TABLE 2		
SEQ ID NO.	**DESCRIPTION**	**SEQUENCE (NUCLEOTIDE SEQUENCES ARE 5'-3')**
		tctccgggtaaagtcgacggagctagcagccccgtgaacgtgagcagccccagc gtgcaggatatcatgggccctggagctcgcagacagggcaggattgtgcaggga aggcctgagatgtgcttctgcccacccccctaccccactccctccccttcggatc ttaacactgggcactcacacacccaccccatgctcctctccaggctcagcagca ggtacgtacccaaccatgggctcgcaggccctgcccccggggcccatgcagacc ctcatctttttcgacatggaggccactggcttgcccttctcccagcccaaggtc acggagctgtgcctgctggctgtccacagatgtgccctggagagccccccccacc tctcaggggccacctcccacagttcctccaccaccgcgtgtggtagacaagctc tccctgtgtgtggctccggggaaggcctgcagccctgcagccagcgagatcaca ggtctgagcacagctgtgctggcagcgcatgggcgtcaatgttttgatgacaac ctggccaacctgctcctagccttcctgcggcgccagccacagccctggtgcctg gtggcacacaatggtgaccgctacgacttccccctgctccaagcagagctggct atgctgggcctcaccagtgctctggatggtgccttctgtgtggatagcatcact gcgctgaaggccctggagcgagcaagcagcccctcagaacacggcccaaggaag agctacagcctaggcagcatctacactcgcctgtatgggcagtcccctccagac tcgcacacggctgagggtgatgtcctggccctgctcagcatctgtcagtggaga ccacaggccctgctgcggtgggtggatgctcacgccaggcctttcggcaccatc aggcccatgtatggggtcacagcctctgctaggaccaaatgataatctaga
207	huVK3LP-hDNase1L3-hIgG1-WT-NLG-hTREX1-72AA	metpaqllfllllwlpdttgmricsfnvrsfgeskqedknamdvivkvikrcdi ilvmeikdsnnricpilmeklnrnsrrgitynyvissrlgrntykeqyaflyke klvsvkrsyhyhdyqdgdadvfsrepfvvwfqsphtavkdfviiplhttpetsv keidelvevytdvkhrwkaenfifmgdfnagcsyvpkkawknirlrtdprfvwl igdqedttvkkstncaydrivlrgqeivssvvpksnsvfdfqkayklteeeald vsdhfpvefklqssraftnskksvtlrkktkskrsdlepkssdkthtcppcpap ellggpsvflfppkpkdtlmisrtpevtcvvvdvshedpevkfnwyvdgvevhn aktkpreeqynstyrvvsvltvlhqdwlngkeykckvsnkalpapiektiskak gqprepqvytlppsrdeltknqvsltclvkgfypsdiavewesngqpennyktt ppvldsdgsfflyskltvdksrwqqgnvfscsvmhealhnhytqkslslspgkv dgasspvnvsspsvqdimgpgarrqgrivqgrpemcfcppptplpplriltlgt htptpcsspgsaagtyptmgsqalppgpmqtliffdmeatglpfsqpkvtelcl lavhrcalespptsqgppptvpppprvvdklslcvapgkacspaaseitglsta vlaahgrqcfddnlanlllaflrrqpqpwclvahngdrydfpllqaelamlglt saldgafcvdsitalkalerasppsehgprksyslgsiytrlygqsppdshtae gdvlallsicqwrpqallrwvdaharpfgtirpmygvtasartk*
208	(G4S)10	ggggsggggsggggsggggsggggsggggsggggsggggsggggsggggs
209	(G4S)3	ggggsggggsggggs
210	(G4S)	ggggs
211	(G4S)6	ggggsggggsggggsggggsggggsggggs
212	OligodT 18mer	ttttttttttttttttt
213	mRNase-mIgG2a P238S, K322S, P331S (nucleotide sequence)	gttaagcttg ccacc atg ggt ctg gag aag tcc ctc att ctg ttt cca ttg ttt ttc ctg ctg ctt gga tgg gtc cag cct tcc ccg ggc agg gaa tct gca gca cag aag ttt cag cgg cag cac atg gat cca gat ggt tcc tcc atc aac agc ccc acc tac tgc aac caa atg atg aaa cgc cgg gat atg aca aat ggg tca tgc aag ccc gtg aac acc ttc gtg cat gag ccc ttg gca gat gtc cag gcc gtc tgc tcc cag gaa aat gtc acc tgc aag aac agg aag agc aac tgc tac aag agc agc tct gcc ctg cac atc act gac tgc cac ctg aag ggc aac tcc aag tat ccc aac tgt gac tac aag acc act caa tac cag aag cac atc att gtg gcc tgt gaa ggg aac ccc tac gta cca gtc cac ttt gat gct act gtg ctc gag ccc aga ggt ctc aca atc aag ccc tct cct cca tgc aaa tgc cca gca cct aac ctc ttg ggt gga tca tcc gtc ttc atc ttc cct cca aag atc aag gat gta ctc atg atc tcc ctg agc ccc atg gtc aca tgt gtg gtg gtg gat gtg agc gag gat gac cca gac gtc cag atc agc tgg ttt gtg aac aac gtg gaa gta cac aca gct cag aca caa acc

