

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 45

UNITED STATES PATENT AND TRADEMARK OFFICE

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

Ex parte VICTOR J. DZAU,
GARY H. GIBBONS, and
RYUICHI MORISHITA

Appeal No. 2001-0490
Application No. 08/524,206

ON BRIEF

Before WILLIAM F. SMITH, ADAMS, and GRIMES, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the final rejection of claims 1, 3, 5-8, 13 and 14, all the claims pending in the application.

Claim 1 is illustrative of the subject matter on appeal and is reproduced below:

1. A method of modulating gene transcription in vivo within mammalian cells, said method comprising:
 - administering to a mammal a composition comprising dsDNA having a sequence specific for binding to a transcription factor which modulates the transcription of at least one gene,
 - whereby said dsDNA is introduced into the nuclei of said cells in an amount sufficient to competitively inhibit the binding of said transcription factor to said gene,
 - whereby the transcription of said gene is modulated.

The references relied upon by the examiner are:

Chu et al. (Chu '985)	5,683,985	Nov. 4, 1997
Chu et al. (Chu '522)	WO 92/18522	Oct. 29, 1992

Mannino et al. (Mannino), "Liposome Mediated Gene Transfer," BioTechniques, Vol. 6, No. 7, pp. 682-690 (1988)

Bielinska et al. (Bielinska), "Regulation of Gene Expression with Double-Stranded Phosphorothioate Oligonucleotides," Science, Vol. 250, pp.997-999 (1990)

Uhlmann et al. (Uhlmann), "Antisense Oligonucleotides: A New Therapeutic Principle," Chemical Reviews, Vol. 90, No. 4, pp. 544-584 (1990)

Hug et al. (Hug), "Liposomes for the transformation of eukaryotic cells," Biochimica et Biophysics Acta, Vol. 1097, pp. 1-17 (1991)

Libby et al. (Libby), "A Cascade Model for Restenosis - A Special Case of Atherosclerosis Progression," Circulation, Vol. 86, Suppl. III, pp. III-47-III-52 (1992)

Tomita et al. (Tomita), "Direct in vivo gene introduction into rat kidney," Biochemical and Biophysical Research Communications, Vol. 186, No. 1, pp. 129-134 (1992)

Chien, "Molecular Advances in Cardiovascular Biology," Science, Vol. 260, pp. 916-917 (1993)

Milligan et al. (Milligan), "Current Concepts in Antisense Drug Design," Journal of Medicinal Chemistry, Vol. 36, No. 14, pp. 1923-1937 (1993)

Stein et al. (Stein), "Antisense Oligonucleotides as Therapeutic Agents – Is the Bullet Really Magical?" Science, Vol. 261, pp. 1004-1012 (1993)

Schwartz et al. (Schwartz), "Subspecialty Clinics: Cardiology – Coronary Restenosis: Prospects for Solution and New Perspectives From a Porcine Model," Mayo Clin Proc, Vol. 68, No. 1, pp. 54-62 (1993)

Rubin et al. (Rubin), "Atherosclerosis in mice: getting to the heart of a polygenic disorder," TIG, Vol. 10, No. 6, pp. 199-204 (1994)

Barinaga, "Gene Therapy for Clogged Arteries Passes Test in Pigs," Science, Vol. 265, p. 265 (1994)

Tseng et al. (Tseng), "Antisense oligonucleotide technology in the development of cancer therapeutics," Cancer Gene Therapy, Vol. 1, No. 1, pp. 65-71 (1994)

GROUND OF REJECTION

Claims 1, 3, 5-8, 13 and 14 stand rejected under 35 U.S.C. § 112, first paragraph, as being based on an insufficient disclosure to support or enable the scope of the claimed invention.

Claims 1, 3 and 6 stand rejected under 35 U.S.C. 102(a) or (e) as anticipated by Chu '985 or Chu '522 in light of Bielinska.

Claims 1, 5, 7, 13 and 14 stand rejected under 35 U.S.C. § 103. As evidence of obviousness the examiner relies on Chu '985 or Chu '522 in the alternative, in addition to Bielinska, Mannino, Marishita and Tomita.

