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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
6 March 2003 (06.03.2003)

PCT

(10) International Publication Number
WO 03/018755 A2

(51) International Patent Classification[7]: C12N

(21) International Application Number: PCT/US02/26830

(22) International Filing Date: 23 August 2002 (23.08.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/314,693 24 August 2001 (24.08.2001) US

(71) Applicant *(for all designated States except US)*: **THE OHIO STATE UNIVERSITY RESEARCH FOUNDATION** [US/US]; 1960 Kenny Road, Columbus, OH 43210-1036 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **YOU, Ming** [US/US]; 7688 Hidden Hollow Drive, Columbus, OH 43235 (US). **WANG, Yian** [US/US]; 7688 Hidden Hollow Drive, Columbus, OH 43235 (US). **ZHANG, Zhongqui** [CN/US]; 1238 Waterford Drive, Columbus, OH 43220 (US).

(74) Agent: **DOCHERTY, Pamela, A.**; Calfee, Halter & Griswold LLP, 1400 McDonald Investment Center, 800 Superior Avenue, Cleveland, OH 44114 (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, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

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 03/018755 A2

(54) Title: WILD-TYPE RAS AS A CANCER THERAPEUTIC AGENT

(57) Abstract: Methods for inhibiting proliferation of a cell, particularly a cancer cell are provided. The method comprises increasing intracellular levels of one or more wild-type ras proteins in the cell. In one aspect, the method comprises introducing and expressing a nucleic molecule that encodes a wild-type ras protein in the cell. In another aspect, intracellular levels of one more ras proteins are increased by introducing one or more wild-type ras proteins into the cell. The present invention also relates to the therapeutic use of wild-type ras proteins or nucleic acids that encode one or more wild-type ras proteins in the treatment of tumors or cancer, or prophylactically to prevent formation of tumors or cancer. Methods of characterizing or evaluating cancer in a humans or other mammals are provided. In one embodiment, the method comprises assaying for a loss of function mutation in one or more endogenous ras alleles in the genome of tumor cells obtained from the subject. In another embodiment, the method comprises assaying for a loss of function mutation in one or more endogenous ras alleles and an activating mutation in one or more ras alleles in tumor cells obtained from the subject.