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- (71) Applicant (*for all designated States except US*): **DANA-FARBER CANCER INSTITUTE, INC.** [US/US]; 44 Binney Street, Boston, MA 02115 (US).
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- (72) Inventors; and
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- (75) Inventors/Applicants (*for US only*): **KAELIN, William, G.** [US/US]; 177 Commonwealth Avenue, Boston, MA 02116 (US). **IVAN, Mircea** [RO/US]; 107 Norfolk Street, #7, Cambridge, MA 02139 (US).
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- Published:**
- *with international search report*
 - *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*
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- 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.*

(54) Title: MUTEINS OF HYPOXIA INDUCIBLE FACTOR ALPHA AND METHODS OF USE THEREOF

(57) Abstract: The present invention provides hypoxia inducible factor alpha muteins, DNA sequences encoding these hypoxia inducible factor alpha muteins, recombinant DNA molecules containing those DNA sequences operatively linked to expression control sequences and capable of inducing expression of an hypoxia inducible factor alpha muteins, hosts transformed with those recombinant DNA molecules, pharmaceutical compositions containing hypoxia inducible factor alpha muteins and methods of using those compositions to treat hypoxia and ischemic related tissue damage.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/08946

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07K 16/00; C12N 15/12, 15/74, 15/85

US CL : 435/325, 69.1, 252.3, 320.1; 536/23.1, 23.5; 530/350, 388.21

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. : 435/325, 69.1, 252.3, 320.1; 536/23.1, 23.5; 530/350, 388.21

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 00/10578 A1 (THE JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE) 02 March 2000 (02.03.2000), pages 12-16.	1-11 and 13
Y, P	US 6,124,131 A (SEMENZA) 26 September 2000 (26.09.2000) columns 2, 3, 5 and 6.	1-11 and 13
A	SEMENZA et al. Structural and functional analysis of hypoxia-inducible factor 1.	1-11 and 13
---	Kidney International. February 1997, Vol. 31, pages 553-555. See whole document.	
A		
A, P	TANIMOTO et al. Mechanism of regulation of the hypoxia-inducible factor-1alpha by the von-Hippel-Lindo tumor suppressor protein. The EMBO Journal. August 2000, Vol. 19, No. 16, pages 4298-4309. See pages 4299-4306.	1-11 and 13

A, P		



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"I" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

19 July 2002 (19.07.2002)

Date of mailing of the international search report

23 SEP 2002

Name and mailing address of the ISA/US

Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. (703)305-3230

Authorized officer

Chun Min Kain

Telephone No. (703) 308-0196

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/08946

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/08946

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This international Search Authority has found 6 inventions claimed in the International Application covered by the claims indicated below:

- I. Claims 1-11, drawn to a hypoxia inducible factor (HIF) mutein polypeptide.
- II. Claims 13, drawn to a nucleic acid encoding the mutein peptide.

This international Searching Authority considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the special technical feature of the Group I invention is the specific polypeptide claimed therein while the special technical feature of the Group II invention is the particular nucleic acid claimed therein. Since the special technical feature of the Group I invention is not present in the Group II claims and the special technical feature of the Group II invention are not present in the Groups I claims, unity of invention is lacking.

Continuation of B. FIELDS SEARCHED Item 3:

EAST search on USPAT, DERWENT, EPO, JPO, USPGPUB; STN search on MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA. Search terms: hypoxia inducible factor, hif, mutein, mutation, von hippel lindau, vhl, transactivation domain. Nucleotide sequence search: SEQ ID NO:1 and SEQ ID NO:3. Amino acid sequence: SEQ ID NO:2 and SEQ ID NO:4.