We reverse the rejection under 35 U.S.C. § 112, first paragraph, and affirm the prior art rejections.

CLAIM GROUPING

According to appellants (Brief, page 5), “[f]or each ground of rejection, the claims stand or fall together.” Since all claims stand or fall together, we limit our discussion to representative independent claim 1. Claims 3, 5-8, 13 and 14 will stand or fall together with claim 1. In re Young, 927 F.2d 588, 590, 18 USPQ2d 1089, 1091 (Fed. Cir. 1991).

DISCUSSION

THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH:

According to the examiner (Answer, page 6), “[t]he specification does not enable any person skilled in the art to make and use the invention commensurate in scope with the current claims.” The examiner did not argue the claims separately therefore for the reasons set forth above we limit our discussion to representative independent claim 1.

With reference to Uhlmann, Milligan, Stein and Tseng the examiner finds (Answer, page 7), “[a]t the time the application was filed therapeutic administration of oligonucleotides to an animal or human subject by any route was considered by those skilled in the art to be an undeveloped and unpredictable method of treatment....” However, in contrast to the claimed invention, each of the references relied upon by the examiner are drawn to anti-sense therapies. Reply Brief, page 6. Apparently recognizing this deficiency in the references, the examiner simply concludes (Answer, page 7):

The obstacles to providing sufficient mRNA-binding oligonucleotides to a patient’s cells ... are even greater for the claimed method, wherein the DNA molecules are targeted to a DNA-binding protein, because the affinity of oligonucleoties for their complementary target mRNAs is expected to be greater than the affinity of double-strand DNAs for their binding site of the protein.

However, as appellants recognize (Reply Brief, page 6), “the [e]xaminer provided no evidence to support this statement.” We remind the examiner that our reviewing court has held that findings of fact must be supported by substantial evidence within the record. In re Gartside, 203 F.3d 1305, 1315, 53 USPQ2d 1769, 1775 (Fed. Cir. 2000) (“because our review of the board’s decision is

confined to the factual record compiled by the board ... the 'substantial evidence' standard is appropriate for our review of board fact findings, see 5 U.S.C. § 706(2)(E).” See also In re Lee, 277 F.3d 1338, 61 USPQ2d 1430 (Fed. Cir. 2002) (a board decision denying patent must be founded on necessary findings and must provide an administrative record showing the evidence which the findings are based; the board must assure the requisite findings are made, based on evidence of record).

On a different tack the examiner finds (Answer, page 8), the “[e]fficiency of liposome-mediated transfection is strongly dependent on the lipid composition, and some lipid mixtures give little or no transfection (Hug et al., p. 7; Mannino et al., p. 687)” apparently suggesting that the claimed invention be limited to the precise liposome described in appellants’ specification. See Specification, pages 12-18. However, as appellants point out (Reply Brief, pages 8-9), “[i]n addition to HVJ liposomes, which are described in detail in the Examples, the specification states that other well known DNA delivery methods can be used in the methods of the invention.” The examiner does not address these “other well known DNA delivery methods.” We remind the examiner, it is not a function of the claims to specifically exclude all possible inoperative embodiments. As set forth in Atlas Powder Co. v. E.I. DuPont De Nemours & Co., 750 F.2d 1569, 1576-77, 224 USPQ 409, 414 (Fed. Cir. 1984):

Even if some of the claimed combinations were inoperative, the claims are not necessarily invalid. “It is not a function of the claims to specifically exclude ... possible inoperative substances....” In re Dinh-Nguyen, 492 F.2d 856, 859-59, 181 USPQ 46, 48 (CCPA 1974)(emphasis omitted). Accord, In re Geerdes, 491 F.2d 1260, 1265, 180 USPQ 789, 793 (CCPA 1974); In re Anderson, 471 F.2d

1237, 1242, 176 USPQ 331, 334-35 (CCPA 1971). Of course, if the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention, the claims might indeed be invalid. See e.g., In re Cook, 439 F.2d 730, 735, 169 USPQ 298, 302 (CCPA 1971).

