NEWS & ANALYSIS

Recent patents related to p53

The tumour suppressor p53 — which regulates genes that are involved in DNA repair, metabolism, cell cycle arrest, apoptosis and senescence — is the most frequently mutated gene in human cancer. On p217, Lane *et al.* highlight the development of drugs and new targets within the p53 pathway, as well as challenges such as targeting protein– protein interactions and a fragile mutant transcription factor. Here in TABLE 1 we highlight selected patent applications published in the past year related to p53. Data were researched using the <u>Espacenet</u> database.



Table 1 Published patent applications related to p53		
Publication numbers	Applicants	Subject
WO 2013176623	A*STAR	An isolated peptide that consists of the amino-terminal end of MDM2, which is capable of inhibiting the interaction between TCTP and p53 and/or MDM2; useful for treating cancer
WO 2013036208	A*STAR	Peptides that activate p53; useful for treating cancers that are associated with mutant p53 or a disorder characterized by an undesirably low activity of p53
HK 1104237	Buck Institute	Small molecules that replace or agonize p53 function and can be used to promote cell death in a p53-naive cell $% \left[\frac{1}{2}\right] =0$
WO 2013110007	Columbia University	The use of fatostatin, which inhibits SREBP activation, to reduce the level of mutant p53 binding to the HMG-CoA reductase gene promoter; useful for treating p53-mutant tumours
AU 2013231104	Dana-Farber Cancer Institute	Cross-linked peptides that are related to human p53 and bind to HDM2 or a family member of HDM2; useful for promoting apoptosis
HK 1126216	Roche	2,4,5-triphenyl imidazoline derivatives that inhibit the interaction between p53 and MDM2 proteins; useful for treating cancer
WO 2014018953	Indiana University	Small-molecule inauhzin analogues that activate p53 and inhibit the growth of several human cancer cell lines without causing toxicity in normal human p53-containing cells
HK 1107651	Janssen	Compounds that inhibit the p53–MDM2 interaction
WO 2013113148	S. Lin and M. Zheng	The use of blockers and siRNA against the β_3 -adrenergic receptor — which regulates SIRT1, mTOR and p53 levels or activity — for treating malignancies, rheumatoid arthritis and renal failure
WO 2013062923 JP 2013035852	Merck Sharp & Dohme	Compounds that inhibit HDM2 and increase p53 activity; useful for treating cancer
WO 2013096755	New York University	Peptidomimetics that contain stable, proteolytically resistant, hydrogen-bond surrogate helices and at least one β -amino acid; they promote cell death by inhibiting the p53–HDM2 interaction
MX 2013005631 CN 103221094	Novartis	A crystalline form of an inhibitor of the interaction between p53 and MDM2 and/or MDM4 $$
WO 2014011177	Smith Holdings and Eleos	Antisense p53 phosphorodiamidate morpholino compounds that downmodulate p53 expression
WO 2013009979	Smith Holdings and Eleos	An oligonucleotide that suppresses the expression of p53 and clusterin genes; methods of using it to treat cancer, AIDS, Alzheimer's disease, atherosclerosis and autoimmune diseases
US 2013005769	P. H. Storck et al.	Inhibitors of the p53–MDM2 interaction that are useful for treating breast cancer, colorectal cancer, non-small-cell lung cancer or acute myelogenous leukaemia
US 2013310382	University of Dundee <i>et al</i> .	Small organic molecules that act as p53 mimetics or agonists, and a novel screening system for identifying such compounds
EP 2639240	University of Perugia	Peptides that impair the inhibitory activity of the MDM2–MDM4 heterodimer for p53, and so maintain the association between MDM4 and p53 to restore the oncosuppressive function of p53 in cancer cells containing wild-type p53, directing its function towards an apoptotic outcome
US 2014005386	University of Pittsburgh	p53–MDM2 antagonists that are useful for treating relapsed or refractory acute myeloid leukaemia, lymphoid leukaemia, refractory chronic lymphocytic leukaemia or small-cell lymphocytic lymphomas
WO 2013105037	University of Porto et al.	$Compounds \ that \ can be used \ to \ treat \ diseases \ that \ are \ positively \ influenced \ by \ the \ inhibition \ of \ the \ p53-MDM2 \ or \ p53-MDM4 \ interaction, \ such \ as \ breast \ cancer, \ colorectal \ cancer \ and \ prostate \ cancer$
WO 2013162760	University of Southern California	A p53 cyclotide that inhibits p53 dysregulation or inhibition and has anticancer activity
US 2013345115	University of Southern California	Nuclear penetrating acetylated histone H4 tail peptides that bind to HDAC1 and the methyltransferase G9a and impair their repressive actions on p53 target genes

A*STAR, Agency for Science, Technology and Research; HDAC1, histone deacetylase 1; HMG-CoA, 3-hydroxy-3-methylglutaryl-CoA; MDM2, E3 ubiquitin protein ligase MDM2 (also known as HDM2); mTOR, mammalian target of rapamycin; siRNA, small interfering RNA; SIRT1, sirtuin 1; SREBP, sterol regulatory element binding protein; TCTP, translationally controlled tumour protein.