Exhibit 5

(12) **United States Patent**
Anderson et al.

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(45) **Date of Patent:** *Nov. 24, 2009

(54) **METHOD FOR INHIBITING PRO-ANGIOGENIC ACTIVITIES OF ENDOTHELIAL CELLS SELECTIVELY AT A SITE OF NEOANGIOGENESIS IN A MAMMAL BY ADMINISTRATION OF THE EXTRACELLULAR DOMAIN OF D1-1 POLYPEPTIDES**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 55 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **11/437,755**

(22) Filed: **May 18, 2006**

(65) **Prior Publication Data**

US 2007/0082000 A1 Apr. 12, 2007

Related U.S. Application Data

(63) Continuation-in-part of application No. 10/424,986, filed on Apr. 28, 2003, now Pat. No. 7,538,088.

(60) Provisional application No. 60/375,904, filed on Apr. 26, 2002, provisional application No. 60/682,542, filed on May 18, 2005.

(51) **Int. Cl.**
A61K 38/17 (2006.01)
C07K 14/47 (2006.01)
C07K 14/515 (2006.01)

(52) **U.S. Cl.** **514/12**; 530/300; 530/324

(58) **Field of Classification Search** .... None
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2004/0120955 A1* 6/2004 Anderson et al. 424/146.1

FOREIGN PATENT DOCUMENTS

EP	0561172	A1	9/1993
EP	0682113	A2	11/1995
WO	WO-00/55173	A1	9/2000
WO	WO-00/61623	A1	10/2000
WO	WO-01/57190	A2	8/2001
WO	WO-01/77289	A2	10/2001
WO	WO-02/079492	A2	10/2002

OTHER PUBLICATIONS

Delisser et al., "Platelet Endothelial Cell Adhesion Molecule (CD31)," *Current Topics In Microbiology and Immunology* 184:37-45(1993).

Marra et al., Accession No. AA267694 (Mar. 21, 1997).

(Continued)

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(57) **ABSTRACT**

The disclosure provides, among other things, novel angiogenesis-related nucleic acids, polypeptides and methods of use.

5 Claims, 17 Drawing Sheets

Human D1-1 Polypeptides

A. Full-length sequence (SEQ ID NO:10)

```
MGTAGAMQLCWVILGFLLFRGHNSQPTMTQTSSSQGGLGGLSLTTEPVSS    50
NPGYIPSSEANRPSHLSSTGTPGAGVPSSGRDGGTSRDTFQTVPPNSTTM    100
SLSMREDATILPSPTSETVLTVAAFGVISFIVILVVVVIILVGVVSLRFK    150
CRKSKESEDPQKPGSSGLSESCSTANGEKDSITLISMKNINMNNGKQSLS    200
AEKVL   205
```

B. Extracellular portion (SEQ ID NO:11)

```
QPTMTQTSSSQGGLGGLSLTTEPVSSNPGYIPSSEANRPSHLSSTGTPGA
GVPSSGRDGGTSRDTFQTVPPNSTTMSLSMREDATILPSPTSETVLT
```

C. Conserved portion (SEQ ID NO:12)

```
VAAFGVISFIVILVVVVIILVGVVSLRFKCRKSKESEDPQKPGSSGLSES
```

OTHER PUBLICATIONS

Osborn et al., "Direct Expression Cloning of Vascular Cell Adhesion Molecule1, A Cytokine-Induced Endothelial Protein That Binds to Lymphocytes," *Cell* 59:1203-1211(1989).

Genbank ref. No. XM_148854.

Genbank ref No. XP_148854.

Bork and Bairoch, 1996, Go hunting in sequence databases but watch out for the traps, Trends in Genet. 12(10):425427.

Bork, 2000, Powers and Pitfalls in Sequence Analysis: The 70% Hurdle, Genome Res. 10:398-400.

Brenner, 1999, Errors in genome annotation, Trends in Genet. 15:132-133.

Doerks, 1998, Protein annotation: detective work for function prediction, Trends in Genet. 14(6):248-250.

Ngo et al., 1995, The Protein Folding Problem and Tertiary Structure Prediction, Chapter 14: Computational Complexity Protein Structure Prediction, and the Levinthal Paradox, pp. 492-495.

Skolnick and Fetrow, 2000, From genes to protein structure and function: novel applications of computational approached in the genomic era, Trends in Genet. 18:34-39.

Smith and Zhang, 1997, The challenges of genome sequence annotation of "The devil is in the details," Nature Biotech. 15:1222-1223.

Staton et al., 2004, Current methods for assaying angiogenesis in vitro and in vivo, Int. J. Exp. Path. 85:233-248.

Wells, 1990, Additivity of Mutational Effects in Proteins, Biochem. 29(37):8509-8517.

Antikainen et al., "Altering protein specificity: techniques and applicaitons," *Bioorganic & Medicinal Chemistry*, 13:2701-2716 (2005).