TABLE 2		
SEQ ID NO.	**DESCRIPTION**	**SEQUENCE (NUCLEOTIDE SEQUENCES ARE 5'-3')**
		cat aga gag gat tac aac agt act ctc cgg gtg gtc agt gcc ctc ccc atc cag cac cag gac tgg atg agt ggc aag gag ttc aaa tgc tcg gtc aac aac aaa gac ctc cca gcg tcc atc gag aga acc atc tca aaa ccc aga ggg cca gta aga gct cca cag gta tat gtc ttg cct cca cca gca gaa gag atg act aag aaa gag ttc agt ctg acc tgc atg atc aca ggc ttc tta cct gcc gaa att gct gtg gac tgg acc agc aat ggg cgt aca gag caa aac tac aag aac acc gca aca gtc ctg gac tct gat ggt tct tac ttc atg tac agc aag ctc aga gta caa aag agc act tgg gaa aga gga agt ctt ttc gcc tgc tca gtg gtc cac gag ggt ctg cac aat cac ctt acg act aag agc ttc tct cgg act ccg ggt aaa tgataatcta gaa
214	mRNase-mIgG2a P238S, K322S, P331S (amino acid sequence)	Met Gly Leu Glu Lys Ser Leu Ile Leu Phe Pro Leu Phe Phe Leu Leu Leu Gly Trp Val Gln Pro Ser Pro Gly Arg Glu Ser Ala Ala Gln Lys Phe Gln Arg Gln His Met Asp Pro Asp Gly Ser Ser Ile Asn Ser Pro Thr Tyr Cys Asn Gln Met Met Lys Arg Arg Asp Met Thr Asn Gly Ser Cys Lys Pro Val Asn Thr Phe Val His Glu Pro Leu Ala Asp Val Gln Ala Val Cys Ser Gln Glu Asn Val Thr Cys Lys Asn Arg Lys Ser Asn Cys Tyr Lys Ser Ser Ser Ala Leu His Ile Thr Asp Cys His Leu Lys Gly Asn Ser Lys Tyr Pro Asn Cys Asp Tyr Lys Thr Thr Gln Tyr Gln Lys His Ile Ile Val Ala Cys Glu Gly Asn Pro Tyr Val Pro Val His Phe Asp Ala Thr Val Leu Glu Pro Arg Gly Leu Thr Ile Lys Pro Ser Pro Pro Cys Lys Cys Pro Ala Pro Asn Leu Leu Gly Gly Ser Ser Val Phe Ile Phe Pro Pro Lys Ile Lys Asp Val Leu Met Ile Ser Leu Ser Pro Met Val Thr Cys Val Val Val Asp Val Ser Glu Asp Asp Pro Asp Val Gln Ile Ser Trp Phe Val Asn Asn Val Glu Val His Thr Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser Thr Leu Arg Val Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met Ser Gly Lys Glu Phe Lys Cys Ser Val Asn Asn Lys Asp Leu Pro Ala Ser Ile Glu Arg Thr Ile Ser Lys Pro Arg Gly Pro Val Arg Ala Pro Gln Val Tyr Val Leu Pro Pro Pro Ala Glu Glu Met Thr Lys Lys Glu Phe Ser Leu Thr Cys Met Ile Thr Gly Phe Leu Pro Ala Glu Ile Ala Val Asp Trp Thr Ser Asn Gly Arg Thr Glu Gln Asn Tyr Lys Asn Thr Ala Thr Val Leu Asp Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu Arg Val Gln Lys Ser Thr Trp Glu Arg Gly Ser Leu Phe Ala Cys Ser Val Val His Glu Gly Leu His Asn His Leu Thr Thr Lys Ser Phe Ser Arg Thr Pro Gly Lys

CLAIMS

1. A polypeptide comprising an RNase and a variant Fc domain, wherein the RNase is operatively coupled, optionally with a linker, to the variant Fc domain, wherein the variant Fc domain is a variant human IgG1 Fc domain comprising an amino acid substitution which decreases binding, compared to wild-type, to an Fcγ receptor or a complement protein or both, wherein the polypeptide has a reduced effector function optionally selected from the group consisting of opsonization, phagocytosis, complement dependent cytotoxicity, and antibody-dependent cellular cytotoxicity.

