



(51) International Patent Classification:

G01N 33/53 (2006.01) C07K 14/435 (2006.01)
C12Q 1/68 (2006.01) C12N 9/00 (2006.01)

(21) International Application Number:

PCT/SG2013/000460

(22) International Filing Date:

25 October 2013 (25.10.2013)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

201207942-2 25 October 2012 (25.10.2012) SG

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903031 (SG).(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,
KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,
MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ,
OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA,
SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM,
ZW.(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ,
UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ,
TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV,
MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— of inventorship (Rule 4.17(iv))

Published:

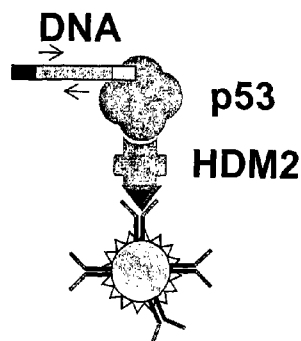
— with international search report (Art. 21(3))

— with sequence listing part of description (Rule 5.2(a))

(54) Title: METHODS FOR DETERMINING RESISTANCE AGAINST MOLECULES TARGETING PROTEINS

Figure 1

A.



(57) **Abstract:** The present disclosure provides a method of determining resistance of a biological molecule to inhibition of its interaction with a target molecule by an inhibitor of the biological molecule, the method comprising the steps of: a) co-compartmentalizing a gene encoding the biological molecule with the target molecule, or a gene encoding the biological molecule with a gene encoding the target molecule into an aqueous droplet disposed within a water-in-oil emulsion, and b) assaying for a complex comprising the biological molecule and the target molecule upon expression of the gene encoding the biological molecule and the gene encoding the target molecule, wherein detection of the complex in the presence of the inhibitor indicates that the biological molecule is resistant to inhibition of its interaction with the target molecule by the inhibitor. Also provided are mutated HDM2 ubiquitin ligase polypeptides exhibiting resistance to Nutlin inhibition of p53 binding.