

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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. 19

UNITED STATES PATENT AND TRADEMARK OFFICE

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

Ex parte BEI SHAN, R. MARC LEARNED, M. CATHERINE AMARAL,
STEVEN L. MCKNIGHT, FABIENNE CHARLES DE LA BROUSSE
and JIN-LONG CHEN

Appeal No. 2000-0441¹
Application No. 08/866,942

ON BRIEF

Before WILLIAM F. SMITH, SCHEINER and GRIMES, Administrative Patent Judges.
SCHEINER, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 1-3 and 5-14, the only claims remaining in the application. Claims 1 and 5 are representative of the subject matter on appeal:

1. An isolated genetic knock-in cell, wherein said cell is, or is a progeny of, a genetic knock-in primary cell obtained from a transgenic mouse made by homologous recombination of a targeted native allele with a transgene comprising a sequence encoding a reporter flanked by flanking sequences which effect the homologous recombination of said transgene with said native allele, wherein the expression of said reporter is under the control of native gene expression regulatory sequences of said native allele.

¹ Application for patent filed May 31, 1997. According to appellants, this application is a continuation-in-part of application no. 08/707,408, filed September 4, 1996, now U.S. Patent no. 5,780,258.

5. A cell-based method for screening for modulators of a targeted gene expression, said method comprising steps:

(a) isolating a genetic knock-in primary cell from a transgenic mouse made by homologous recombination of a targeted native allele with a transgene comprising a sequence encoding a reporter flanked by flanking sequences which effect the homologous recombination of said transgene with said native allele, wherein the expression of said reporter is under the control of native gene expression regulatory sequences of said native allele,

(b) determining a first reporter expression level in a first isolated cell wherein said first isolated cell is, or is a progeny of said genetic knock-in cell;

(c) contacting a second isolated cell wherein said second isolated cell is, or is a progeny of said genetic knock-in cell with a candidate agent under conditions whereby but for the presence of said agent, said reporter is expressed at said first reporter expression level;

(d) determining a second reporter expression level in said second isolated cell;

(e) comparing said first expression level with said second expression level, wherein a difference between said first and second expression levels indicates that said candidate agent modulates the targeted gene expression.

The references relied on by the examiner are:

Foulkes et al. (Foulkes)	5,665,543	Sep. 9, 1997
Wadsworth et al. (Wadsworth)	5,720,936	Feb. 24, 1998
Skoultchi et al. (Skoultchi)	WO 91/06667	May 16, 1991

The issue presented for review is whether claims 1-3 and 5-14 are unpatentable under 35 U.S.C. § 103 in view of Foulkes, Wadsworth and Skoultchi.

DISCUSSION

According to the examiner, Foulkes describes genetic knock-in cells derived from established cells lines by homologous recombination of a targeted native allele with a transgene encoding a reporter, wherein the expression of the reporter is under the control of the native gene expression regulatory sequences. Paper No. 4. The cells are used in a reporter assay to screen candidate compounds for the ability to modulate expression of the targeted native allele.

As indicated above, the claims stand rejected as unpatentable under 35 U.S.C. § 103, nevertheless, the examiner argues that “Applicant has not demonstrated any patentable distinction conferred upon the claimed cell(s) as a result of being isolated from a transgenic animal.” Paper. No. 7, page 4. The implication is that Foulkes anticipates the claimed invention. Further, “[i]t is the Examiner’s position that Appellant’s [sic] have not met their burden to illustrate that structural differences do indeed exist in the first place and that these differences translate or result in activities or functions that are distinct from those of cultured primary cells that have been “knocked-in” after isolation from a non-transgenic animal.” Answer, page 3.

“[E]very limitation of a claim must identically appear in a single prior art reference for it to anticipate the claim.” Gechter v. Davidson, 116 F.3d 1454, 1457, 43 USPQ2d 1030, 1032 (Fed. Cir. 1997). Moreover, “the Patent Office has the initial burden of coming forward with some sort of evidence tending to disprove novelty.” In re Wilder, 429 F.2d 447, 450, 166 USPQ2d 545, 548 (CCPA 1970).

