

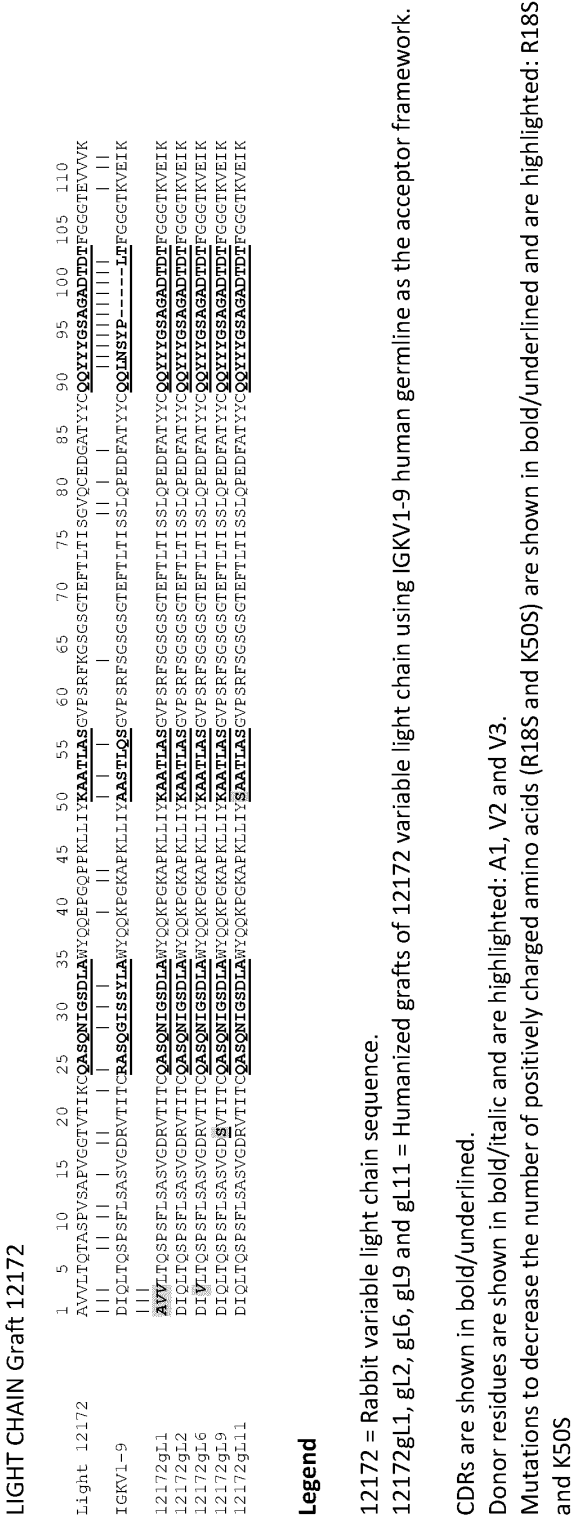


Figure 1

HEAVY CHAIN Graft 12172

Heavy 12172	1	5	10	15	20	25	30	35	40	45	50	55	60	65	70	75	80	85	90	95	100	105	110	115	120
	-QSLVESGGRLVPTGTLTCTAS GFLSSSYAMTWVRQAPCKGLEWIGLIYAGGSPSYASWAKGRFTIS KTST--TVDLKMTSTPTEDTATYFCAR GTGD TVYTVYFNIWGQGLVTVSS																								
IGHV3-66	EVQLVESGGGLVQPGGSLRLSCAAS GFTVYSNNYMSWVRQAPCKGLEWISYIYSGGSPYYADSVKGRFTIS RDNKNTLYLQNNSLRAEDTAVYYCAR-----YFDYWGQGLVTVSS																								
12172gH1	EVQLVESGGGLVQPGGSLRLSCAAS GFSLS SYAMTWVRQAPCKGLEWIGLIYAGGSPSYASWAKGRFTISKDSKNTLYLQNNSLRAEDTAVYYCAR GTGD TVYTVYFNIWGQGLVTVSS																								
12172gH2	EVQLVESGGGLVQPGGSLRLSCAAS GFSLS SYAMTWVRQAPCKGLEWIGLIYAGGSPSYASWAKGRFTISKDSKNTLYLQNNSLRAEDTAVYYCAR GTGD TVYTVYFNIWGQGLVTVSS																								
12172gH4	EVQLVESGGGLVQPGGSLRLSCAAS GFSLS SYAMTWVRQAPCKGLEWIGLIYAGGSPSYASWAKGRFTISKDSKNTLYLQNNSLRAEDTAVYYCAR GTGD TVYTVYFNIWGQGLVTVSS																								
12172gH6	EVQLVESGGGLVQPGGSLRLSCAAS GFSLS SYAMTWVRQAPCKGLEWIGLIYAGGSPSYASWAKGRFTISKDSKNTLYLQNNSLRAEDTAVYYCAR GTGD TVYTVYFNIWGQGLVTVSS																								
12172gH8	EVQLVESGGGLVQPGGSLRLSCAAS GFSLS SYAMTWVRQAPCKGLEWIGLIYAGGSPSYASWAKGRFTISKDSKNTLYLQNNSLRAEDTAVYYCAR GTGD TVYTVYFNIWGQGLVTVSS																								
12172gH9	EVQLVESGGGLVQPGGSLRLSCAAS GFSLS SYAMTWVRQAPCKGLEWIGLIYAGGSPSYASWAKGRFTISRDNSKNTLYLQNNSLRAEDTAVYYCAR GTGD TVYTVYFNIWGQGLVTVSS																								
12172gH10	EVQLVESGGGLVQPGGSLRLSCAAS GFSLS SYAMTWVRQAPCKGLEWIGLIYAGGSPSYASWAKGRFTISRDNSKNTLYLQNNSLRAEDTAVYYCAR GTGD TVYTVYFNIWGQGLVTVSS																								
12172gH11	EVQLVESGGGLVQPGGSLRLSCAAS GFSLS SYAMTWVRQAPCKGLEWIGLIYAGGSPSYASWAKGRFTISKDSKNTLYLQNNSLRAEDTAVYYCAR GTGD TVYTVYFNIWGQGLVTVSS																								
12172gH12	EVQLVESGGGLVQPGGSLRLSCAAS GFSLS SYAMTWVRQAPCKGLEWIGLIYAGGSPSYASWAKGRFTISKDSKNTLYLQNNSLRAEDTAVYYCAR GTGD TVYTVYFNIWGQGLVTVSS																								
12172gH26	EVQLVESGGGLVQPGGSLRLSCAAS GFSLS SYAMTWVRQAPCKGLEWIGLIYAGGSPSYASWAKGRFTISKDSKNTLYLQNNSLRAEDTAVYYCAR GTGD TVYTVYFNIWGQGLVTVSS																								
12172gH48	EVQLVESGGGLVQPGGSLRLSCAAS GFSLS SYAMTWVRQAPCKGLEWIGLIYAGGSPSYASWAKGRFTISKDSKNTLYLQNNSLRAEDTAVYYCAR GTGD TVYTVYFNIWGQGLVTVSS																								
12172gH49	EVQLVESGGGLVQPGGSLRLSCAAS GFSLS SYAMTWVRQAPCKGLEWIGLIYAGGSPSYASWAKGRFTISKDSKNTLYLQNNSLRAEDTAVYYCAR GTGD TVYTVYFNIWGQGLVTVSS																								

