gln Met  Asn Glu His Arg Ser  Lys Ala Glu
    1250                1255                1260

Glu Thr  Gln Arg Ser Val Asn  Asp Leu Thr Ser Gln  Arg Ala Lys
    1265                1270                1275

Leu Gln  Thr Glu Asn Gly Glu  Leu Ser Arg Gln Leu  Asp Glu Lys
    1280                1285                1290

Glu Ala  Leu Ile Ser Gln Leu  Thr Arg Gly Lys Leu  Thr Tyr Thr
    1295                1300                1305

Gln Gln  Leu Glu Asp Leu Lys  Arg Gln Leu Glu Glu  Glu Val Lys
    1310                1315                1320

Ala Lys  Asn Ala Leu Ala His  Ala Leu Gln Ser Ala  Arg His Asp
    1325                1330                1335

Cys Asp  Leu Leu Arg Glu Gln  Tyr Glu Glu Glu Thr  Glu Ala Lys
    1340                1345                1350

Ala Glu  Leu Gln Arg Val Leu  Ser Lys Ala Asn Ser  Glu Val Ala
    1355                1360                1365

Gln Trp  Arg Thr Lys Tyr Glu  Thr Asp Ala Ile Gln  Arg Thr Glu
    1370                1375                1380
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Glu Leu  Glu Glu Ala Lys Lys  Lys Leu Ala Gln Arg  Leu Gln Glu
    1385                1390                1395

Ala Glu  Glu Ala Val Glu Ala  Val Asn Ala Lys Cys  Ser Ser Leu
    1400                1405                1410

Glu Lys  Thr Lys His Arg Leu  Gln Asn Glu Ile Glu  Asp Leu Met
    1415                1420                1425

Val Asp  Val Glu Arg Ser Asn  Ala Ala Ala Ala Ala  Leu Asp Lys
    1430                1435                1440

Lys Gln  Arg Asn Phe Asp Lys  Ile Leu Ala Glu Trp  Lys Gln Lys
    1445                1450                1455

Tyr Glu  Glu Ser Gln Ser Glu  Leu Glu Ser Ser Gln  Lys Glu Ala
    1460                1465                1470

Arg Ser  Leu Ser Thr Glu Leu  Phe Lys Leu Lys Asn  Ala Tyr Glu
    1475                1480                1485

Glu Ser  Leu Glu His Leu Glu  Thr Phe Lys Arg Glu  Asn Lys Asn
    1490                1495                1500

Leu Gln  Glu Glu Ile Ser Asp  Leu Thr Glu Gln Leu  Gly Ser Ser
    1505                1510                1515

Gly Lys  Thr Ile His Glu Leu  Glu Lys Val Arg Lys  Gln Leu Glu
    1520                1525                1530

Ala Glu  Lys Met Glu Leu Gln  Ser Ala Leu Glu Glu  Ala Glu Ala
    1535                1540                1545

Ser Leu  Glu His Glu Glu Gly  Lys Ile Leu Arg Ala  Gln Leu Glu
    1550                1555                1560

Phe Asn  Gln Ile Lys Ala Glu  Ile Glu Arg Lys Leu  Ala Glu Lys
    1565                1570                1575

Asp Glu  Glu Met Glu Gln Ala  Lys Arg Asn His Leu  Arg Val Val
    1580                1585                1590

Asp Ser  Leu Gln Thr Ser Leu  Asp Ala Glu Thr Arg  Ser Arg Asn
    1595                1600                1605

Glu Ala  Leu Arg Val Lys Lys  Lys Met Glu Gly Asp  Leu Asn Glu
    1610                1615                1620

Met Glu  Ile Gln Leu Ser His  Ala Asn Arg Met Ala  Ala Glu Ala
    1625                1630                1635

Gln Lys  Gln Val Lys Ser Leu  Gln Ser Leu Leu Lys  Asp Thr Gln
    1640                1645                1650

Ile Gln  Leu Asp Asp Ala Val  Arg Ala Asn Asp Asp  Leu Lys Glu
    1655                1660                1665

Asn Ile  Ala Ile Val Glu Arg  Arg Asn Asn Leu Leu  Gln Ala Glu
    1670                1675                1680

Leu Glu  Glu Leu Arg Ala Val  Val Glu Gln Thr Glu  Arg Ser Arg
    1685                1690                1695

Lys Leu  Ala Glu Gln Glu Leu  Ile Glu Thr Ser Glu  Arg Val Gln
    1700                1705                1710

Leu Leu  His Ser Gln Asn Thr  Ser Leu Ile Asn Gln  Lys Lys Lys
    1715                1720                1725

