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(54) **Title:** NOVEL COLLECTION OF HCDR3 REGIONS AND USES THEREFOR

(57) **Abstract:** The present invention is directed to the preparation and use of a collection of antibody heavy chain complementarity determining region 3 (HCDR3) members, where diversity of the collection is a function of the length of the HCDR3 members. The diversity of the collection of HCDR3 regions substantially represents the natural amino acid distribution of HCDR3 in the human repertoire. This natural amino acid distribution can be represented by biasing the complete random distribution of amino acids, accordingly, in the HCDR3 encoding DNA sequence by using trinucleotide mutagenesis (TRIM) technology. A collection of HCDR3 members of the invention each can be comprised within a variable region of an antibody (or fragment thereof) to form a library of synthetic antibodies or antibody fragments. Synthetic antibody libraries of the present invention may be designed to include modular features, such as chemically synthesized "master gene" framework regions, which may contain unique restriction sites flanking one or more CDR regions, including an HCDR3 region prepared as described herein. The invention also provides nucleic acid molecules encoding such diverse collection and methods of making and using the same.