Legend

12172 = Rabbit variable heavy chain sequence.
12172gH1, gH2, gH4, gH6, gH8, gH9, gH10, gH11, gH12, gH26, gH48 and gH49 = Humanized grafts of 12172 variable heavy chain using IGHV3-66 human germline as the acceptor framework.

CDRs are shown in bold/underlined.
Donor residues are shown in bold/italic and are highlighted: T23, I48, G49, K71, S73 and V78.
Mutations to decrease the number of positively charged amino acids (K75S, K75Q and K75E) are shown in bold/underlined and are highlighted.

Figure 2

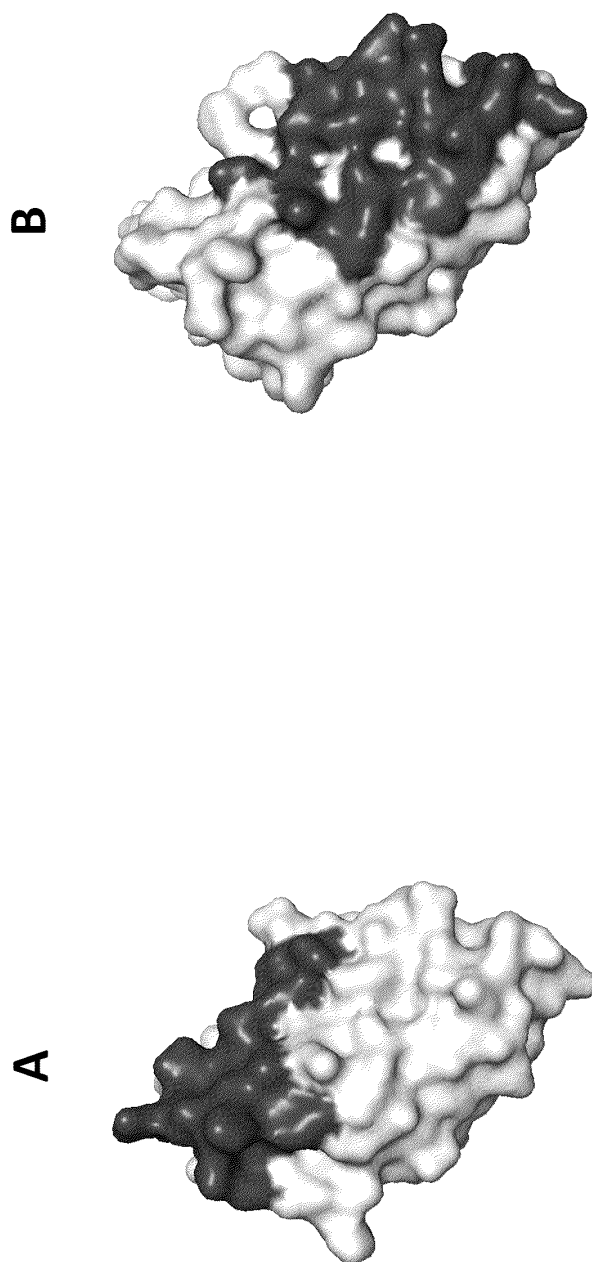


Figure 3

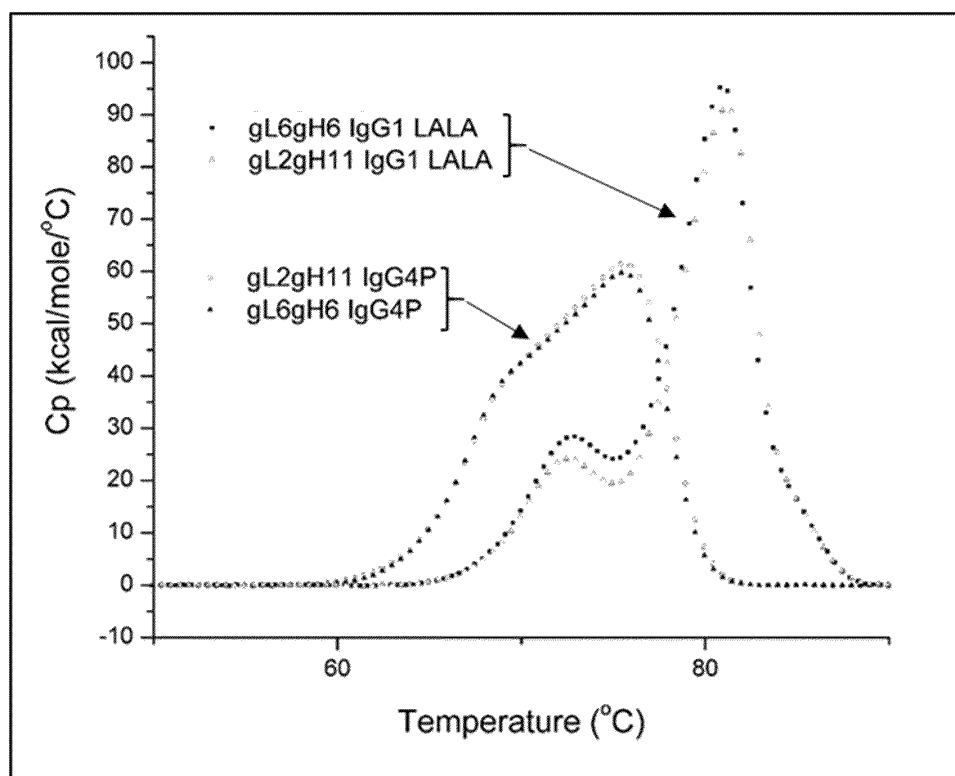


Figure 4

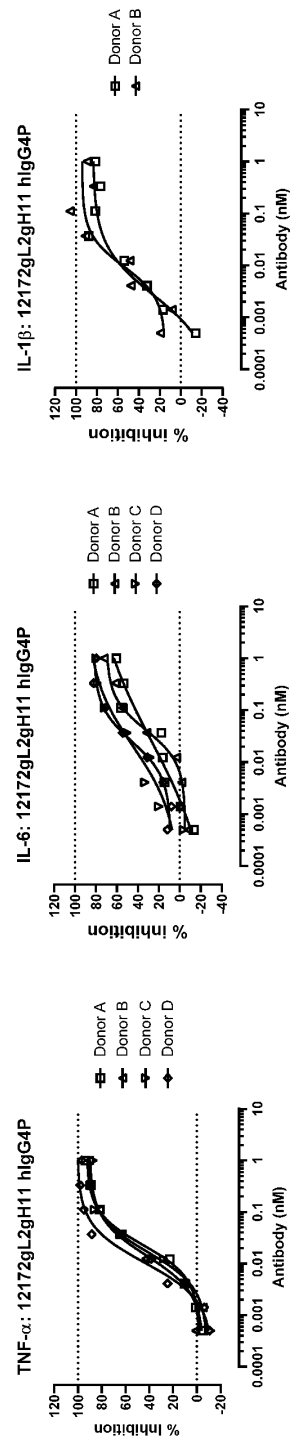


Figure 5

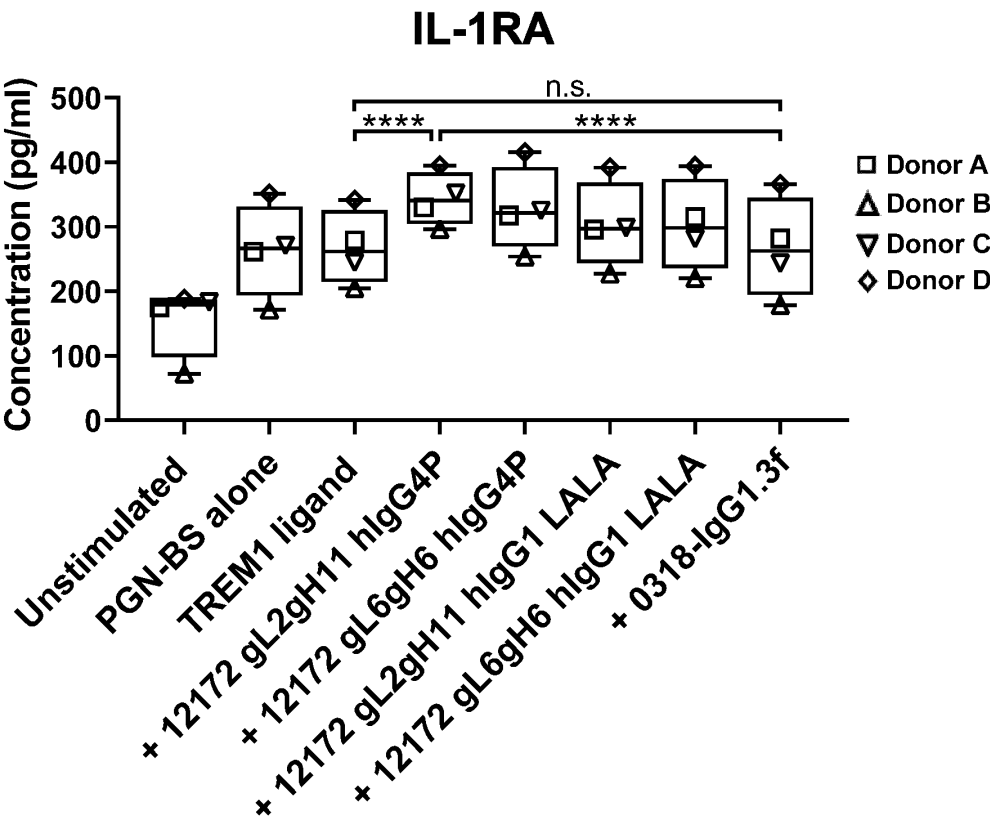


Figure 6

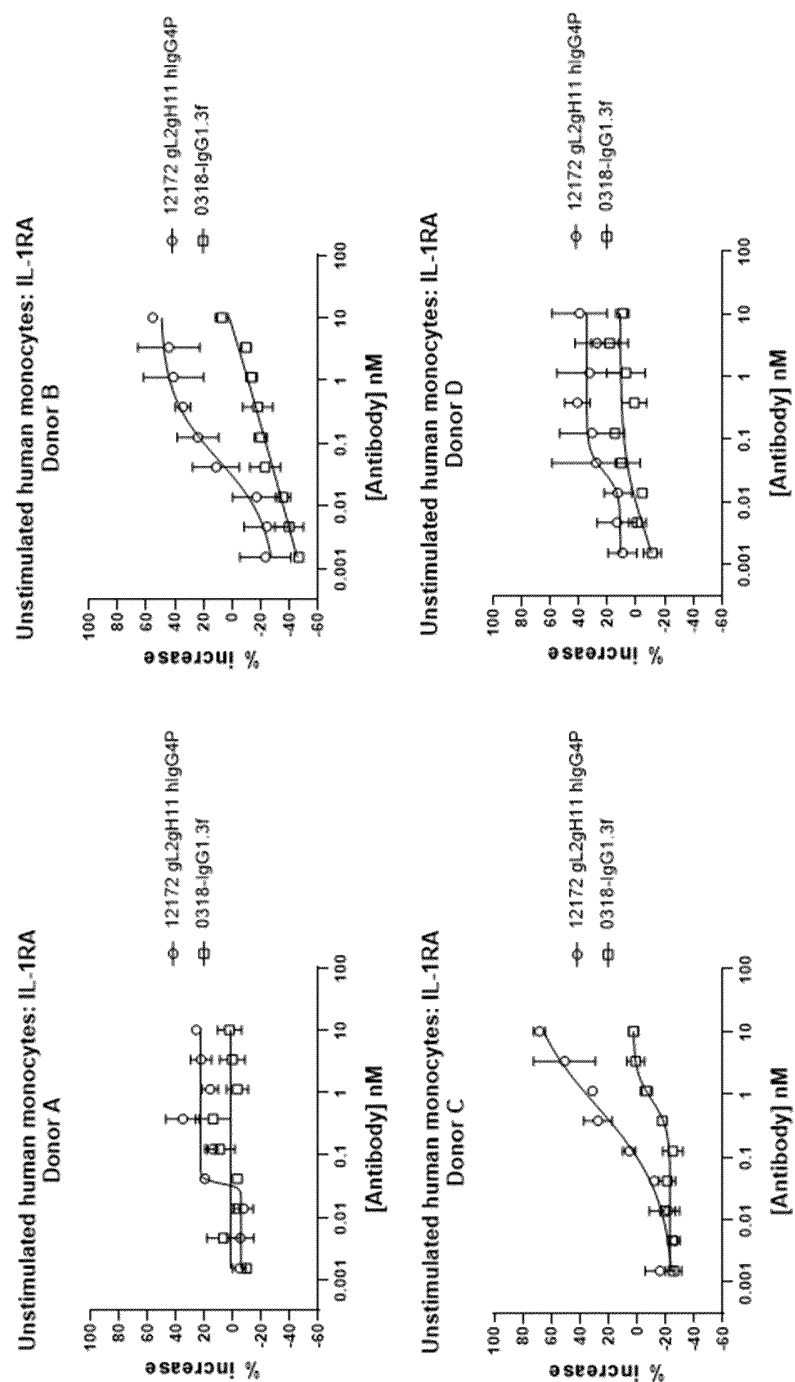


