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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte PAOLA NISTICO, FRANCESCA DI MODUGNO, and MARIA SIMONA PINO

Appeal 2017-010301
Application 12/997,795[1]
Technology Center 1600

Before ULRIKE W. JENKS, JOHN G. NEW, and ELIZABETH A. LAVIER, *Administrative Patent Judges*.

LAVIER, *Administrative Patent Judge.*

DECISION ON APPEAL

Pursuant to 35 U.S.C. § 134(a), Appellants seek review of the Examiner's rejections of claims 1–5, 10, 20–24, and 29. We have jurisdiction under 35 U.S.C. § 6(b). For the reasons set forth below, we AFFIRM.

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[1] Appellants identify the real party in interest as Istituti Fisioterapici Ospitalieri (IFO) – Istituto Regina Elena Per Lo Studio E La Cura Dei Tumori. Br. 3.

BACKGROUND

The Specification relates to a method for determining whether a tumor is sensitive or resistant to EGFR[2] inhibitor drugs by testing for expression of the hMena^{+11a} splicing variant of hMena. Spec. 4:5–8.

Claim 1 is illustrative, and recites:

> 1. A method for discriminating between sensitive and resistant tumours to a treatment with EGFR inhibitor drugs comprising:
>
> - *in vitro* testing whether tumour material expresses the hMena^{+11a} splicing variant of hMena, a tumour comprising the tumour material positive for said testing being sensitive to the treatment, wherein said testing is carried out by detecting hMena^{+11a} isoform protein with an antibody or fragment thereof that specifically recognises the hMena^{+11a} isoform without cross reacting with other hMena isoforms.

Br. 21 (Claims Appendix).

REJECTIONS MAINTAINED ON APPEAL

1. Claims 1–5, 20, and 29 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Di Modugno[3,4] and Adolf.[5] Ans. 3.

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[2] Epidermal growth factor receptor (EFGR) "is commonly over expressed in a number of epithelial malignancies and its up regulation is often associated with an aggressive phenotype of the tumour," and thus represents a promising target for cancer treatment. Spec. 1:5–8; *see also id.* at 1:14–20.

[3] Di Modugno et al., *Molecular Cloning of hMena (ENAH) and Its Splice Variant hMena^{+11a}: Epidermal Growth Factor Increases Their Expression and Stimulates hMena^{+11a} Phosphorylation in Breast Cancer Cell Lines*, 67 CANCER RES. 2657 (2007).

[4] Di Modugno is sometimes referred to in the record as "Di Modugno II." We have left unaltered such references in the passages quoted herein.

[5] Adolf et al., US 6,972,324 B2, issued Dec. 6, 2005.

2. Claims 10 and 21–24 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Di Modugno, Adolf, and Baker.[6] Ans. 7.

DISCUSSION

Upon consideration of the evidence on this record and each of Appellants' contentions, we find that the preponderance of evidence on this record supports the Examiner's conclusions that the appealed claims are unpatentable over the cited prior art. Accordingly, we sustain Rejections 1 and 2 for the reasons set forth in the Answer at pages 3–8 and 10–15, which we incorporate herein by reference. We offer the following discussion for emphasis only.

A. Rejection 1

Di Modugno reports the cloning of hMena and hMena^{+11a} from a breast carcinoma cell line, and reports that EGF treatment in breast cancer cell lines promotes upregulation of hMena and hMena^{+11a}, "resulting in an increase of the fraction of phosphorylated hMena^{+11a} isoform only." Di Modugno Abstract. hMena and hMena^{+11a} differ from one another insofar as hMena^{+11a} contains an additional exon corresponding to 21 amino acids. *Id.; see also id.* at Figs. 1C, 1D. Di Modugno teaches using an anti-hMena antibody, CKLK1, which recognizes both isoforms, for Western blot analysis to study protein expression in tumor cell lines. *See id.* at 2660. Di Modugno notes that "[t]he hMena and hMena^{+11a} isoforms are not clearly distinguishable by Western blot because they comigrate (88–90 kDa)." *Id.*

[6] Baker et al., US 2007/0128636 A1, published June 7, 2007.

The Examiner relies on Di Modugno as teaching the elements of claim 1 with the exception that "Di Modugno II does not teach discriminating between tumors that are sensitive or resistant to treatment with EGFR inhibitor drugs via the detection of the hMena^{+11a} variant using an antibody that is specific for the hMena^{+11a} variant and does not cross-react with other isoforms." Non-Final Action 8.[7] To remedy this deficiency, the Examiner turns to Adolf, which teaches "the production of two CD44v6 antibodies with different properties." Non-Final Action 9 (citing Adolf 3:1–13). The Examiner finds that "[b]y substituting the hMena^{+11a} variant that was disclosed and sequenced by Di Modugno II for the CD44v6 variant of Adolf et al., one could produce an antibody that is specific for the hMena^{+11a} variant and does not cross-react with other isoforms," and that it would have been obvious to do so in part[8] because "Di Modugno II teaches that detecting the hMena^{+11a} variant would provide a method for discriminating between tumors that are sensitive or resistant to treatment with EGFR inhibitor drugs." *Id.*