Met Asp  Ala Asp Leu Ser Gln  Leu Gln Thr Glu Val  Glu Glu Ala
    1730                1735                1740

Val Gln  Glu Cys Arg Asn Ala  Glu Glu Lys Ala Lys  Lys Ala Ile
    1745                1750                1755
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```
Thr Asp  Ala Ala Met Met Ala  Glu Glu Leu Lys Lys  Glu Gln Asp
    1760                1765                1770

Thr Ser  Ala His Leu Glu Arg  Met Lys Lys Asn Met  Glu Gln Thr
    1775                1780                1785

Ile Lys  Asp Leu Gln His Arg  Leu Asp Glu Ala Glu  Gln Ile Ala
    1790                1795                1800

Leu Lys  Gly Gly Lys Lys Gln  Leu Gln Lys Leu Glu  Ala Arg Val
    1805                1810                1815

Arg Glu  Leu Glu Asn Glu Leu  Glu Ala Glu Gln Lys  Arg Asn Ala
    1820                1825                1830

Glu Ser  Val Lys Gly Met Arg  Lys Ser Glu Arg Arg  Ile Lys Glu
    1835                1840                1845

Leu Thr  Tyr Gln Thr Glu Glu  Asp Arg Lys Asn Leu  Leu Arg Leu
    1850                1855                1860

Gln Asp  Leu Val Asp Lys Leu  Gln Leu Lys Val Lys  Ala Tyr Lys
    1865                1870                1875

Arg Gln  Ala Glu Glu Ala Glu  Glu Gln Ala Asn Thr  Asn Leu Ser
    1880                1885                1890

Lys Phe  Arg Lys Val Gln His  Glu Leu Asp Glu Ala  Glu Glu Arg
    1895                1900                1905

Ala Asp  Ile Ala Glu Ser Gln  Val Asn Lys Leu Arg  Ala Lys Ser
    1910                1915                1920

Arg Asp  Ile Gly Thr Lys Gly  Leu Asn Glu Glu
    1925                1930


<210> SEQ ID NO 11
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 11

Ser Ser Asp Ala Ala Arg Glu Pro Arg Pro Ala Pro Ala Pro Ile
1               5                   10                  15


<210> SEQ ID NO 12
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 12

Val Asp Glu Glu Arg Tyr Asp Ile Glu Ala Lys Val Thr Lys Asn
1               5                   10                  15


<210> SEQ ID NO 13
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 13

Asp Ile Glu Ala Lys Val Thr Lys Asn Ile Thr Glu Ile Ala Asp
1               5                   10                  15


<210> SEQ ID NO 14
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 14
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Leu Asp Leu Arg Ala His Leu Lys Gln Val Lys Lys Glu Asp Thr
1               5                   10                  15