Figure 7

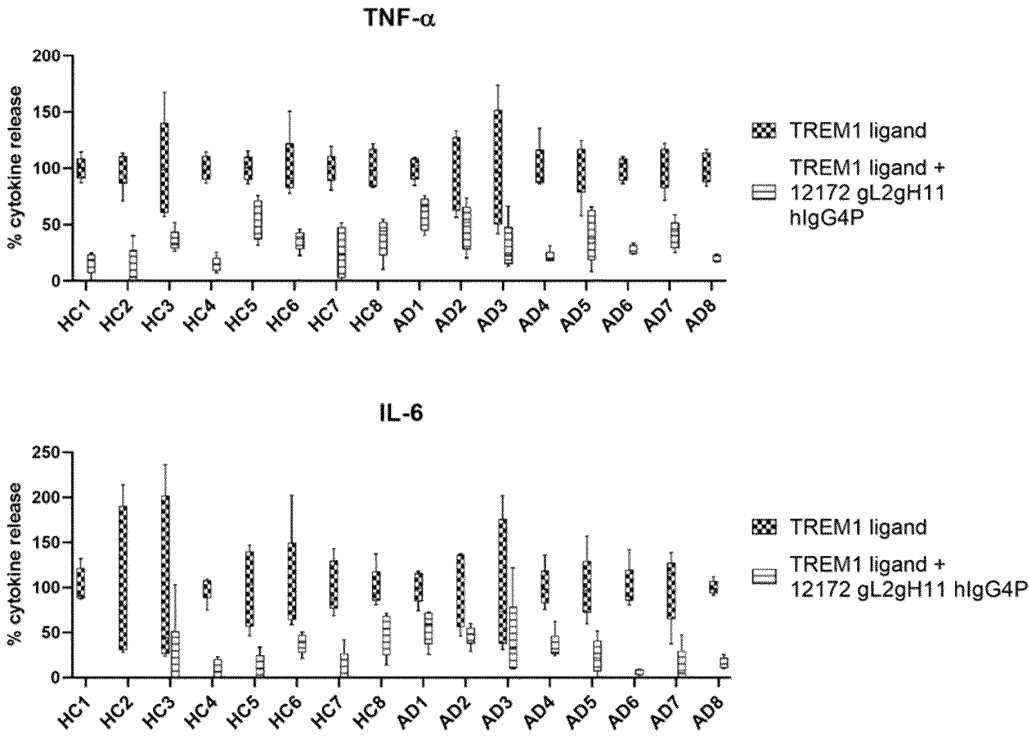


Figure 8

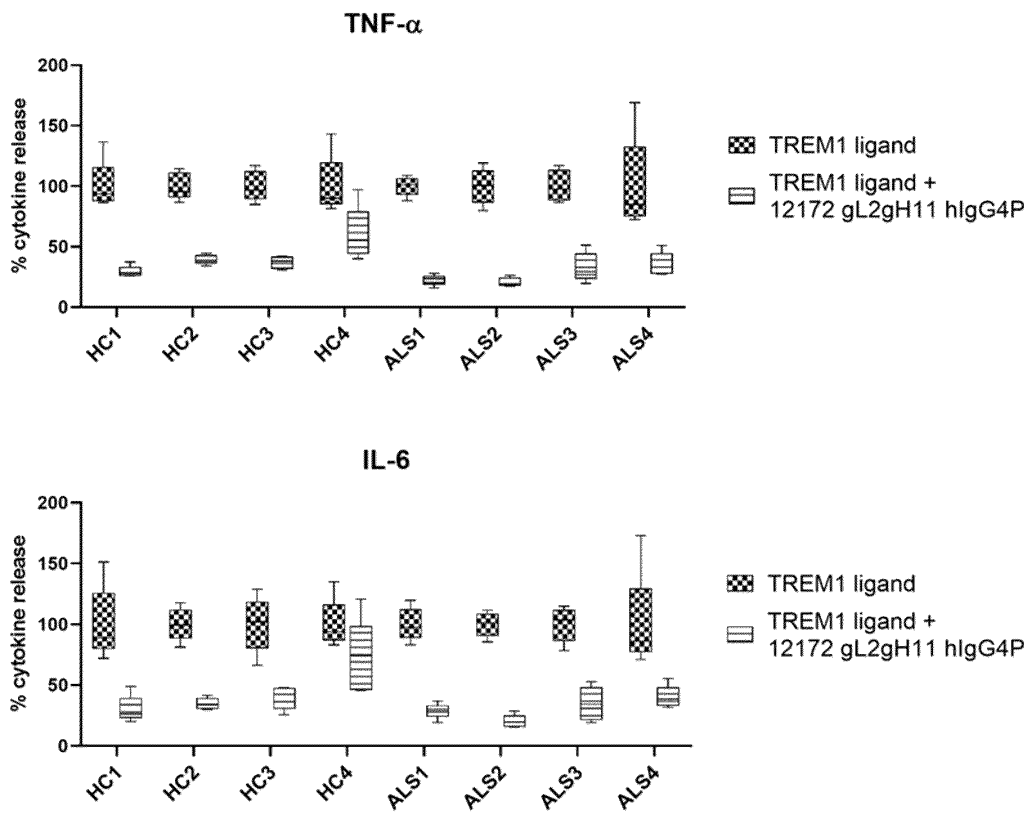


Figure 9

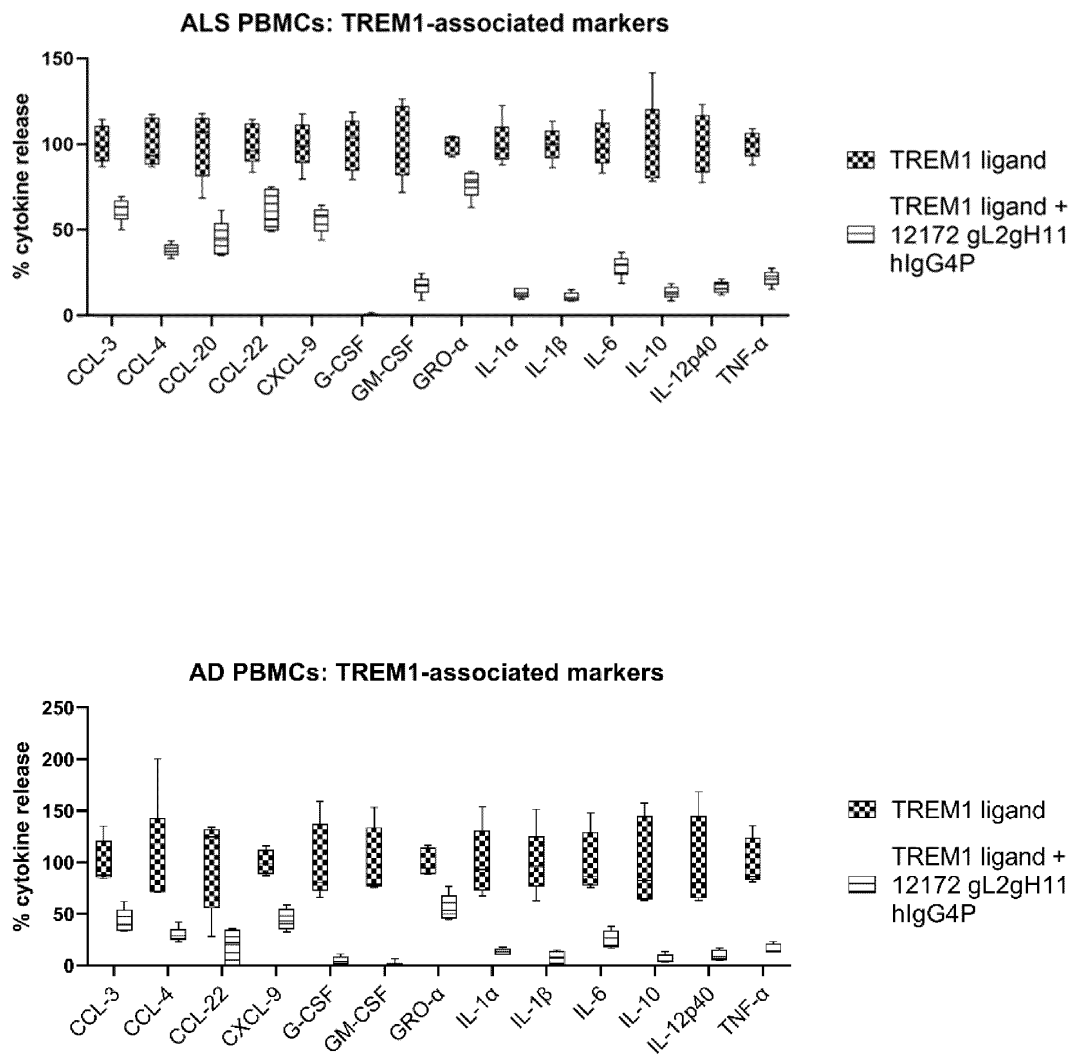


Figure 10

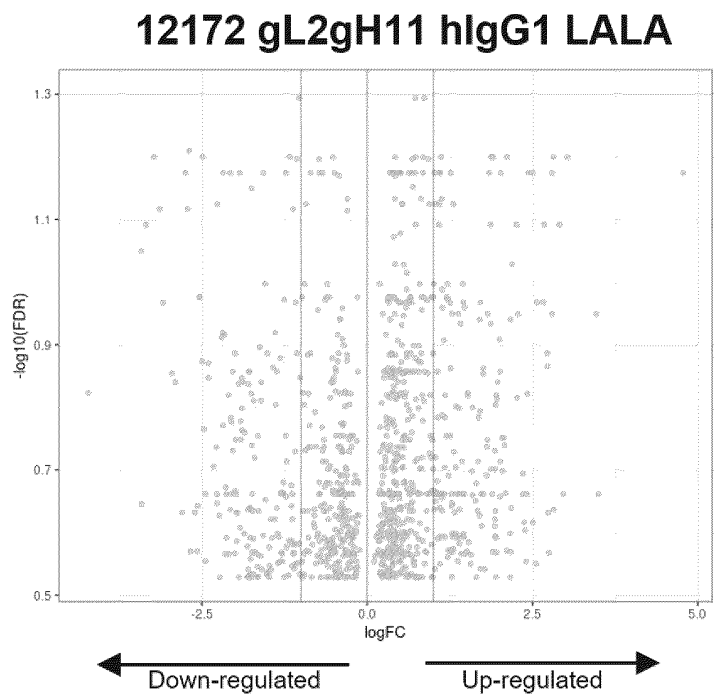
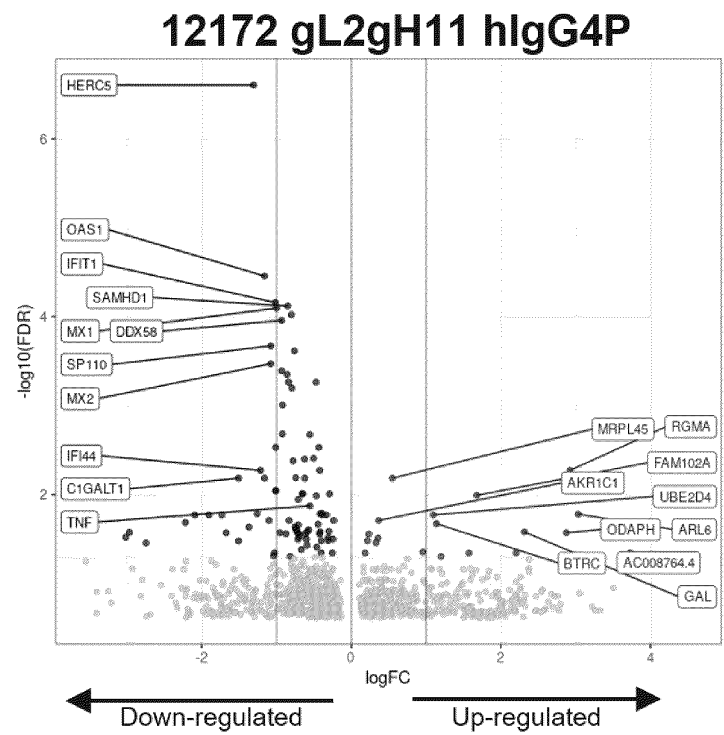


