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(54) Title: POCKET ENGINEERING OF HLA ALLELES FOR TREATING AUTOIMMUNITY

(57) Abstract: Methods of preventing or treating autoimmune disease are disclosed. In some cases, subjects with having or at risk of developing autoimmune disease are identified as possessing one or more autoimmunity-susceptibility HLA alleles at one or more HLA loci. In many cases, the HLA loci are selected from Class I and Class II loci, for example Class I A, B, and C, and Class II DQ, DR, and DP. In many cases, subjects suffering from or at risk of developing an autoimmune disease may be administered a plurality engineered autologous HSCs modified to carry and express a variant susceptibility allele having at least one mutation in the antigen binding cleft that alters antigen binding and/or specificity of that variant HLA molecule. In many embodiments, the engineered HSCs are CD34+ immune cells that express one or more modified HLA proteins.



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