<210> SEQ ID NO 15
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 15

Ala Leu Ser Gly Met Glu Gly Arg Lys Lys Lys Phe Glu Ser
1               5                   10
```

What is claimed is:

1. A reagent for use in an immunoassay for determining the presence or amount of at least one protein in a test sample, the reagent comprising:

at least one peptide comprising at least 5 consecutive amino acid residues wherein the peptide is derived from said protein and further wherein said reagent is used to block the interaction between an endogenous antibody and said protein in the test sample.

2. The reagent of claim **1**, wherein the protein is selected from the group consisting of: cardiac troponin I (SEQ ID NO:1), cardiac troponin T (SEQ ID NO:2), thyroid stimulating hormone (TSH) (SEQ ID NO:3), beta-human chorionic gonadotropin (beta-HCG) (SEQ ID NO:4), myeloperoxidase (MPO) (SEQ ID NO:5), prostate specific antigen (PSA) (SEQ ID NO:6), human B-type natriuretic peptide (hBNP) (SEQ ID NO:7), myosin light chain 2 (SEQ ID NO:8), myosin-6 (SEQ ID NO:9) and myosin-7 (SEQ ID NO:10).

3. The reagent of claim **1**, wherein the peptide has a length of 5 consecutive amino acids to 15 consecutive amino acids.

4. The reagent of claim **1**, wherein the protein is cardiac troponin I, and the peptide has a sequence comprising at least five consecutive amino acid residues from a sequence selected from the group consisting of SSDAAREPRPAPAPI (SEQ ID NO:11), VDEERYDIEAKVTKN (SEQ ID NO:12), DIEAKVTKNITEIAD (SEQ ID NO:13), LDLRAHLKQVKKEDT (SEQ ID NO:14), and ALSGMEGRKKKFES (SEQ ID NO:15).

5. A reagent for use in an immunoassay for determining the presence or amount of at cardiac troponin I in a test sample, the reagent comprising a peptide having a sequence comprising at least five consecutive amino acid residues from a sequence selected from the group consisting of SSDAAREPRPAPAPI (SEQ ID NO:11), VDEERYDIEAKVTKN (SEQ ID NO:12), DIEAKVTKNITEIAD (SEQ ID NO:13), LDLRAHLKQVKKEDT (SEQ ID NO:14), and ALSGMEGRKKKFES (SEQ ID NO:15).

6. A method of detecting at least one protein of interest in a test sample, the method comprising the steps of:

a. preparing a first mixture comprising a test sample suspected of containing at least one protein of interest and at least one reagent, wherein said reagent (1) is at least one peptide comprising at least 5 consecutive amino acid residues derived from said protein that binds to the antibody of interest; and (2) disrupts the interaction between an endogenous antibody in the test sample and the antigen;

b. preparing a second mixture comprising the first mixture and a first specific binding partner, wherein the first specific binding partner comprises an antibody, wherein the antibody binds with the protein of interest to form a first specific binding partner-protein complex; and

c. contacting the second mixture with a second specific binding partner, wherein the second specific binding partner comprises an antibody that has been conjugated to a detectable label and further wherein the second specific binding partner binds to the first specific binding partner-protein complex to form a first specific binding partner-protein-second specific binding partner complex; and

d. measuring the signal generated by or emitted from the detectable label and detecting the protein of interest in the test sample.

7. The method of claim **6**, wherein the protein is selected from the group consisting of: cardiac troponin I, cardiac troponin T, thyroid stimulating hormone (TSH), beta-human chorionic gonadotropin (beta-HCG), myeloperoxidase (MPO), prostate specific antigen (PSA), human B-type natriuretic peptide (hBNP), myosin light chain 2, myosin-6 and myosin-7.

8. The method of claim **6**, wherein the test sample is whole blood, serum or plasma.

9. The method of claim **6**, wherein the first specific binding partner is immobilized to a solid phase either before or after the formation of the first specific binding partner-protein complex.

10. The method of claim **6**, wherein the second specific binding partner is immobilized to a solid phase either before or after formation of the first specific binding partner-protein-second specific binding partner complex.