Figure 11A

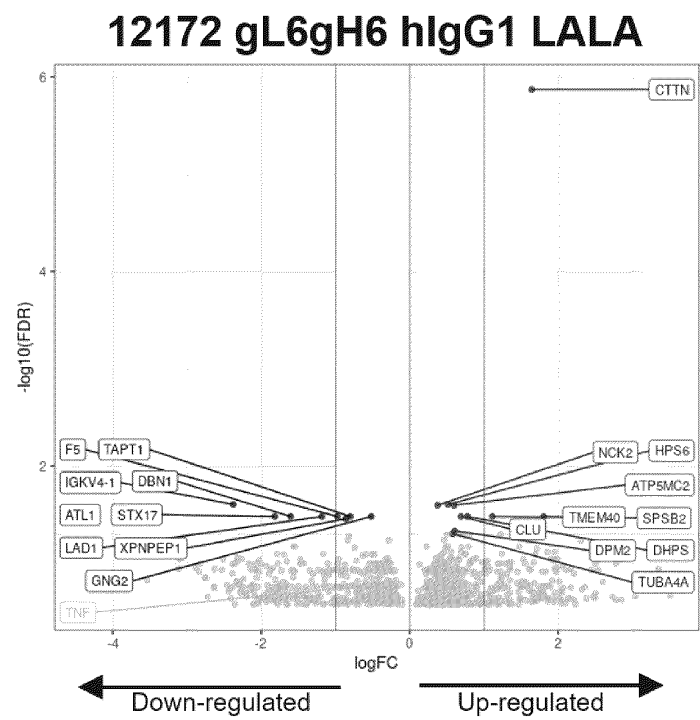
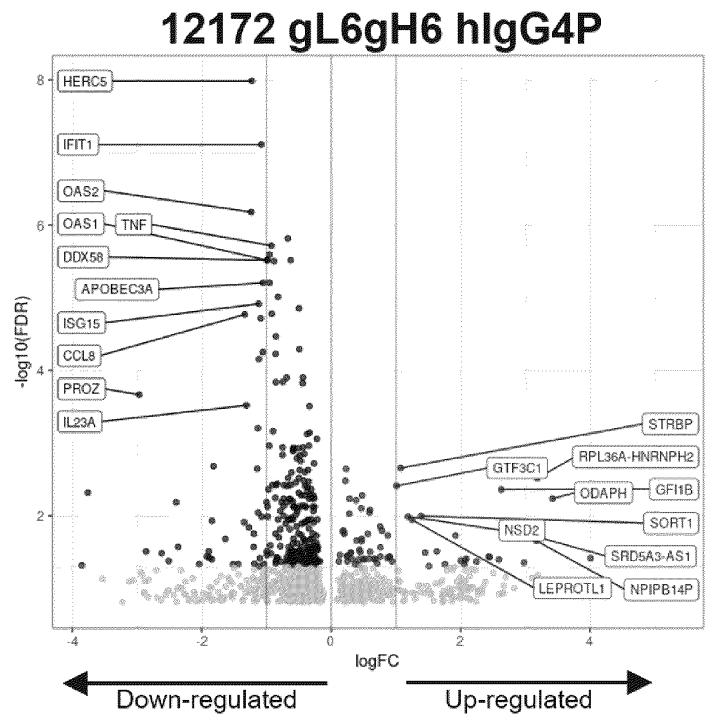


