

UNITED STATES BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte ROBERT J. LEFKOWITZ,
MARTIN J. LOHSE, JEFFREY L. BENOVIC,
and MARC G. CARON

Appeal No. 1996-1307
Application No. 08/038,072

ON BRIEF

Before McKELVEY, Senior Administrative Patent Judge, and
SCHAFER and TORCZON, Administrative Patent Judges.

TORCZON, Administrative Patent Judge.

DECISION ON APPEAL

Appellants seek review under 35 U.S.C. § 134 of the
examiner's final rejection of claims 2-4, 7, and 15-19 under
35 U.S.C. § 103. (Paper No. 31 (Not. App.)). We reverse.

BACKGROUND

We select claim 15, reproduced below, as representative
of the claimed invention:

15. A method of inhibiting desensitization of a
cell to the effects of a compound comprising causing
the cell to be contacted with a pharmaceutically
acceptable agent that inhibits β_2 adrenergic
receptor protein kinase-induced phosphorylation of
 β_2 adrenergic receptors for said compound, which β_2
adrenergic receptors are present on the surface of
said cell, wherein said contacting is effected under
conditions such that said inhibition is effected.

The examiner rejected claims 2-4, 7, and 15-19 under 35 U.S.C. § 103 as being unpatentable over

R.J. Lefkowitz & M.G. Caron, "Adrenergic receptors: models for the study of receptors coupled to guanine nucleotide regulatory proteins", 263 J. Biol. Chem. 4993-96 (1988) ("Lefkowitz")

or

R.L. Huganir & P. Greengard, "Regulation of receptor function by protein phosphorylation", 8 Trends Pharm. Sci. 472-77 (1987) ("Huganir")

in view of Appellants' own admissions (Paper No. 33 (Ex. Ans.) at 3).

Lefkowitz and Huganir teach that phosphorylation of the β adrenergic receptor (" β_2 AR")¹ desensitizes the receptor to an agonist. The desensitization may be heterologous (i.e., without the receptor being occupied by agonist) or homologous (i.e., only occurs in agonist occupied receptor). Heterologous desensitization is thought to be caused by phosphorylation of the β_2 AR by cAMP²-dependent protein kinase while homologous desensitization is thought to be caused by

¹In referring to the β adrenergic receptor, Appellants use the term " β_2 AR". In referring to the receptor's kinase, Appellant uses the shorthand term " β AR kinase" (Paper No. 1(Spec.) at e.g., 10, 13). We will use the same shorthand terminology that Appellants use.

²Cyclic adenosine monophosphate.

phosphorylation of the β_2 AR by β adrenergic receptor kinase (β ar kinase) (Lefkowitz at 4995 and Haganir at 474-475).

The examiner states that "[t]he primary references do not teach inhibition of the phosphorylation by using an inhibitor of the kinase."³ The examiner relies upon Appellants' "own admissions" at page ten of Appellants' specification for teaching "known compounds capable of inhibiting receptor kinases involved in mediating homologous desensitization of adenylyl cyclase-coupled receptors" (Paper No. 33 at 3). The relevant disclosure at page ten of Appellants' specification is as follows:

Compounds suitable for use in the present invention include those capable of inhibiting receptor kinases, for example, specific protein kinases involved in mediating homologous desensitization of adenylyl cyclase-coupled receptors (i.e. β ar kinase). (See also Blackshear (1988) FASEB J. 2:2957; Middleton (1988) Ann. Allergy 61:53; Hunnan [sic, Hannun] (1988) Science 243:500.)

DISCUSSION

³Claim 15 requires inhibition of β ar kinase-induced **phosphorylation** which does not necessarily require inhibition of

the kinase. An agent capable of inhibiting the β ar kinase would be expected to inhibit phosphorylation of the receptor and in fact this does appear to be how the claimed invention works(Paper No. 1 (Specification) at 10).

In the context of Appellants' claims, we find that β_2 adrenergic receptor protein kinase-induced phosphorylation is phosphorylation of the receptor induced specifically by β kinase. Appellants describe (Paper No. 1 at 1:25-2:12) β kinase, as do Lefkowitz (at 4995) and Haganir (at 475). β kinase appears to phosphorylate a particular portion of β_2AR that differs from the portions phosphorylated by other kinases (Haganir at 474 and 475 (Fig. 4)).

Lefkowitz and Haganir would have suggested to one skilled in the art that an agent capable of inhibiting β kinase or β kinase induced phosphorylation would inhibit desensitization. Neither reference, however, teaches such an agent.

The examiner relies on a portion of the Appellants' disclosure that refers to three references (Blackshear, Middleton, and Hannun) that teach inhibitors of protein C kinase and cAMP-dependent kinase (See Blackshear at 2957, Middleton at 56, and Hannun at 243). The examiner has not shown where these references teach an agent that inhibits β kinase or β kinase induced phosphorylation. Absent such showing, we do not find that the cited disclosure is an

admission that agents known to inhibit Sar kinase or Sar kinase induced phosphorylation were known in the art.

To establish obviousness of a claimed invention under 35 U.S.C. § 103, all the claim limitations must be taught or suggested by the prior art. In re Royka, 490 F.2d 981, 985, 180 USPQ 580, 583 (CCPA 1974). The examiner has not pointed out where the prior art teaches or suggests an agent capable of inhibiting Sar kinase or Sar kinase induced phosphorylation. Without such a teaching or suggestion, the references suggest a course for further research, but not the present invention. In re O'Farrell, 853 F.2d 894, 903, 7 USPQ2d 1673, 1680-81 (Fed. Cir. 1988). (An invitation to experiment is not obviousness). The rejection of claim 15 under 35 U.S.C. § 103 is reversed.

Claims 2-4, 7, and 16-19 are also directed to methods of inhibiting desensitization that require an agent that inhibits Sar kinase-induced phosphorylation. Accordingly, the rejection of these claims under 35 U.S.C. § 103 is also reversed.

DECISION

The examiner's rejection of claims 2-4, 7, and 15-19 under 35 U.S.C. §§ 103 is

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REVERSED

PATENT

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