

THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 15

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JOEL S. GREENBERGER

Appeal No. 1996-0927
Application 07/888,203¹

ON BRIEF

Before WILLIAM F. SMITH, JOHN D. SMITH and ROBINSON, Administrative Patent Judges.

ROBINSON, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 3-9 and 22-23, which are all of the claims pending in this application.

Claim 22 is illustrative of the claims on appeal and is reproduced below:

¹Application for patent filed May 26, 1992. According to appellant, the application is a continuation of Application 07/415,186, filed September 29, 1989, now abandoned.

22. A method for homing hematopoietic stem cells to transplanted bone marrow stromal cells and inducing proliferation of those stem cells in a host, comprising

administering to the host stromal cells genetically engineered to express a first member of a ligand-receptor binding pair, and subsequently

administering to the host hematopoietic stem cells genetically engineered to express a second member of said ligand-receptor binding pair, whereby binding of said first member to said second member homes said stem cells to said stromal cells and induces proliferation of said stem cells.

The references relied upon by the examiner are:

Anklesaria et al. (Anklesaria), "Engraftment of a Clonal Bone Marrow Stromal Cell Line *in vivo* Stimulates Hematopoietic Recovery from Total Body Irradiation," Proceedings of the National Academy of Science, Vol. 84, pages 7681-7685, 1987.

Ohkawa et al. (Ohkawa), "Effect of Direct Cell-to-Cell Interaction between the KM-102 Clonal Human Marrow Stromal Cell Line and the HL-60 Myeloid Leukemic Cell Line on the Differentiation and Proliferation of the HL-60 Line," Cancer Research, Vol. 47, pages 2879-2882, 1987.

Pierce et al. (Pierce), "Signal Transduction Through the EGF Receptor Transfected in IL-3-Dependent Hematopoietic Cells," Science, Vol. 239, pages 628-631, 1988.

Grounds of Rejection

Claims 3-9 and 22-23 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Anklesaria, Ohkawa and Pierce.

We reverse.

BACKGROUND

At page 4 of the specification, the applicant describes the invention as relating to a method for homing hematopoietic stem cells to bone marrow stromal cells in a host by administering to a host stromal cells which have been genetically engineered to express a first member of a ligand-receptor binding pair and hematopoietic stem cells genetically engineered to express a second member of a ligand-receptor binding pair under conditions which permit the first member of the ligand-receptor binding pair to bind to the second member of the ligand-receptor binding pair and thereby resulting in the "homing" of the stem cells to the stromal cells. The method is described as being useful for transplanting bone marrow in a host or for treating a host afflicted with a disease associated with a disorder of the bone marrow.

Discussion:

Claim Interpretation:

Claim 22, the sole independent claim, is directed to a method of homing hematopoietic stem cells to transplanted bone marrow stromal cells and inducing proliferation of the stem cells in a host, comprising administering to the host both stromal cells which have been genetically engineered to express a first member of a ligand-receptor binding pair and, subsequently, stem cells which have been genetically engineered to express a second member of the ligand receptor binding pair. While not

specifically defined by the specification, "homing" appears to describe the interaction or binding between the altered stromal cells and the altered stem cells, in the host, which results from the binding of the ligand-receptor binding pair. (Specification, pages 4-5).

The rejections under 35 U.S.C. § 103

Claims 3-9 and 22-23 stand rejected under 35 U.S.C. § 103 as being unpatentable over Anklesaria taken with Pierce and Ohkawa.

In describing Anklesaria, the examiner states (Answer, page 4):

Anklesaria discloses engraftment of a murine bone marrow stromal cell line in vivo (GB1/6) and that the transplanted stromal marrow cells homed to the bone marrow sinuses (page 7682, column 2, "Homing and Function of GB1/6 Cells in Transplanted Mice"). Anklesaria further discloses that the stromal cell line (GB1/6) was transformed with a retroviral vector containing the Neo gene (Abstract). Anklesaria discloses that the homed stromal cells were capable of supporting stem cell (nonadherent cells) proliferation (page 7683, columns 1 and 2).

