(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
26 September 2002 (26.09.2002)

PCT

(10) International Publication Number
WO 02/074929 A3

(51) International Patent Classification[7]: C07H 19/00, 21/00, 21/02, 21/04, C12Q 1/68

(21) International Application Number: PCT/US02/08546

(22) International Filing Date: 19 March 2002 (19.03.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/277,081	19 March 2001 (19.03.2001)	US
60/277,094	19 March 2001 (19.03.2001)	US
60/306,691	20 July 2001 (20.07.2001)	US
10/101,030	19 March 2002 (19.03.2002)	US

(71) Applicant *(for all designated States except US)*: **PRESIDENT AND FELLOWS OF HARVARD COLLEGE** [US/US]; 17 Quincy Street, Cambridge, MA 02139 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **LIU, David, R.** [US/US]; Lexigton, MA (US). **GARTNER, Zev, J.** [US/US]; Cambridge, MA (US). **KANAN, Mattew, W.** [—/—]; Cambridge, MA (US).

(74) Agent: **SHAIR, Karoline, K., M.**; Choate, Hall & Stewart, Exchange Place, 53 State Street, Boston, MA 02109 (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report:
30 May 2003

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 02/074929 A3

(54) Title: EVOLVING NEW MOLECULAR FUNCTION

(57) Abstract: Nature evolves biological molecules such as proteins through iterated rounds of diversification, selection, and amplification. The present invention provides methods, compositions, and systems for syntheiszing, selecting, amplifying, and evolving non-natural molecules based on nucleic acid templates. The sequence of a nucleic acid template is used to direct the synthesis of non-natural molecules such as unnatural polymers and small molecules. Using this method combinatorial libraries of these molecules can be prepared and screened. Upon selection of a molecule, its encoding nucleic acid template may be amplified and/or evolved to yield the same molecule of the present invention allow for the amplification and evolution of non-natural molecules in a manner analogous to the amplification of natural biopolymer such as polynucleotides and protein.