Armstrong, et al., "ECSM2, An Endothelial Specific Filamin A Binding Protein That Mediates Chemotaxis," *Arterioscler Thromb Vasc Biol*, 28:1-7 (2008).

Auerbach, et al. "Angiogenisis Assays: A Critical Overview," *Clinical Chemistry*, 49(1):32-40 (2003).

Ferrer-Costa, et al., "Characterization of Compensated Mutations in Terms of Structural and Physico-Chemical Properties," *J. Mol. Biol.*, 365:249-256 (2007).

Ponce et al., "The Chick Chorioallantoic Membrane as an In Vivo Angiogenesis Model," *Current Protocols in Cell Biology*, Supplement 18:19.5.1-19.5.6 (2003).

Genbank ref. No. XM_148854, Date: May 17, 2002.

Genbank ref No. XP_148854, Date: May 17, 2002.

* cited by examiner

Figure 1

Figure 2

DOCKET ALARM
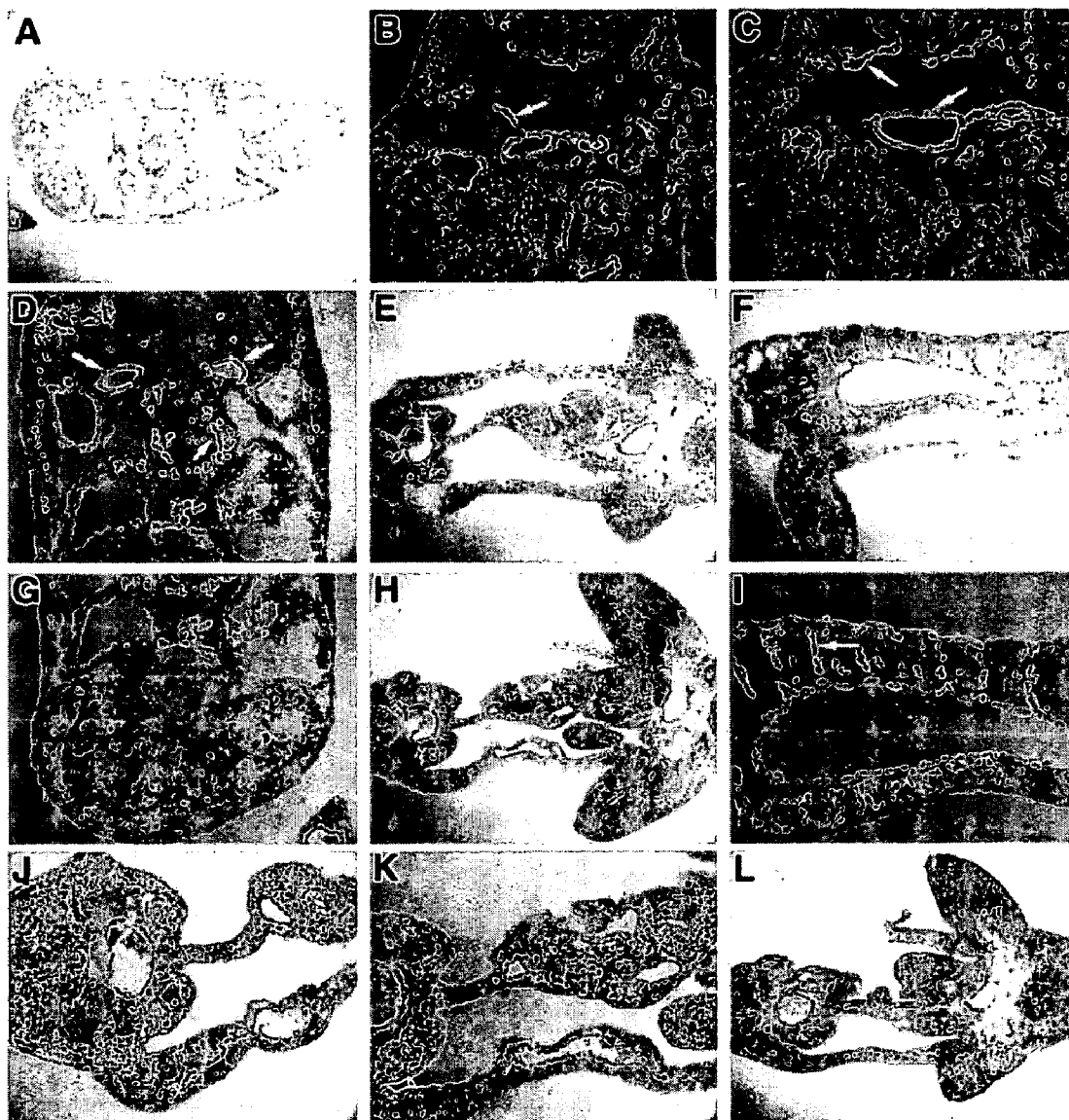
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