Appellants argue the rejection of claim 1 is the product of hindsight and unsupported opinions. *See* Br. 11–12. Specifically, Appellants assert that Di Modugno "is completely silent on whether tumors are resistant (or not) to EGFR inhibitor drugs," and further that "[n]owhere does Di Modugno suggest or otherwise make obvious the conclusion that detection of hMena^{+11a} would allow discrimination between tumors that are sensitive or resistant to treatment with EGFR inhibitor!" *Id.* at 12.

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[7] Non-Final Action dated May 5, 2014.
[8] A full description of the Examiner's rationale for combining the references as claimed can be found at pages 9–10 of the Non-Final Action.

We are not persuaded. The "discriminat[ion] between sensitive and resistant tumours to a treatment with EGFR inhibitor drugs" recited in claim 1 amounts to an intended purpose, not a claim limitation.[9] As the Examiner points out, "the only meaningful limitation of claim 1 comprises detecting the hMena^{+11a} isoform of hMena using an antibody that specifically recognizes the hMena^{+11a} isoform without cross reacting with other hMena isoforms." Ans. 13. We discern no error in the Examiner's conclusion that this step would have been obvious to the ordinarily skilled artisan at the time of the invention, because (1) Di Modugno provides the 21-amino acid sequence of the exon unique to the hMena^{+11a} isoform (*see* Ans. 11), and (2) "[i]n view of the teachings of Di Modugno et al. and Adolf et al., one of ordinary skill in the art would reason that detecting the hMena^{+11a} variant of hMena could be carried out by using antibodies that are hMena^{+11a} variant-specific" (*id.*).[10] Accordingly, for these reasons and those already of record, we affirm the rejection of claim 1.

With respect to Appellants' allegation that the Examiner impermissibly relied upon hindsight in performing the obviousness analysis:

> Any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning, but so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made and does not include knowledge gleaned only from applicant's disclosure, such a reconstruction is proper.

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[9] Our analysis likewise applies to the similar (but not identical) intended use language in the preambles of claims 10 and 29.

[10] Even if we were to construe the preamble of claim 1 as limiting, we would still affirm the Examiner's rejection for claim 1, for the reasons articulated by the Examiner on pages 14–15 of the Answer.

In re McLaughlin, 443 F.2d 1392, 1395 (CCPA 1971). Appellants point to no knowledge that the Examiner relied upon which could have been gleaned only from Appellants' Specification. The Examiner, relying solely upon the teachings of the cited prior art, concluded that a skilled artisan would have had a reasonable expectation of success in combining the references for the reasons we set forth *supra*, and additionally based upon the teachings of Baker. Final Act. 6. Appellants have, for the reasons we have explained, not persuaded us to the contrary; indeed, Appellants do not address the Examiner's latter conclusion in this respect.

Appellants group claims 2–5 and 20 along with claim 1 (*see* Br. 9) and do not separately argue these claims. Thus, claims 2–5 and 20 fall with claim 1. *See* 37 C.F.R. § 41.37(c)(1)(iv). Although Appellants state that claim 29 forms a separate group (*see* Br. 9), Appellants do not argue it separately from claim 1. *See generally* Br. 10–14. As such, we affirm the rejection of claim 29 for substantially the same reasons as claim 1.

B. Rejection 2

Appellants' arguments in favor of the patentability of claims 10 and 21–24 largely retrace their arguments with respect to claim 1. *Compare* Br. 14–16 *with id.* at 10–14. In regard to Baker, the additional reference unique to Rejection 2, Appellants state:

> At best, Baker shows it would have been desirable to identify a specific marker for circulating tumor-cells in the blood. *There is no evidence or reasoning, however, that it would have been obvious to make an antibody or fragment thereof that specifically recognizes the hMena^{+11a} isoform without cross reacting with other hMena isoforms.* Thus, even the broadest claim is not made obvious by the combination of Di Modugno and Adolf, further in view of Baker.

Br. 15–16 (emphasis added). As is apparent from the emphasized sentence, the essence of this argument is about Di Modugno, not Baker. For the reasons discussed above with respect to Rejection 1 and those already of record, we are not persuaded of any reversible error in the Examiner's reliance on Di Modugno, nor in the combination of Di Modugno with Adolf. As such, Appellants have not demonstrated any reversible error by the Examiner in rejecting claim 10. Appellants group claims 21–24 with claim 10 (*see* Br. 9) and argue them only by virtue of their dependency on claim 10 (*see id.* at 16). Accordingly, claims 21–24 fall with claim 10.

CONCLUSION

The rejections of claims 1–5, 10, 20–24, and 29 are affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED