

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte
MARIE RANSON, BARRY JOHN ALLEN, and
CLIVE LEIGHTON BUNN

Appeal 2007-4158
Application 09/790,900
Technology Center 1600

Decided: March 21, 2008

Before, DEMETRA J. MILLS, LORA M. GREEN, and
RICHARD M. LEBOVITZ, *Administrative Patent Judges*.

MILLS, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134. The Examiner has rejected claims 14-19, 21, and 33-42, all of the claims on appeal, for obviousness. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

The following claim is representative.

39. A PAI-2 conjugate molecule that is internalized by a cell that expresses a uPA/uPAR complex, said molecule comprising a component (i) that is PAI-2 and, bound or linked via a chelator thereto, a component (ii) that is a radioisotope, wherein component (i) binds to uPA.

Cited References

Gansow	US 5,124,471	Jun. 23, 1992
Jankun	US 5,679,350	Oct. 21, 1997
Piwnica-Worms	US 6,348,185 B1	Feb. 19, 2002

Conese et al., "Urokinase/Urokinase Receptor System: Internalization/Degradation of Urokinase-Serpin Complexes: Mechanism and Regulation", 376 *Biol. Chem. Hoppe-Seyler*, 143-155 (1995).

Allen et al., "Alpha-and beta-emitting radio lanthanides in targeted cancer therapy: The potential role of terbium-149", 17 *Nuclear Medicine Communications*, 40-47 (1996).

Tsatas et al., "Tissue-specific Expression of the Relaxed Conformation of Plasminogen Activator Inhibitor-2 and Low density Lipoprotein Receptor-related Protein in Human Term Gestational Tissues", 45(12) *The Journal of Histochemistry & Cytochemistry*, 1593-1602 (1997).

Kennel et al., "Radioimmunotherapy f micrometastases in lung with vascular targeted 213 Bi", 80(1/2) *British Journal of Cancer*, 175-184 (1999).

Grounds of Rejection

1. Claims 14-17, 21, 33-37 and 39-42 stand rejected under 35 U.S.C. § 103(a) over Jankun in view of Allen and Gansow.
2. Claims 14-16, 21, 33-35, and 39-42 stand rejected under 35 U.S.C. § 103(a) over Jankun in view of Kennel and Gansow.

3. Claims 17-19, 21, and 36-42 stand rejected under 35 U.S.C. § 103(a) over Jankun in view of Piwnica-Worms.

DISCUSSION

Background

“Proteolytic enzymes such as urokinase plasminogen activator (herein referred to as ‘uPA’) play a role in tumor angiogenesis and metastatic cell migration; both of which are processes that require tissue barriers to be breached. Under normal physiologic conditions, most cells express little or no uPA.” (Spec. 2.) The activity of uPA is physiologically inhibited by the serpins plasminogen activator inhibitors type 1 and 2 (PAI-1 and PAI-2). (Spec. 2.)

1. Claims 14-17, 21, 33-37 and 39-42 stand rejected under 35 U.S.C. § 103(a) over Jankun in view of Allen and Gansow.

The Examiner finds that Jankun teaches

a plasminogen activator inhibitor material (PAI-2)/conjugated medicament, see abstract and column 7, lines 10-20. The medicaments may be a toxin such as “... saporin” . . . The [Jankun] patent does not teach that the PAI-2 conjugate molecule comprises the alpha particle emitting radioisotope, terbium-149 (Tb-149) which is radioactive detectable. Nor does the patent teach utilization of the chelator, cyclic diethylenetriaminepentaacetic acid (DTPA) in order to manufacture a PAI-2 conjugate molecule.

(Ans. 4.)

To make up for this deficiency the Examiner relies on Allen and Gansow. (Ans. 4.)

Allen... teach[es] the use of the alpha-emitting radionuclide, Tb-149 with a molecular carrier such as monoclonal antibodies for targeted cancer therapy. ... [Gansow¹] teaches that DTPA derivatives have proven useful for labeling proteins with radioactive metals, see column 2, lines 38-41.

(*Id.* at 4-5.)