2. The polypeptide of claim 1 wherein:

(a) the RNase is a human RNase, such as a human pancreatic RNase 1; and/or

(b) the Fc domain comprises a hinge domain, a CH2 domain and a CH3 domain; and/or

(c) a leader sequence, such as the human VK3LP peptide, is coupled to the N-terminus of the RNase.

3. The polypeptide of claim 1 or claim 2, wherein:

(a) the Fc domain comprises a modified hinge domain comprising at least one substitution, optionally wherein the modified hinge domain comprises a mutation in one or more of the three hinge cysteines, such as SCC or SSS; and/or

(b) wherein the Fc domain comprises a modified CH2 domain comprising at least one substitution, optionally wherein the substitution is selected from the group consisting of P238S, P331S, N297S or a combination thereof.

4. The polypeptide of claim 1 or claim 2, wherein

(a) the RNase comprises an amino acid sequence at least 90% identical to the amino acid sequence set forth in SEQ ID NO:149 optionally without its leader sequence, or comprises 100 or more contiguous amino acids from SEQ ID NO. 149; and/or

(b) the Fc domain comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97% or 98% identical to the amino acid sequence set forth in SEQ ID NO:145, optionally comprising a modified hinge domain comprising at least one substitution, optionally

wherein the modified hinge domain comprises a mutation in one or more of the three hinge cysteines, such as SCC or SSS; and/or optionally comprising one or more Fc mutations selected from P238S, P331S, K322S, and N279S.

5. The polypeptide of claim 1, wherein:

the polypeptide comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97% or 98% identical to the amino acid sequence set forth in SEQ ID NO:163, optionally without its leader sequence; or

the polypeptide comprises an amino acid sequence at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97% or 98% identical to the amino acid sequence set forth in SEQ ID NO:161, optionally without its leader sequence;

optionally wherein the Fc domain comprises a modified hinge domain comprising at least one substitution, optionally wherein the modified hinge domain comprises a mutation in one or more of the three hinge cysteines, such as SCC or SSS; and/or a modified CH2 domain comprising at least one substitution selected from the group consisting of P238S, P331S, N297S or combination thereof.

6. The polypeptide of any preceding claim, wherein:

the RNase is operatively coupled to the Fc domain via a linker domain, optionally wherein the linker domain is a polypeptide linker, such as a gly-ser linker; and/or

wherein the RNase is operatively coupled to the N-terminus of the Fc domain, optionally with a linker; and/or

wherein the RNase is operatively coupled to the C-terminus of the Fc domain, optionally with a linker; and/or

wherein the polypeptide comprises a human VK3LP peptide leader sequence coupled to the N-terminus of the RNase.

7. A composition comprising the polypeptide of any of the preceding claims and a pharmaceutically acceptable carrier.

8. A nucleic acid molecule encoding the polypeptide according to any of claims 1 to 6.

9. A recombinant expression vector comprising a nucleic acid molecule according to claim 8.

10. A host cell transformed with the recombinant expression vector according to claim 9.

11. A method of making the polypeptide of any of claims 1 to 6, comprising: providing a host cell comprising a nucleic acid sequence that encodes the polypeptide; and maintaining the host cell under conditions in which the polypeptide is expressed.

12. A polypeptide of any of claims 1 to 6 for use in a method for treating a condition associated with an abnormal immune response;

optionally wherein the condition is an autoimmune disease, optionally systemic lupus erythematosus (SLE), or optionally selected from the group consisting of insulin-dependent diabetes mellitus, multiple sclerosis, experimental autoimmune encephalomyelitis, rheumatoid arthritis, experimental autoimmune arthritis, myasthenia gravis, thyroiditis, an experimental form of uveoretinitis, Hashimoto's thyroiditis, primary myxoedema, thyrotoxicosis, pernicious anaemia, autoimmune atrophic gastritis, Addison's disease, premature menopause, male infertility, juvenile diabetes, Goodpasture's syndrome, pemphigus vulgaris, pemphigoid, sympathetic ophthalmia, phacogenic uveitis, autoimmune haemolytic anaemia, idiopathic leucopenia, primary biliary cirrhosis, active chronic hepatitis Hbs-ve, cryptogenic cirrhosis, ulcerative colitis, Sjogren's syndrome, scleroderma, Wegener's granulomatosis, polymyositis, dermatomyositis, discoid LE, systemic lupus erythematosus (SLE), and connective tissue disease.

13. A dimeric polypeptide comprising a polypeptide of any one of claims 1-6, optionally a homodimer.

14. A composition comprising the dimeric polypeptide of claim 13 and a pharmaceutically acceptable excipient.

15. A polypeptide of any of claims 1 to 6, a composition of claim 7, a dimeric polypeptide of claim 13 or a composition of claim 14, for use in a method of treating systemic lupus erythematosus (SLE).