Similarly we are not persuaded by the examiner's arguments (Answer, pages 8-9) with regard to restenosis, the scope of claim 1 is not limited to the treatment of restenosis.

For the foregoing reasons, it is our opinion that the examiner failed to provide the evidence necessary to establish a prima facie case of non-enablement. Accordingly, we reverse the rejection of claim 1 under 35 U.S.C. § 112, first paragraph. As set forth above, claims 3, 5-8, 13 and 14 stand together with claim 1.

THE REJECTION UNDER 35 U.S.C. § 102:

Since the teachings of the two Chu references are essentially identical (see Answer, page 10) we will focus our attention on Chu '522.¹ Appellants do not dispute that Chu '522 teach a method of modulating the transcription of products which are subject to regulation by transcriptional control recognition sequences by administering a therapeutically effective amount of an oligonucleotide comprised of three segments, wherein the second segment links

¹ We note that appellants do not argue the two references separately.

the first segment to the third segment, and the first and third segments are complementary to each other.

Instead, appellants argue that the oligonucleotide disclosed by Chu '522 is not double stranded DNA (dsDNA). According to appellants (Brief, bridging paragraph, pages 11-12):

It is a basic and fundamental fact of molecular biology that double stranded DNA consists of two DNA strands that are linked to one another only by base pairing (*i.e.*, hydrogen bonding) between nucleotide bases that make up each of the strands; there is no form of covalent linkage between the two DNA strands that make up double stranded DNA.

However, as the examiner points out (Answer, page 14), “[t]his restriction on dsDNA is not disclosed in the instant specification.” Furthermore, claim 1 recites “a composition comprising dsDNA having a sequence specific for binding to a transcription factor which modulates the transcription of at least one gene...” Even assuming the specification did restrict the meaning of dsDNA, the use of the open transitional term “comprising” does not exclude the presence of a linker region connecting the two complementary strands of DNA together, as in Chu '522.

For the foregoing reasons, we find no error in the examiners rejection². Our reasoning applies equally to Chu '522 and Chu '985. Accordingly, we affirm the rejection of claim 1 under 35 U.S.C. 102(a) as anticipated by Chu '522, or under 102(e) as anticipated by Chu '985. As discussed supra claims 3 and 6 fall together with claim 1.

² We recognize the examiner's reliance on Bielinska as evidence that the HIV enhancer sequence taught by both Chu references is an NF-κB binding site. In re Samour, 571 F.2d 559, 563, 197 USPQ 1, 4-5 (CCPA 1978).

THE REJECTION UNDER 35 U.S.C. § 103:

As set forth above, claims 5, 7, 13 and 14 stand or fall together with representative claim 1. As discussed above, we have found that claim 1 is anticipated by Chu '522 and Chu '985. As set forth in Structural Rubber Prods. Co. v. Park Rubber Co., 749 F.2d 707, 716, 223 USPQ 1264, 1271 (Fed. Cir. 1984), "a disclosure that anticipates under § 102 also renders the claim invalid under § 103, for 'anticipation is the epitome of obviousness,' In re Fracalossi, 681 F.2d 792, 215 USPQ 569 (CCPA 1982)."

Accordingly we find no error in, and therefore affirm, the rejection of claim 1 under 35 U.S.C. § 103 as obvious over Chu '985 or Chu '522 in the alternative, in view of Bielinska, Mannino, Marishita and Tomita. As discussed supra claims 5, 7, 13 and 14 fall together with claim 1.

OTHER ISSUE

If upon further prosecution, the examiner remains of the opinion that the specification does not provide an enabling description of the method of treating restenosis set forth in claim 8, the examiner should clearly articulate his position with regard that claim and provide appellants with a full and fair opportunity to respond.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN-PART

William F. Smith)	
Administrative Patent Judge)	
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)	BOARD OF PATENT
Donald E. Adams)	
Administrative Patent Judge)	APPEALS AND
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)	INTERFERENCES
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Eric Grimes)	
Administrative Patent Judge)	

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Clark & Elbing, LLP
176 Federal Street
Boston, MA 02110-2214

DEA/jlb