The examiner acknowledges that (Answer, page 4):

Anklesaria differs from the claims in that the reference fails to disclose genetically engineered stem cells and stromal cells, wherein the stem cells are engineered to express a first member of a ligand-receptor binding pair and the stromal cells engineered to express the second member of the ligand-binding pair.

The examiner relies on Pierce as disclosing a stem cell line which has been genetically engineered to express the EGF receptor and Ohkawa as disclosing that hematopoiesis is controlled by cell-cell interaction between hematopoietic cells and marrow stromal cells.

(Id.)

The examiner concludes that (Answer, paragraph bridging pages 4-5):

it would have been obvious to one of ordinary skill to genetically engineer stem cells and stromal cells with the genes encoding the ligand and receptor, respectively, of a ligand-receptor pair, in order to increase the cell-to-cell interaction of the stem cells with the stromal cells

It is the initial burden of the patent examiner to establish that claims presented in an application for patent are unpatentable. In re Oetiker, 977 F.2d 1443, 1446, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992). We have carefully considered the evidence and discussion in support of the rejection presented by the examiner. However, a fair evaluation of the references, applicant's specification and consideration of the claimed subject matter as a whole, dictates a conclusion that the construction of the claimed method from the prior art teachings is not suggested.

As urged by appellant, Anklesaria 1) does not disclose stromal cells which have been genetically engineered to express a member of a ligand-receptor binding pair, 2) does not disclose the administration of genetically altered stem cells to a host, and 3) does not disclose stem cells that have been genetically engineered to express a member of a ligand-receptor binding pair and then administered to a host. (Principal Brief, page 6). While disclosing genetically engineered stem cells which includes a EGF receptor, Pierce does not suggest the administration of these stem cells, in combination with a genetically altered stromal cells, to a host. Ohkawa describes hematopoietic cellular interaction with a clonal human marrow stromal cell line. However, none of the cells or cell lines, of Ohkawa,

are described as being genetically engineered.

To establish a prima facie case of obviousness, there must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill in the field of the invention would make the substitutions required. That knowledge can not come from the applicant's invention itself. Diversitech Corp. v. Century Steps, Inc., 850 F.2d 675, 678-79, 7 USPQ2d 1315, 1318 (Fed. Cir. 1988); In re Geiger, 815 F.2d 686, 688, 2 USPQ2d 1276, 1278 (Fed. Cir. 1987); Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1143, 227 USPQ 543, 551 (Fed. Cir. 1985). The extent to which such suggestion must be explicit in or may be fairly inferred from the references, is decided on the facts of each case, in light of the prior art and its relationship to the invention. In re Gorman, 933 F.2d 983, 986-987, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991).

Here, the examiner has not provided evidence or facts which would have reasonably suggested the use of genetically altered stromal cells and genetically altered stem cells to achieve the homing of the stem cells when administered to a host in the manner claimed. To the extent that the examiner urges that appellant has recreated a naturally occurring mechanism by using known members of ligand-receptor binding pairs and therefore the invention is obvious over the known naturally occurring homing mechanism, we note that none of the references, relied upon by the examiner, explicitly describe the natural mechanism alluded to by the examiner. Therefore, it is not possible to compare the natural interaction between stromal cells and stem cells.

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On the record before us, the examiner appears to have made use of appellant's disclosed invention to interpret and construe the references relied upon. The examiner provides no tie to bind these references together and points to no reason, suggestion, or motivation which would have lead one of ordinary skill in this art to genetically alter a stromal cell and a stem cell in a manner which would result in each expressing a member of a ligand-receptor binding pair and administering these altered cells to a host in order to "home" the stem cells to the stromal cells. Where, as here, the examiner fails to establish a prima facie case, the rejection is improper and will be overturned. In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir.1988). Therefore, the rejection of claims 3-9 and 22-23 under 35 U.S.C. § 103 is reversed.

Summary

The decision of the examiner to reject claims 3-9 and 22-23 under 35 U.S.C. §

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103 is reversed.

REVERSED

WILLIAM F. SMITH)	
Administrative Patent Judge)	
)	
)	
)	BOARD OF PATENT
JOHN D. SMITH)	
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