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(54) **Title:** WDR13 AS A NOVEL BIOMARKER USEFUL FOR TREATING DIABETES AND CANCER

(57) **Abstract:** WD-repeat proteins are very diverse, yet these are structurally related proteins that participate in a wide range of cellular functions. WDR13, a member of this family, is conserved from fishes to humans and localizes into the nucleus. To understand the in vivo function(s) of *Wdr13* gene, we have created and characterized a mutant mouse strain lacking this gene. The mutant mice had higher serum insulin levels and increased pancreatic islet mass as a result of the enhanced beta cell proliferation. While a known cell cycle inhibitor, p21, was down regulated in the mutant islets overexpression of WDR13 in the pancreatic MIN6 cell line resulted in upregulation of p21, accompanied by retardation of cell proliferation. We suggest that WDR13 is a novel negative regulator of the pancreatic beta cell proliferation. Co-immunoprecipitation experiments showed that this protein interacts with estrogen receptors and various HDACs. We provide evidence to show that WDR13 can regulate estrogen receptors-mediated transcription both in HDAC-dependent and HDAC-independent manner. Given the higher insulin levels, better glucose clearance and the lack of insulin resistance in WDR13 deficient mice, we propose that this protein may be a potential candidate drug target for ameliorating impaired glucose metabolism in diabetes.



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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A01K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

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EPO-Internal, BIOSIS, CHEM ABS Data, Sequence Search, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2005/260572 A1 (KATO KIKUYA [JP] ET AL) 24 November 2005 (2005-11-24)	6,11
Y	claims 1-21; sequence 155 -----	1-3
X	WO 2010/037134 A2 (STEMLIFELINE INC [US]; KRTOLICA ANA [US]; ILIC DUSKO [US]) 1 April 2010 (2010-04-01)	6,11
Y	page 48, paragraph 89 - paragraph 90 paragraph [0107] - paragraph [0110] -----	1-3
X	WO 2004/048938 A2 (PROTEIN DESIGN LABS INC [US]; AZIZ NATASHA [US]; GINSBURG WENDY M [US]) 10 June 2004 (2004-06-10)	6
Y	claims 1-16; table 4A ----- -/-	1-3

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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INTERNATIONAL SEARCH REPORT

Information on patent family members

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