11. The method of claim **6**, wherein the detectable label is selected from the group consisting of a radioactive label, an enzymatic label, a chemiluminescent label, a fluorescence label, a thermometric label, and an immuno-polymerase chain reaction label.

12. The method of claim **6**, wherein said detectable label is an acridinium compound.

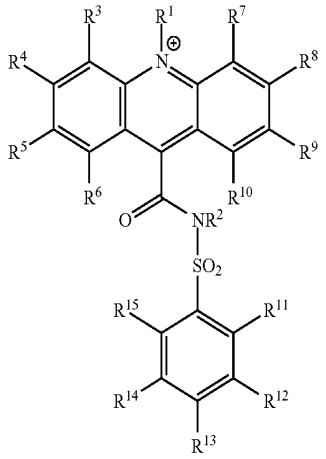
13. The method of claim **12** further comprising:

a. generating or providing a source of hydrogen peroxide to the second mixture contacted with a second specific binding partner;

b. adding a basic solution to the mixture of step (a);

c. measuring the light signal generated or emitted in step (b) and detecting the protein of interest in the sample.

14. The method of claim **12**, wherein the acridinium compound is an acridinium-9-carboxamide having a structure according to formula I:

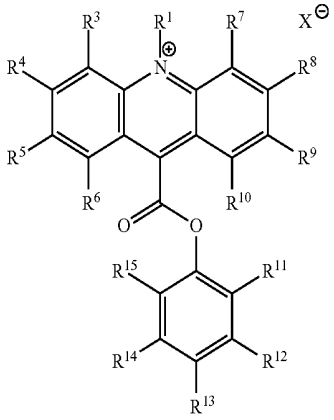


I

wherein R^1 and R^2 are each independently selected from the group consisting of: alkyl, alkenyl, alkynyl, aryl or aralkyl, sulfoalkyl, carboxyalkyl and oxoalkyl, and

wherein R^3 through R^{15} are each independently selected from the group consisting of: hydrogen, alkyl, alkenyl, alkynyl, aryl or aralkyl, amino, amido, acyl, alkoxyl, hydroxyl, carboxyl, halogen, halide, nitro, cyano, sulfo, sulfoalkyl, carboxyalkyl and oxoalkyl; and optionally, if present, $X^{\ominus}$ is an anion.

15. The method of claim **12**, wherein the acridinium compound is an acridinium-9-carboxylate aryl ester having a structure according to formula II:



II

wherein R1 is an alkyl, alkenyl, alkynyl, aryl or aralkyl, sulfoalkyl, carboxyalkyl and oxoalkyl; and

wherein R3 through R15 are each independently selected from the group consisting of: hydrogen, alkyl, alkenyl, alkynyl, aryl or aralkyl, amino, amido, acyl, alkoxyl, hydroxyl, carboxyl, halogen, halide, nitro, cyano, sulfo, sulfoalkyl, carboxyalkyl and oxoalkyl; and optionally, if present, XΘ is an anion.

16. The method of claim **6**, wherein the reagent is a peptide having a length of 5 consecutive amino acids to 15 consecutive amino acids.

17. The method of claim **6**, wherein the protein is cardiac troponin I, and the peptide has a sequence comprising at least five consecutive amino acid residues from a sequence selected from the group consisting of SSDAAREPRPAPAPI (SEQ ID NO:11), VDEERYDIEAKVTKN (SEQ ID NO:12), DIEAKVTKNITEIAD (SEQ ID NO:13), LDLRAHLKQVKKEDT (SEQ ID NO:14), and ALSGMEGRKKKFES (SEQ ID NO:15).

18. The method of claim **6**, further comprising the step of quantifying the amount of protein of interest in the test sample by relating the amount of signal in step (d) to the amount of the one or more proteins of interest in the test sample either by use of a standard curve for the protein of interest or by comparison to a reference standard.

19. The method of claim **7**, wherein the method is adapted for use in an automated system or semi-automated system.

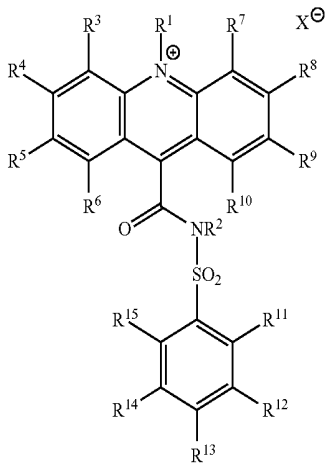
20. A kit for detecting and/or quantifying at least one protein of interest in a test sample, the kit comprising: the reagent of claim **1**; a capture reagent comprising an antibody that binds to the protein of interest; and instructions for detecting and/or quantifying at least one protein of interest in a test sample.

21. The kit of claim **20**, wherein the kit further comprises a conjugate comprising an antibody conjugated to a detectable label.

22. The kit of claim **21**, wherein the detectable label is selected from the group consisting of a radioactive label, an enzymatic label, a chemiluminescent label, a fluorescence label, a thermometric label, and an immuno-polymerase chain reaction label.

23. The kit of claim **22**, wherein the detectable label is an acridinium compound.

24. The kit of claim **23**, wherein the acridinium compound is an acridinium-9-carboxamide having a structure according to formula I:



I

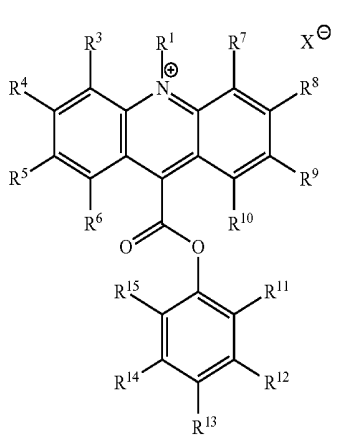
wherein R^1 and R^2 are each independently selected from the group consisting of: alkyl, alkenyl, alkynyl, aryl or aralkyl, sulfoalkyl, carboxyalkyl and oxoalkyl, and

wherein R^3 through R^{15} are each independently selected from the group consisting of: hydrogen, alkyl, alkenyl,

alkynyl, aryl or aralkyl, amino, amido, acyl, alkoxyl, hydroxyl, carboxyl, halogen, halide, nitro, cyano, sulfo, sulfoalkyl, carboxyalkyl and oxoalkyl; and

optionally, if present, $X^{\ominus}$ is an anion.

