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(54) Title: PRODUCTION OF FUNCTIONAL HYBRID GENES AND PROTEINS

(57) Abstract: The invention relates to an improved method for creating gene and protein libraries, particularly random gene libraries encoding for hybrid proteins containing fragments from one or two parent proteins. The method may be used to make libraries of circularly permuted variants of genes encoding a single protein or hybrid proteins, especially single chain proteins. In addition, the invention can be used to make libraries for protein fragment complementation, in which the two fragments originate from one parent protein or from two different parent proteins. The method can produce a library of genes mostly of the correct size, leading to a high fraction of functional hybrids or complements. When coupled with suitable screening or selection, the method can be used to create and identify hybrid proteins, including new proteins with new or altered properties. The invention also provides libraries of hybrid proteins, especially single-chain proteins, that include an N-terminal sequence originating from one parent protein, fused to a C-terminal sequence of a second parent protein, with both sequences varying in length among the hybrids of the library.