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**Declarations under Rule 4.17:**
— *as to the identity of the inventor (Rule 4.17(i)) for all designations*
— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for all designations*
— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations*

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(54) Title: MECHANISMS OF MYOBLAST TRANSFER IN TREATING HEART FAILURE

(57) Abstract: Bioengineering the regenerative heart provides a novel treatment for heart failure. On May 14, 2002, a 55-year-old man suffering ischemic myocardial infarction received 25 injections carrying 465 million cGMP-produced *pure* myoblasts into his myocardium after coronary artery bypass grafting. Three myogenesis mechanisms were elucidated with 17 human/porcine xenografts using cyclosporine as immunosuppressant. Some myoblasts developed to become cardiomyocytes. Others transferred their nuclei into host cardiomyocytes through natural cell fusion. As yet others formed skeletal myofibers with satellite cells. *De novo* production of contractile filaments augmented heart contractility. Human myoblasts transduced with $VEGF_{165}$ gene produced six times more capillaries in porcine myocardium than placebo. Xenograft rejection was not observed for up to 20 weeks despite cyclosporine discontinuation at 6 weeks.

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# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/24600

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : C12N 15/85; A61K 48/00
US CL : 435/325; 514/44

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; 514/44

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)
STN: EMBASE BIOSIS CAPLUS

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X<br>---<br>Y | SUZUKI, K. et al. Cell Transplantation for the Treatment of Acute Myocardial Infarction Using Vascular Endothelial Growth Factor-Expressing Skeletal Myoblasts. Circulation. 18 September 2001, Vol. 104, [suppl 1]. pages I-207-I-212 especially page I-209. | 1-4,8<br>---<br>5-7, 9 |
| A | POWELL, C. et al. Tissue-Engineered Human Bioartificial Muscles Expressing a Foreign Recombinant Protein for Gene Therapy. Human Gene Therapy. 01 March 1999, Vol. 10, No. 4, pages 565-577. | 1-20 |

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