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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte CASEY CASE

Appeal 2017-000729[1]
Application 12/736,665
Technology Center 1600

Before DONALD E. ADAMS, RICHARD M. LEBOVITZ, and FRANCISCO C. PRATS, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

This appeal involves claims directed to a neural regenerating cell descended from a mesenchymal adherent stem cell. The Examiner rejected the claims under 35 U.S.C. § 102 as anticipated, or alternatively under 35 U.S.C. § 103 as obvious, and as patent ineligible subject matter under 35 U.S.C. § 101. Appellant appeals the Examiner's determination under 35 U.S.C. § 134 that the claims are unpatentable. We have jurisdiction under 35 U.S.C. § 6(b). The Examiner's decision is reversed.

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[1] The Appeal Brief ("Appeal Br.") identifies SanBio, Inc., as the real-party-in-interest.

STATEMENT OF THE CASE

The Examiner finally rejected claims 25–27 as follows:[2]

Claims 25–27 under pre-AIA 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under pre-AIA 35 U.S.C. § 103(a) as unpatentable over Xiaoxiao Long et al. (*Neural Cell Differentiation In Vitro from Adult Human Bone Marrow Mesenchymal Stem Cells*, Stem Cells and Development, 2005, 14(1):65-69) ("Long"). Ans. 2.

Claims 25–27 under 35 U.S.C. § 101 because the claimed invention is directed to a naturally-occurring cell which is patent eligible subject matter. Ans. 2.

Claim 25, which is the only independent claim on appeal, is reproduced below:

> 25. A neural regenerating cell that is descended from a MASC *in vitro,* wherein:
>
> (a) the cell supports the growth and/or regeneration of neural tissue;
>
> (b) the methylation state of one or more genes in the cell is altered compared to the MASC, wherein the alterations in methylation comprise:
>
> (i) increased methylation of the PITX2, DNMT3b, IGF2R and SDF4 genes, and
>
> (ii) decreased methylation the ROPN1L and TMEM179 genes; and
>
> (c) during culture *in vitro,* neither the MASC nor any of its descendants were transfected with a polynucleotide comprising sequences encoding a Notch intracellular domain.

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[2] The rejections appeared in the Non-Final Office Action mailed November 19, 2014 ("Office Act.").

REJECTIONS BASED ON LONG

Claim 25 is directed to a neural regenerating cell ("NRC") descended from a marrow adherent stem cell ("MASC"). The claim recites that the cell has three properties: (a) supports the growth and/or regeneration of neural tissue; (b) has a specifically recited gene methylation pattern; and (c) the MASC cell or its descendants were *not* transfected with a polynucleotide comprising sequences encoding a Notch intracellular domain ("NID").

The Examiner found that the claimed cell is the same, or obvious over, the cell disclosed in Long. Ans. 11. Long describes a bone marrow (BM) mesenchymal stem cell (MASC) which is capable of expanding and differentiating into neural cells (NCs). Long Abstract. The Examiner found that "a MASC derived cell produced by the method taught by Long et al. would be the same as the MASC derived cell recited in claim 25." Office Act. 10. The Examiner stated that the inventors "may have devised a new method for generating MASC derived cells, but not new MASC derived cells." *Id.* The Examiner stated "the characteristics of the neural regenerating cell in claim 25 amount to no more than newfound characteristics of a known product." Ans. 11. Citing *In re Best*, 562 F.2d 1252, 1255 (CCPA 1977), the Examiner stated that "[b]ecause the Office does not have the facilities for examining and comparing the Applicants' product with the products of the prior art the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art." Office Act. 9.

With respect to the recited gene methylation pattern, the Examiner found that because the claimed cell is derived from the same progenitor MASC cell as Long's cell, "the suspicion then is that the changes in

methylation occur naturally and are inherent to the process of deriving the neural regenerating cell from a MASC, which is clearly taught by Long." Ans. 11.

The Examiner also found that the claimed methylation pattern, as described in the Specification, was obtained by transfecting cells with NID, but this step is excluded from the claim. Ans. 7–8. For this reason, the Examiner stated that it is improper to rely on the methylation pattern of an NID transfect cell as a basis for distinguishing Long. *Id.* 7.

Discussion

The NRC cells described in the Specification were prepared from MASC cells that were transfected with a plasmid encoding NID. Spec. ¶ 40. The inventors derived a transfected cell line ("NRC") and compared its methylation pattern to the progenitor MASC cells. *Id.* ¶¶ 49–50. The inventors disclosed that the methylation patterns between the two cell types are different (*id.* ¶¶ 51, 52, Tables 3 and 5–7) and several of these differences are recited in claim 25.