Figure 11B

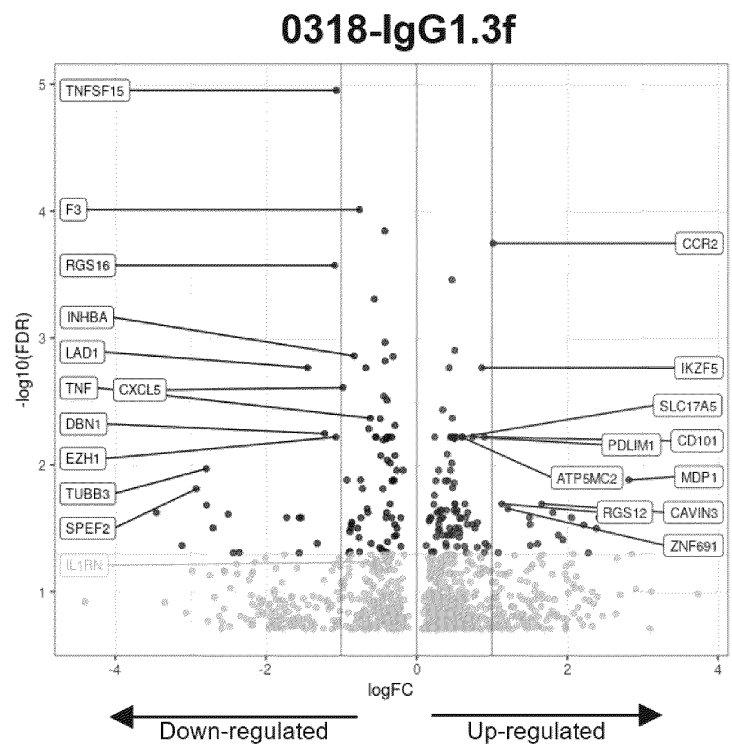


Figure 11C

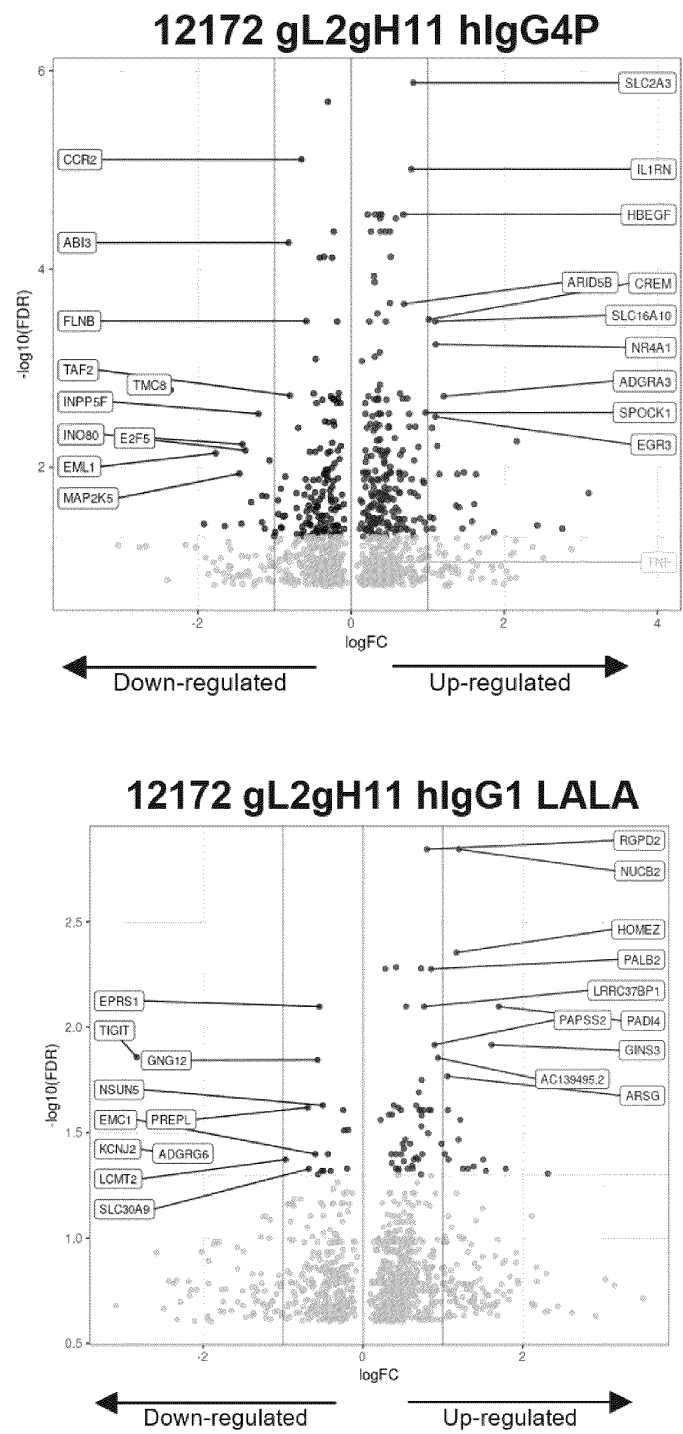


Figure 12A

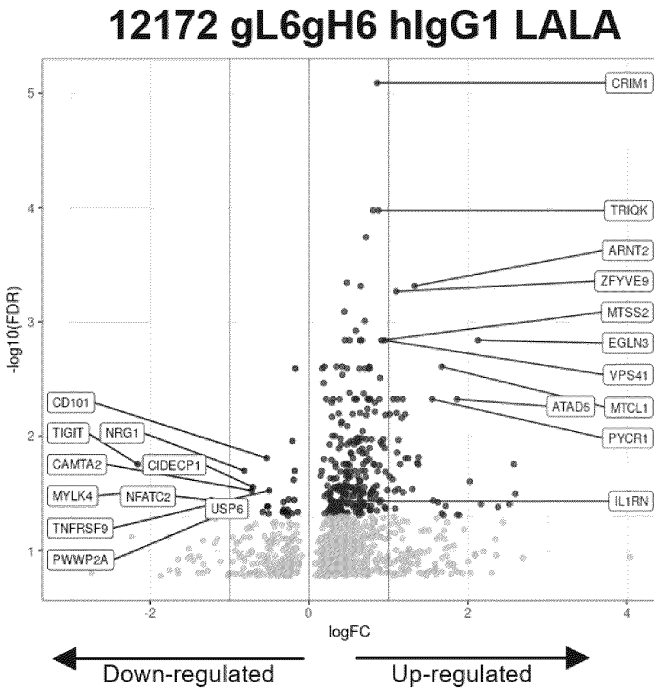
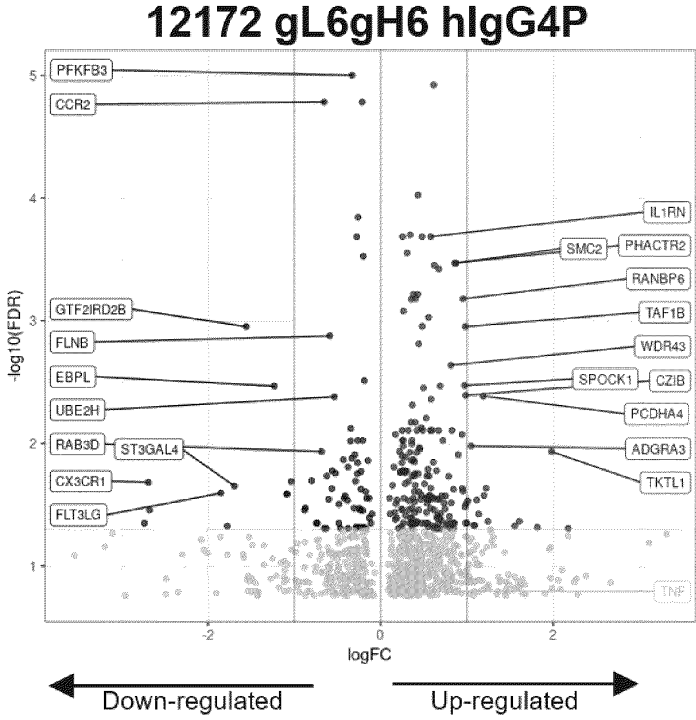