25. The kit of claim **23**, wherein the acridinium compound is an acridinium-9-carboxylate aryl ester having a structure according to formula II:



II

wherein R1 is an alkyl, alkenyl, alkynyl, aryl or aralkyl, sulfoalkyl, carboxyalkyl and oxoalkyl; and

wherein R3 through R15 are each independently selected from the group consisting of: hydrogen, alkyl, alkenyl, alkynyl, aryl or aralkyl, amino, amido, acyl, alkoxyl, hydroxyl, carboxyl, halogen, halide, nitro, cyano, sulfo, sulfoalkyl, carboxyalkyl and oxoalkyl; and

optionally, if present, $X^{\ominus}$ is an anion.

26. The kit of claim **23**, further comprising a basic solution.

27. The kit of claim **26**, wherein the basic solution is a solution having a pH of at least about 10.

28. The kit of claim **23**, further comprising a hydrogen peroxide source.

29. The kit of claim **28**, wherein the hydrogen peroxide source comprises a buffer or a solution containing hydrogen peroxide.

30. The kit of claim **28**, wherein the hydrogen peroxide source comprises a hydrogen peroxide generating enzyme.

31. The kit of claim **30**, wherein the hydrogen peroxide generating enzyme is selected from the group consisting of: (R)-6-hydroxynicotine oxidase, (S)-2-hydroxy acid oxidase, (S)-6-hydroxynicotine oxidase, 3-aci-nitropropanoate oxidase, 3-hydroxyanthranilate oxidase, 4-hydroxymandelate oxidase, 6-hydroxynicotinate dehydrogenase, abscisic-aldehyde oxidase, acyl-CoA oxidase, alcohol oxidase, aldehyde oxidase, amine oxidase, amine oxidase (copper-containing), amine oxidase (flavin-containing), aryl-alcohol oxidase, aryl-aldehyde oxidase, catechol oxidase, cholesterol oxidase, choline oxidase, columbamine oxidase, cyclohexylamine oxidase, cytochrome c oxidase, D-amino-acid oxidase, D-arabinono-1,4-lactone oxidase, D-arabinono-1,4-lactone oxidase, D-aspartate oxidase, D-glutamate oxidase, D-glutamate(D-aspartate) oxidase, dihydrobenzophenanthridine oxidase, dihydroorotate oxidase, dihydrouracil oxidase, dimethylglycine oxidase, D-mannitol oxidase, ecdysone oxidase, ethanolamine oxidase, galactose oxidase, glucose oxidase, glutathione oxidase, glycerol-3-phosphate oxidase, glycine oxidase, glyoxylate oxidase, hexose oxidase, hydroxyphytanate oxidase, indole-3-acetaldehyde oxidase, lactic acid oxidase, L-amino-acid oxidase, L-aspartate oxidase, L-galactonolactone oxidase, L-glutamate oxidase, L-gulonolactone oxidase, L-lysine 6-oxidase, L-lysine oxidase, long-chain-alcohol oxidase, L-pipecolate oxidase, L-sorbose oxidase, malate oxidase, methanethiol oxidase, monoamino acid oxidase, N^6-methyl-lysine oxidase, N-acylhexosamine oxidase, NAD(P)H oxidase, nitroalkane oxidase, N-methyl-L-amino-acid oxidase, nucleoside oxidase, oxalate oxidase, polyamine oxidase, polyphenol oxidase, polyvinyl-alcohol oxidase, prenylcysteine oxidase, protein-lysine 6-oxidase, putrescine oxidase, pyranose oxidase, pyridoxal 5'-phosphate synthase, pyridoxine 4-oxidase, pyrroloquinoline-quinone synthase, pyruvate oxidase, pyruvate oxidase (CoA-acetylating), reticuline oxidase, retinal oxidase, rifamycin-B oxidase, sarcosine oxidase, secondary-alcohol oxidase, sulfite oxidase, superoxide dismutase, superoxide reductase, tetrahydroberberine oxidase, thiamine oxidase, tryptophan α,β-oxidase, urate oxidase (uricase, uric acid oxidase), vanillyl-alcohol oxidase, xanthine oxidase, xylitol oxidase and combinations thereof.

32. The kit of claim **20**, wherein the protein is cardiac troponin I, cardiac troponin T, thyroid stimulating hormone (TSH), beta-human chorionic gonadotropin (beta-HCG), myeloperoxidase (MPO), prostate specific antigen (PSA), human B-type natriuretic peptide (hBNP), myosin light chain 2, myosin-6 or myosin-7.

33. The kit of claim **20**, wherein the reagent is a peptide having a length of 5 consecutive amino acids to 15 consecutive amino acids.

34. The kit of claim **33**, wherein the protein is cardiac troponin I, and the peptide has a sequence comprising at least five consecutive amino acid residues from a sequence selected from the group consisting of SSDAAREPRPAPAPI (SEQ ID NO:11), VDEERYDIEAKVTKN (SEQ ID NO:12), DIEAKVTKNITEIAD (SEQ ID NO:13), LDLRAHLKQVKKEDT (SEQ ID NO:14), and ALSGMEGRKKKFES (SEQ ID NO:15).

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摘要(译)

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