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(54) Title: GENETICALLY MODIFIED MICE COMPRISING HUMANIZED CELLULAR IMMUNE SYSTEM COMPONENTS WITH IMPROVED DIVERSITY OF TCRB REPERTOIRE

(57) Abstract: Disclosed herein are non-human animals (e.g., rodents, e.g., mice or rats) genetically engineered to express a humanized T cell co-receptor (e.g., humanized CD4 and/or CD8 (e.g., CD8 α and/or CD8 β)), a human or humanized T cell receptor (TCR) comprising a variable domain encoded by at least one human TCR variable region gene segment and/or a human or humanized major histocompatibility complex that binds the humanized T cell co-receptor (e.g., human or humanized MHC II (e.g., MHC II α and/or MHC II β chains) and/or MHC I (e.g., MHC I α) respectively, and optionally human or humanized β 2 microglobulin). Also provided are embryos, tissues, and cells expressing the same. Methods for making a genetically engineered animal that expresses at least one humanized T cell co-receptor (e.g., humanized CD4 and/or CD8), at least one humanized MHC that associates with the humanized T cell co-receptor (e.g., humanized MHC II and/or MHC I, respectively) and/or the humanized TCR are also provided. Methods for using the genetically engineered animals that mount a substantially humanized T cell immune response for developing human therapeutics are also provided.



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