Figure 12B

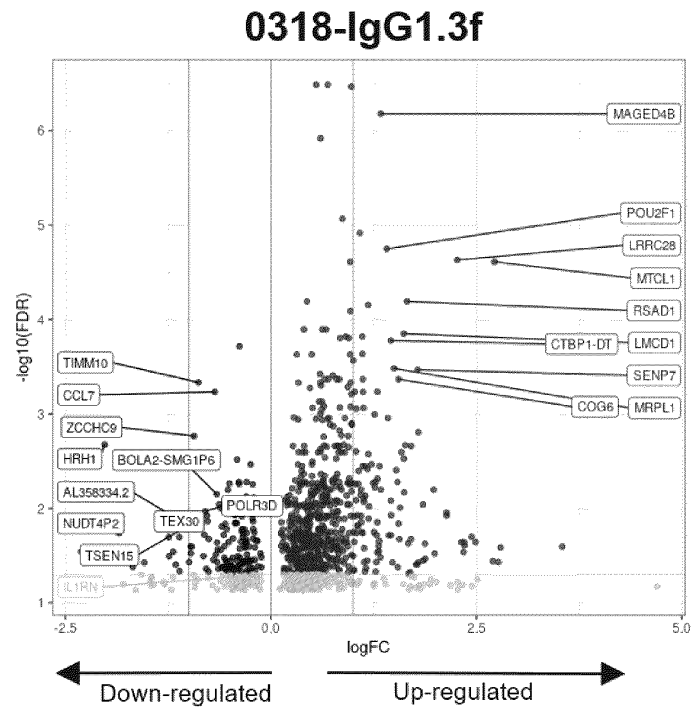


Figure 12C

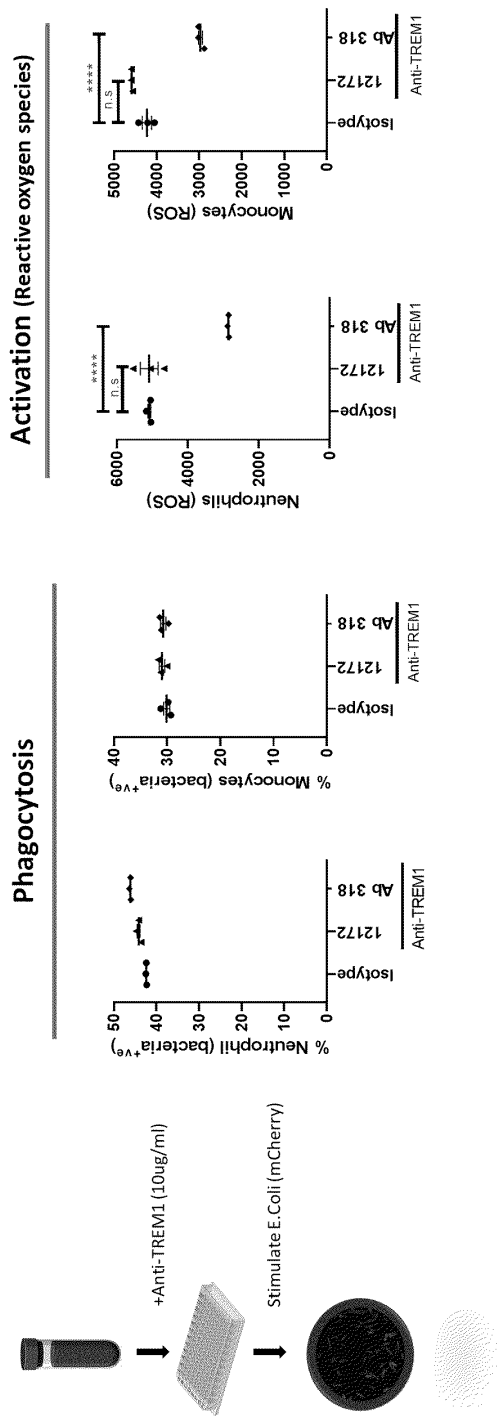


Figure 13

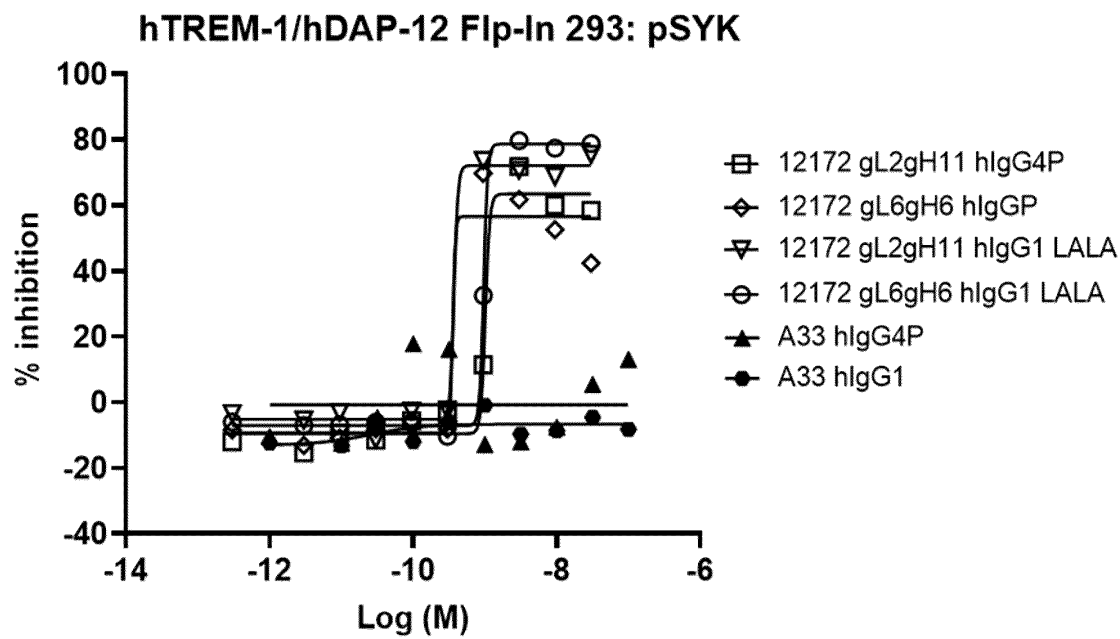


Figure 14