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(71) Applicant *(for all designated States except US)*: **ABMAXIS, INC.** [US/US]; 453 Ravendale Drive, Suites A & B, Mountain View, CA 94043 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **LUO, Peizhi** [US/US]; 415 Madera Ave., Apt.#3, Sunnyvale, CA 94086 (US). **HSIEH, Mark** [US/US]; 4171 Byron Street, Apt. #D, Palo Alto, CA 94306 (US). **ZHONG, Pingyu** [US/US]; 1475 Tyler Parkway, Mountain View, CA 94040 (US). **WANG, Caili** [CN/US]; 2316 20th Avenue, San Francisco, CA 94116 (US). **CAO, Yicheng** [CN/US]; 260 N. Mathilda Avenue, #E6, Sunnyvale, CA 94086 (US). **LIU, Shengjiang** [US/US]; 535 Devonshire Court, Mountain View, CA 94043 (US).

(74) Agent: **CHEN, Shirley**; Wilson Sonsini Goodrich & Rosati, 650 Page Mill Road, Palo Alto, CA 94304-1050 (US).

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(54) Title: GENERATION AND SELECTION OF PROTEIN LIBRARY IN SILICO

(57) Abstract: The present invention provides a methodology for efficiently generating and screening protein libraries for optimized proteins with desirable biological functions, such as improved binding affinity towards biologically and/or therapeutically important target molecules. The process is carried out computationally in a high throughput manner by mining the ever-expanding databases of protein sequences of all organisms, especially human. In one embodiment, a method for constructing a library of designed proteins, comprising the steps of: providing an amino acid sequence derived from a lead protein, the amino acid sequence being designated as a lead sequence; comparing the lead sequence with a plurality of tester protein sequences; and selecting from the plurality of tester protein sequences at least two peptide segments that have at least 15% sequence identity with the lead sequence, the selected peptide segments forming a hit library; and forming a library of designed proteins by substituting the lead sequence with the hit library. The library of designed proteins can be expressed in vitro or in vivo to produce a library of recombinant proteins that can be screened for novel or improved function(s) over the lead protein, such as an antibody against therapeutically important target.

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