The Examiner concludes that

[i]t would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to conjugate Tb-149 to PAI-2 via DPTA in order to implement an efficacious mode of clinical treatment and diagnostic imaging of cancer. One of ordinary skill in the art would have been motivated by the teachings of Allen . . . and patent '471 [Gansow] because Tb-149 radionuclide labeling has several advantages such as: ... (4) the art established usefulness of radionuclide materials in cancer therapy and the knowledge that DTPA tightly binds metals ions and forms stable complexes in vivo with a wide variety of radiometals useful in cancer detection and therapy, see bridging paragraph of columns 5 and 6; column 7, lines 57-60.

(*Id.* at 5.)

Appellants contend there is no expectation of success provided by the cited references. (App. Br. 16.) In particular, Appellants argue

¹ The Examiner's Answer erroneously cites the patent number of Jankun, instead of the patent number of Gansow here. However, the subject matter described in the Answer corresponds to the disclosure of Gansow at col. 2, lines 38-41.

the cited prior art fails to teach or suggest the conjugation chemistry regarding PAI-2 and radioisotopes. (App. Br. 13.) Appellants argue that Jankun taught conjugation techniques and reagents that necessarily prevented PAI-1 from converting into its latent inactive form (App. Br. 14) which involved cross-linking of PAI-I to a cytotoxin using disulfide reducible or thiol free acid labile linker. (Br. 19.) Appellants argue

a skilled artisan reading the '350 patent [Jankun] would have assumed that one could only prepare PAI-1 or PAI-2 conjugates using the methods and conjugation agents disclosed in that patent, which necessarily held PAI-1 in its non-latent active form. Because nothing in the '350 patent, or any of the other references, suggested that conjugating a radioisotope to PAI could prevent a PAI from converting to its latent form, nothing in the '350 patent, either alone or in combination with the other cited references, taught or suggested that one could make PAI-2 conjugated to a radioisotope.

(App. Br. 14-15.)

Appellants argue that the Andrews Declaration of record supports this argument with evidence and that the Examiner failed to address this argument. (Br. 15.)

In rejecting claims under 35 U.S.C. § 103, the Examiner bears the initial burden of presenting a *prima facie* case of obviousness. *See In re Rijckaert*, 9 F.3d 1531, 1532 (Fed. Cir. 1993). A *prima facie* case of obviousness is established when the teachings from the prior art itself would appear to have suggested the claimed subject matter to a person of ordinary skill in the art. *In re Bell*, 991 F.2d 781, 783 (Fed. Cir. 1993). An

obviousness analysis requires that the prior art both suggest the claimed subject matter and reveal a reasonable expectation of success to one reasonably skilled in the art. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991).

In the present case we find, in view of the evidence before us, that the Examiner has not shown with sufficient evidence that one of ordinary skill in the art would have had a reasonable expectation of success of preparing a radiolabeled PAI-2 molecule, as claimed. We agree with Appellants that

a knowledgeable reader of the '350 patent [Jankun] would have thought himself limited to the conjugation methodology disclosed there, which necessarily addressed the problem of PAI-1, with its latent and active forms. Conversely, the reader of the '350 patent could not have harbored a reasonable expectation of adapting just any known conjugation chemistry to this end.

(Reply Br. 4-5.)

In view of the above, we reverse the rejection of the Examiner.

2. Claims 14-16, 21, 33-35, and 39-42 stand rejected under 35 U.S.C. § 103(a) over Jankun in view of Kennel and Gansow. Claims 17-19, 21, and 36-42 stand rejected under 35 U.S.C. § 103(a) over Jankun in view of Piwnica.

Each of the rejections noted above rely on the primary reference, Jankun, and thus each of the rejections has the deficiency noted above with respect to the failure of the Examiner to establish an expectation of success of preparing a radiolabeled PAI-2 molecule in view of the requisite

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conjugation chemistry described in Jankun required to maintain the active form of the molecule. We do not find any of the secondary references overcome the deficiency of Jankun. For this reason we reverse the above noted rejections.

SUMMARY

The rejections of the claims for obviousness are reversed.

REVERSED

Ssc:

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