The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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. 35

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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Ex parte PAUL R. SCHIMMEL

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Appeal No. 1997-3242[1]
Application No. 07/929,834[2]

_____

HEARD: February 6, 2001

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Before WILLIAM F. SMITH, SCHEINER and MILLS, Administrative Patent Judges.

SCHEINER, 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 1 through 14, all of the claims in the application.

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[1] As a preliminary matter, we note that this appeal is related to an appeal in application serial no. 08/249,689 (Appeal No. 1997-2396). We have considered the two appeals together.

[2] Application for patent filed August 14, 1992 According to appellant, this application is a continuation-in-part of application serial no. 07/586,534, filed September 21, 1990, now abandoned.

Claim 1 is representative:

1. A method for designing a compound specifically inhibiting targeted ribonucleic acid function comprising the steps of:

(a) determining the nucleotide sequence of a site in the targeted ribonucleic acid that is critical to function, wherein the site is referred to as a critical site;

(b) determining the secondary structure of the region of the targeted ribonucleic acid in which the critical site is located;

(c) determining the three-dimensional structure of the targeted RNA, including the position of the critical site relative to the major and minor grooves;

(d) determining the sequence of nucleotides and structure flanking the critical site in the targeted ribonucleic acid that is specific to the critical region of the ribonucleic acid to be inhibited and within the minor groove; and

(e) designing a compound to bind specifically to the critical site within the minor groove of the targeted ribonucleic acid, wherein binding of the compound to the targeted RNA inhibits the function of the targeted RNA.

No prior art references are relied on by the examiner.

The claims stand rejected as follows:

I. Claims 1-14 under 35 U.S.C. § 112, first paragraph, as based on a non-enabling disclosure.

II. Claims 1-5, 8-10 and 12-14 under 35 U.S.C. § 101 (provisional) as claiming the same invention as that of claims 1, 3, 14-16, 4-6 and 8-10 of copending application serial no. 08/249,689.

III. Claims 1, 2, 8-11, 13 and 14 under the doctrine of obviousness-type double patenting (provisional) as unpatentable over claims 1, 3-6, 9 and 10 of copending application serial no. 08/249,689.

IV. Claims 1-5, 7-10 and 12-14 under the doctrine of obviousness-type double patenting (provisional) as unpatentable over claims 1, 3, 14-16, 4-6 and 8-10 of copending application serial no. 08/249,689.

BACKGROUND

According to the specification, the invention "pertains generally to compounds and to the design of these compounds targeted to bind to ribonucleic acid [(RNA)]; and more particularly, to compounds that bind specifically to certain nucleotide base pairs in combination with elements of the secondary structure of the minor groove of [RNA] molecules." Page 1. Further according to the specification (pages 1 and 2):

> Three principal types of RNA exist in cells: messenger RNA, transfer RNA and ribosomal RNA. . . .
>
> The RNAs share a common overall structure, though each kind of RNA has a unique detailed substructure. Generally RNA is a linear, single-stranded . . . , repetitive polymer in which nucleotide subunits are covalently linked to each other in sequence. Each nucleotide subunit consists of a base linked to the ribose-phosphate of the polymeric backbone. The bases in RNA are adenine (A), uracil (U), guanine (G), and cytosine (C). The sequence of bases imparts specific function to each RNA molecule. Nucleotide bases from different parts of the same or different RNA molecules recognize and noncovalently bond with each other to form base pairs. Since RNAs generally are a single covalent strand, base pairing interactions are usually intrastranded . . . [and] play a major part in determining the three-dimensional structure of each of the RNAs and the interaction of RNA molecules with each other and with other molecules. . . .
>
> The RNA molecule forms a helix with major and minor grooves spiraling around the axis . . . Nucleotide bases are arranged near the center of the helix with the ribose phosphate backbone on the outside. The bases are planar, perpendicular to the axis, and stacked on one another. Because the helix is in the alpha form, bases and sequences of bases are most accessible from the minor groove, which is wider and more shallow than the major groove . . .

For a number of reasons discussed at length in the specification (e.g., pages 9, 10, 20, 23 and 46), "the primary basis for sequence discrimination in RNA is believed to be the minor groove." Specification, page 23.

DISCUSSION

Rejection I: Enablement

"The first paragraph of 35 U.S.C. § 112 requires, inter alia, that the specification of a patent enable any person skilled in the art to which it pertains to make and use the claimed invention. Although the statute does not say so, enablement requires that the specification teach those in the art to make and use the invention without 'undue experimentation.' In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). That some experimentation may be required is not fatal; the issue is whether the amount of experimentation required is 'undue.'" In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991) (emphasis in original).

A number of factors are relevant to whether undue experimentation would be required to practice the claimed invention, including "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

The claimed invention is directed to methods of designing compounds that will bind to a critical site within the minor groove of a ribonucleic acid molecule and inhibit its function. The method comprises five fundamental steps: (a) identifying a nucleotide sequence (i.e., the primary structure) in an RNA molecule that is critical to its function; (b) determining the secondary structure of the region where the critical site is located; (c) determining the tertiary structure of the region where the critical site is located, and its position relative to the major and minor grooves of the molecule; (d) determining the sequence of nucleotides and structure flanking the critical site that is specific to the critical region and within the minor groove; and (e) designing a compound that will specifically bind the critical site within the minor groove and inhibit RNA function. See, e.g., claim 1.