Here, the examiner cites no evidence tending to show that Foulkes cells and the claimed cells are the same. Because we find that the examiner’s conclusory statements are insufficient to discharge the Office’s initial burden of establishing a prima facie case of anticipation, we find it unnecessary to address the declaration of coinventor McKnight, wherein he states that “[p]rimary cells obtained from transgenic animals are distinguishable from cell lines or primary cells modified by homologous recombination . . . because genes ‘knocked in’ to a pluripotent stem cell are subject to ontogeny - the many, diverse molecular modifications of the genome that result in differentiation into primary cells, e.g.[,] cytosine methylation.” Paper No. 10.

Moreover, we know of no authority, and the examiner cites none, that supports the proposition that structural differences in the claimed primary cells must “translate or result in activities or functions that are distinct” (Answer, page 3) from those of prior art cells in order to avoid anticipation.

With respect to obviousness, the examiner argues that “even if differences did exist and they also resulted in distinctions in expression activity, [Wadsworth] already provides those differences.” Answer, page 4.

Wadsworth is directed to developing transgenic animal models for Alzheimer’s disease. The models express the three normal forms of the β -amyloid precursor protein (APP) as well as various naturally occurring mutated forms. Abstract. “The transgenic animals and animal cells are used to screen compounds for a potential effect in the treatment of Alzheimer’s disease using standard methodology[;] [a] compound is administered to the animals or introduced into the culture media . . . then the animals or animal cells are examined for alterations in APP expression, histopathology, and/or behavior.” Column 15, line 64 to column 16, lines 1-3. While Wadsworth does teach that “[c]ell cultures can be isolated from the transgenic animals or prepared from established cell lines using the same constructs with standard cell transfection techniques” (column 5, lines 1-4), all of the transgenic cell lines used in the examples were derived from established cell lines, and most have non-native inducible promoters. None of the animals or animal cells contain reporter genes, thus expression of APP is measured using Northern blots, antibody detection, and Western blots.

According to the examiner, Wadsworth, “[t]aken together with the teachings of Foulkes [] who demonstrate that reporter constructs like those of the instant claims are introduced into cells via homologous recombination and the teachings of Skoultchi []

who illustrate that primary cells undergo homologous recombination, [renders] the claimed invention obvious for reasons made of record in the previous office action.” Answer, page 4. Turning to the previous office action for the reasons, we find only the assertion that “[t]he ordinary artisan would have been motivated to apply the teachings of Foulkes [] and Wadsworth [] to generate reporter knock-in transgenic mice from which cells are isolated to screen for modulators of gene expression.” Paper No. 7, page 5.

Clearly, the examiner has established that individual parts of the claimed invention were known in the prior art. However, as explained in In re Kotzab, 217 F.3d 1365, 1369-70, 55 USPQ2d 1313, 1316 (Fed. Cir. 2000) (citations omitted):

A critical step in analyzing the patentability of claims pursuant to section 103(a) is casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field. [] Close adherence to this methodology is especially important in cases where the very ease with which the invention can be understood may prompt one “to fall victim to the insidious effect of a hindsight syndrome wherein that which only the invention taught is used against its teacher.” []

Most if not all inventions arise from a combination of old elements. [] Thus, every element of a claimed invention may often be found in the prior art. [] However, identification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention. [] Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant.

“It is impermissible to use the claimed invention as an instruction manual or ‘template’ to piece together the teachings of the prior art so that the claimed invention is rendered obvious.” In re Fritch, 972 F.2d 1260, 1266, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992), citing In re Gorman, 933 F.2d 982, 987, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991). The examiner may establish a case of prima facie obviousness based on a combination of references “only by showing some objective teaching in the prior art or that knowledge

generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references.” Id., 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992).

The fact that the prior art could have been modified in a manner consistent with appellants’ claims would not have made the modification obvious unless the prior art suggested the desirability of the modification. In re Gordon, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984). On this record, the only reason or suggestion to combine the references in the manner claimed comes from appellants’ specification.

Nor are we persuaded by the examiner’s assertion that “[t]he ordinary artisan would have had an expectation of success because of the teachings” of the prior art. Paper No. 7, page 5. An expectation of success is an element in a prima facie case of obviousness, but it is not enough in the absence of a reason to modify the references in the first place.

Accordingly, the rejection of the claims under 35 U.S.C. § 103 is reversed.

REVERSED

William F. Smith)
Administrative Patent Judge)
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) BOARD OF PATENT
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Toni R. Scheiner) APPEALS AND
Administrative Patent Judge)
) INTERFERENCES
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Appeal No. 2000-0441
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Page 7

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