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ning of each regular issue of the PCT Gazette.*

(54) Title: COMPOSITIONS AND METHODS FOR TREATING DISEASE

(57) Abstract: The present invention discloses for the first time that the insulin receptor (IR) is a target of Herstatin, which modulates IR and IR-mediated intracellular signaling. In preferred aspects, Herstatin binds at nM concentrations to cell-surface IR, up-regulates basal IR expression by several-fold, induces the accumulation of pro-IR, and stimulates insulin activation of the ERK pathway. Moreover, these changes in insulin signaling are accompanied by alterations in IGF-IR expression, IRS-2 levels, and the serine phosphorylation state of both IRS-1 and IRS-2. Preferred aspects provide novel therapeutic methods and pharmaceutical compositions for treatment of conditions associated with altered IR expression or IR-mediated signaling, including but not limited to insulin resistance syndrome, pre-diabetic conditions, metabolic syndrome, type 1 and type 2 diabetes, cardiac disease, diabetes-associated vascular disease, atherosclerosis, hypertension, diabetes-associated lipid metabolism disorders (dyslipidemia), obesity, critical illness, neurodegenerative disorders, and combinations thereof, and cancer.

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INTERNATIONAL SEARCH REPORT

International application No.

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A. CLASSIFICATION OF SUBJECT MATTER

IPC: A61K 38/18(2006.01),38/28(2006.01),39/395(2006.01);C07K 14/475(2006.01)

USPC: 514/2;530/350;424/134.1

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)

U.S. : 514/2;530/350;424/134.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
WEST Keywords: HER-2, erb-2, herceptin, insulin receptor, binding, diabetes, IGF-1R

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2003/0143568 A1 (SINGER et al.), 31 July 2003 (31.07.2003); paragraphs 0007, 0029, 0030, 0073, 0079, 0082, 0083, 0149, 0150, 0215, 0126 and 0220	1-4, 12-17, 20-25
A	US 6,414,130 B1 (DOHERTY et al.) 02 July 2002 (02.07.2002); abstract; column 2, lines 34-39; column 3, lines 52-67; column 4, lines 35-65 column 8, line 20-column 9, line 42; column 10, lines 25-46; column 19-36 and claims	4-11, 18, 19, 25-27

☐ Further documents are listed in the continuation of Box C.	☐ See patent family annex.
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"O" document referring to an oral disclosure, use, exhibition or other means	
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