The examiner concedes that "steps (a)-(d) [were] known in the prior art at the time of the instant invention as being reasonably reliably performed." Examiner's Answer, page 15. Nevertheless, following an analysis of step (e) under the Wands factors, the examiner concludes that the specification enables nothing more than "trial and error methodology," which "is not design but instead a screening method of the type that is well known as random mutagenesis." Id., page 10.

Thus, the dispositive issue is this: having identified both the sequence and the local three-dimensional structure of a critical site within the minor groove of a target RNA molecule by performing steps (a) through (d) of the claimed method, would it have required

undue experimentation for one skilled in the art to design a compound that would specifically bind the critical site and inhibit RNA function?

According to the examiner, the claims are extremely broad; the quantity of experimentation required to design or obtain an inhibitory compound would be significant; there are no working examples in the specification beyond determining the location and sequence of a critical site in the minor groove of an RNA molecule; there is no guidance other than directing one skilled in the art to target critical sites within the minor groove using complementary nucleotides and hydrogen bond acceptors and donors. Examiner's Answer, pages 3 through 10. Finally, the examiner points to Wilson[3] as evidence that, even three years after the instant filing date, "relatively little progress has been made towards generating compounds that specifically interact and inhibit critical sites on RNA molecules, especially in the minor groove." Id., page 8.

The specification, on the other hand, indicates that at the time of the invention, various computer modeling systems had been used to resolve the three-dimensional structures of specific proteins, and also to design molecules specifically interactive with them. According to the specification, at the time of the invention, computer modeling had found limited use in the design of compounds interactive with nucleic acids because the generation of structural information about nucleic acids had lagged behind computer

[3] Wilson et al (Wilson), "The Search for Structure-Specific Nucleic Acid-Interactive Drugs: Effects of Compound Structure on RNA versus DNA Interaction Strength," Biochemistry, Vol. 32, pp. 4098-4104 (1993).

technology. Specification, pages 47-49. However, further according to the specification, at the time of the invention, advances in RNA synthesis had made previously scarce RNA molecules available for structural analysis by computer modeling. Id., pages 11 and 47.

In reviewing the specification as a whole, it appears that appellant's focus on critical sites within the minor groove of an RNA molecule, where the nucleotide bases and their primary sequence are most accessible, takes the claimed invention out of the realm of trial and error methodology. Once the sequence and local three-dimensional structure of a critical site in a targeted RNA molecule are elucidated by computer modeling, the specification teaches that "[s]pecific binding to the targeted molecule can be achieved by including in the molecule [a] complementary nucleic acid sequence that forms base pairs with the targeted RNA . . . or by inclusion of chemical groups having the correct spatial location and charge." Id., page 49. Finally, Wilson does not appear to describe anything beyond screening known DNA-binding compounds for preferential binding to RNA, thus, it does not provide evidence of failed attempts to design a compound to specifically bind a critical site (of known sequence and local three-dimensional structure) within the minor groove of an RNA molecule.

It is well settled that the examiner bears the initial burden of providing reasons why a supporting disclosure does not enable a claim. As stated in In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971):

> [A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in

> scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

While the factors relied on by the examiner are relevant in determining whether the claimed invention is enabled by the specification, we hold that, on balance, they are insufficient to establish a reasonable basis to doubt the objective truth of statements regarding design of compounds to bind and inhibit the function of RNA molecules. Accordingly, we hold that the examiner has not established that the experimentation required to practice the claimed invention would be undue. The examiner's rejection of claims 1 through 14 for lack of enablement under 35 U.S.C. § 112, first paragraph, is reversed.

Rejections II-IV: Double Patenting

Claims 1 through 5, 8 through 10 and 12 through 14 stand provisionally rejected under 35 U.S.C. § 101 as claiming the same invention as that of claims 1, 3, 14 through 16, 4 through 6 and 8 through 10 of copending application 08/249,689. Claims 1, 2, 8 through 11, 13 and 14 stand provisionally rejected under the judicially-created doctrine of obviousness-type double patenting as unpatentable over claims 1, 3 through 6, 9 and 10 of copending application 08/249,689. Finally, claims 1 through 5, 7 through 10 and 12 through 14 stand provisionally rejected under the judicially-created doctrine of obviousness-type double patenting as unpatentable over claims 1, 3, 14 through 16, 4

through 6 and 8 through 10 of copending application 08/249,689. Appellant does not dispute the merits of any of these rejections. See page 4 of the Brief. As appellant has not argued that the rejections are improper, we affirm them.

CONCLUSION

We have reversed the rejection of claims 1 through 14 for lack of enablement, but affirmed the provisional double patenting rejections of claims 1 through 5 and 7 through 14. As a result of our action today, claim 6 is free of rejection.

AFFIRMED-IN PART

	)
William F. Smith	)
Administrative Patent Judge	)
	)
	)
	) BOARD OF PATENT
Toni R. Scheiner	)
Administrative Patent Judge	) APPEALS AND
	)
	) INTERFERENCES
	)
Demetra J. Mills	)
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