

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

**UNITED STATES PATENT AND TRADEMARK OFFICE**

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**BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES**

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Ex parte HOLGER N. LODE, RALPH A. REISFELD,  
DAVID A. CHERESH and STEPHEN D. GILLIES

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Appeal No. 2006-0273  
Application No. 09/502,732

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HEARD: March 23, 2006

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Before SCHEINER, MILLS, and GRIMES, Administrative Patent Judges.  
MILLS, 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 22, 23, 25, 31, 33, 36, 38, 44, and 46-51, which are all of the claims pending in this application. Claim 22 is representative and reads as follows:

22. A therapeutic composition comprising at least one angiogenesis inhibiting agent, which is an  $\alpha_v\beta_3$  antagonist, and at least one anti-tumor immunotherapeutic agent, which is a fusion protein comprising cytokine IL-2 and an Ig heavy chain that immunoreacts with a tumor associated antigen target.

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The references cited by the examiner are:

Brooks et al. (Brooks)	5,753,230	May 19, 1998 (filed Mar. 18, 1994)
Zasloff et al (Zasloff)	6,147,060	Nov. 14, 2000 (filed Apr. 25, 1997)

Xiang et al. (Xiang), "Elimination of Established Murine Colon Carcinoma Metastases by Antibody-Interleukin 2 Fusion Protein Therapy," Cancer Research, Vol. 57, No. 21, pp. 4948-4955 (1997)

Folkman et al. (Folkman), "Angiogenesis in cancer, vascular, rheumatoid and other disease," Nature Medicine, Vol. 1, No. 1, pp. 27-31 (1995)

#### Grounds of Rejection

Claims 22, 23, 25, 31, 33, 36, 38, 44, and 46-51 stand rejected under 35 U.S.C. §103(a) as obvious over Brooks and Xiang in view of Folkman and Zasloff.

We reverse this rejection.

#### DISCUSSION

#### Procedural History

We previously remanded this application to the examiner on November 21, 2003 (Appeal No. 2003-1039) to revisit evidence of synergism submitted by appellants, and to review the relevance of the disclosures of the Folkman publication and Zasloff patent to the then pending claims. At the time of the remand, the claims were directed to a therapeutic composition comprising at least one angiogenesis inhibiting agent; and at least one anti-tumor immunotherapeutic agent, said anti-tumor immunotherapeutic agent comprising a cell-effector component joined to a tumor associated antigen

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targeting component. Following the remand, the examiner reopened prosecution and the appellants amended the application claims to recite a specific angiogenesis inhibitor and immunotherapeutic agent. The amended claims are now before us on appeal. The examiner rejects the claims for obviousness over Brooks and Xiang in view of Folkman and Zasloff.

### Obviousness

Claims 22, 23, 25, 31, 33, 36, 38, 44, and 46-51 stand rejected under 35 U.S.C. §103(a) as obvious over Brooks and Xiang in view of Folkman and Zasloff.

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, 28 USPQ2d 1955, 1956 (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, 26 USPQ2d 1529, 1531 (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, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). With this as background, we analyze the prior art applied by the examiner in the rejection of the claims on appeal.

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The examiner argues that the two primary references, Brooks and Xiang, anticipate each therapeutic agent. The examiner acknowledges that neither Brooks or Xiang teaches the combination of both an angiogenesis inhibiting agent and an anti-tumor immunotherapeutic agent, but cites In re Kerkhoven<sup>1</sup> in support of the rejection stating that it is “prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for the same purpose, in order to form a third composition that is to be used for the very same purpose” since “the idea of combining them flows logically from their having been individually taught in the prior art.” Answer, page 4.

In addition, the examiner argues that Folkman suggests a greater additive advantage in combining antiangiogenic agents with cytotoxic agents and that Zasloff “successfully demonstrate[d] synergistic effects with a known anti-angiogenic agent in combination with cytotoxic therapy.” Answer, page 6. We further note that the examiner admits that the data in the specification evidence a synergistic result for the claimed composition (Answer, page 5), but submits that such a synergistic result would have been expected in view of the teachings of Folkman and Zasloff.

Assuming, arguendo, that the examiner has established a prima facie case of obviousness, we turn to appellants’ argument and evidence of unexpected synergistic effects for the claimed combination of therapeutic agents.

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<sup>1</sup> 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Appellants argue that Folkman does not teach or suggest the specific combination now claimed and that Folkman does not teach or suggest that any specific combination of therapeutic agents will provide synergistic results. Brief, page 5.

Appellants further argue that (Brief, pages 5-6)

The Folkman article, ... cites a single article by Teicher et al. *Int. J. Cancer*, 1994,57(6):920-925 (of record), [which] ... discusses a number of combinations of antitumor drugs with anti-angiogenic agents. Some combinations, such as TNP-470 and minocycline (both anti-angiogenic) in combination with cyclophosphoramide (a cytotoxic agent) led to significantly reduced numbers and size of metastases (See Tables II, IV and IV) compared to treatment with the agents by themselves. Other combinations, however, such as TNP-470 and/or minocycline in combination with CDDP, melphalan, or BCMU did not provide any significant improvement in number or size of metastases (see Table II, and IV) compared to treatment with the agents by themselves. Thus, even in the Teicher et al. study, the effectiveness of a given combination of antiangiogenic agent and cytotoxic agent was shown to be unpredictable.

... Accordingly, one of ordinary skill in the art would not have had a reasonable expectation of success in combining the agents of Brooks et al., and Xiang et al. to afford the presently claimed invention...

In our view, the examiner has not adequately addressed appellants' evidence that synergy would have been unexpected. We conclude that appellants' evidence reasonably establishes that the therapeutic synergistic results obtained from the combination of an  $\alpha_v\beta_3$  antagonist and a fusion protein comprising cytokine IL-2 and an Ig heavy chain would have been unexpected to one of ordinary skill in the art at the time of filing of the present application, and thus overcomes the rejection under 35 U.S.C. § 103.

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In view of the above, the rejection of the claims under 35 U.S.C. § 103 is reversed.

CONCLUSION

We therefore reverse the rejection of the claims for obviousness over Brooks and Xiang in view of Folkman and Zasloff.

REVERSED

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TONI R. SCHEINER )  
Administrative Patent Judge )  
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) BOARD OF PATENT  
DEMETRA J. MILLS )  
Administrative Patent Judge ) APPEALS AND  
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