While the methylation pattern of the NRC cells were identified in NID transfected cells, the Specification teaches that "achieving the same methylation changes by other means is also useful for preparing NRCs." *Id.* ¶ 56. Consistently, the Specification teaches that "targeted alteration of methylation state can be used to convert a progenitor cell to a neural regenerating cell" and describes methods of doing so. *Id.* ¶¶ 23–29. Claims 26 and 27 are directed to cells in which targeted methylation and demethylation is used to make the claims NRC cells. Based on these disclosures, we find that the Examiner improperly ignored the methylation

pattern recited in the claim because the Specification teaches that the NRC cells, and the characteristic methylation pattern of this cell type, can be produced in ways other than transfection with an NID.

The Examiner acknowledges that Long does not describe the recited methylation pattern, but asserts that it would be *inherent* to Long's cells because they are derived from the same MASC progenitor cells as were the claimed NRC cells. This argument is not persuasive.

> Inherency . . . may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. (Citations omitted.) If, however, the disclosure is sufficient to show that the natural result flowing from the operation as taught would result in the performance of the questioned function, it seems to be well settled that the disclosure should be regarded as sufficient.

In re Oelrich, 666 F.2d 578, 581 (CCPA 1981).

It has been well-established by precedent that when inherency is the basis of a rejection, the Examiner must have a "sound basis" for believing that a process carried out in the prior art produces the same product as claimed. *In re Spada*, 911 F.2d 705, 708 (Fed. Cir. 1990). Thus, there must be a factual or other logical basis that provides an Examiner with a reason to find that the prior art product, while silent, possesses the same properties as claimed. Once a sound basis is established, the Examiner can properly shift the burden to applicant to prove that the prior art process does not produce the same product as claimed. *Best*, 562 F.2d at 1255.

In this case, the Examiner did not provide sufficient factual basis to shift the burden to Appellant to prove the Long's cells are the same as those which are claimed.

As argued by Appellant, the claimed cells "are capable of stimulating neural recovery and/or neural regeneration after transplantation to sites of nervous system injury or disease." Spec. ¶ 6; claim 25, limitation (a). In contrast, Long's cells differentiate into neural cells. Long Abstract. Thus, the functions of the two cell types are described as being different. This difference is supported by the disclosure in the Specification which states: "The cells described and characterized in the present disclosure can also be converted, after further treatments, into cells that have the properties of neural cells and neural precursor cells." Spec. ¶ 59. In other words, while the treatment of MASC cells in Long results in their differentiation into neural cells, the NID treatment of MASC disclosed in the Specification produces cells which are not yet neural cells, but instead stimulate neural recovery and regeneration, and which by additional treatment may be converted into neural cells.

Anticipation by inherency cannot be established by probabilities or possibilities. *Oelrich*, 666 F.2d at 581. Because the Examiner did not provide adequate factual evidence that the cells in Long are the same as those which are claimed, the Examiner did not have an adequate factual basis for shifting the burden to Appellant to prove otherwise. Accordingly, the anticipation rejection of claims 25–27 based on Long is reversed. The obviousness rejection is reversed for the same reasons and because the Examiner did not explain why cells having the claimed properties would have been obvious to one of ordinary skill in the art.

REJECTION BASED ON § 101

The Examiner rejected claims 25–27 as being directed to a naturally-occurring cell which is ineligible for a patent under 35 U.S.C. § 101. Office Act. 4–5. The Examiner found that the claimed NRC cell is derived from a naturally occurring MASC which is "not markedly different in structure from [it]." *Id.* 6. The Examiner stated that the Specification does not establish that the claimed methylation pattern of the NRC cells is different from a naturally occurring cell descended from a MASC. *Id.* The Examiner also argues that changes in DNA methylation occur naturally during differentiation and Appellant has not established that the claimed changes would not naturally occur. Ans. 5.

As discussed above, the claimed cells have a methylation pattern diagnostic for NRCs produced by transforming MASC cells with a plasmid encoding Notch intracellular domain. Spec. ¶ 56. The Specification provided evidence that the DNA methylation pattern of the NRC is different from that of the progenitor MASC. *Id.* ¶¶ 51, 52. The cells with the recited methylation pattern are not neural cells, but require additional steps to convert them to a neural cell type. *Id.* ¶ 59. The Examiner did *not* provide evidence that cells with the claimed property of "support[ing] the growth and/or regeneration of neural tissue" occur in nature. Long, as explained above, shows the differentiation of MASC cells into neural cells, but not cells which support the growth and regeneration of neural tissue. Thus, Long is not persuasive evidence that the cells naturally occur.

The Examiner also did not provide adequate evidence that would have given one of ordinary skill in the art a factual or other logical basis to believe that cells having a methylation pattern characteristic of MASC cells

transformed with a plasmid encoding NID occur in nature, which is an artificial and non-naturally occurring DNA construct.

Because the Examiner did not meet the burden of establishing that the claimed cells are found in nature, the § 101 rejection is reversed.

REVERSED