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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte KENJI KANGAWA and HIROSHI HOSODA

Appeal 2018-006922
Application 10/554,875
Technology Center 1600

Before ERIC B. GRIMES, JEFFREY N. FREDMAN, and ULRIKE W. JENKS, *Administrative Patent Judges*.

JENKS, *Administrative Patent Judge*.

DECISION ON APPEAL

Pursuant to 35 U.S.C. § 134(a), Appellant[1] appeals from the Examiner's decision to reject claims for obviousness. We have jurisdiction under 35 U.S.C. § 6(b).

We REVERSE.

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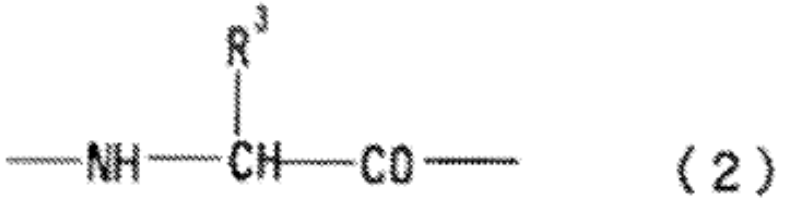
[1] We use the word "Appellant" to refer to "applicant" as defined in 37 C.F.R. § 1.42(a). Appellant identifies the real party in interest as Dr. Kenji Kangawa. Appeal Br. 1. Herein we refer to the Final Office Action of May 5, 2017 (Final Act."), Appeal Brief of October 6, 2017 ("Appeal Br."), Examiner's Answer of March 12, 2018 ("Ans."), Reply Brief of June 25, 2018 ("Reply Br."), Specification of October 31, 2005 ("Spec."), as well as to the prior Board Decision of March 24, 2016 ("Decision").

STATEMENT OF THE CASE

The Specification discloses that "ghrelin is a peptide consisting of 28 amino acids residues which were found in the stomach, and the serine residue at position 3 is modified with an octanoyl group . . . . It is shown that ghrelin acts on [the] Growth Hormone Secretagogue-Receptor (GHS-R) . . . , and is an endogenous brain-gut hormone which stimulates GH secretion from pituitary gland." Spec. 3: 16–20. "[A] polypeptide derivative having an activity of binding to GHS-R . . . ha[s] an activity of promoting hepatocyte proliferation and, as a result, is useful for . . . recovering hapatic regeneration and hepatic function." *Id.* 5: 11–17.

Claims 20, 27, 32, and 48–53 are on appeal, and can be found in the Claims Appendix of the Appeal Brief. Claim 20 is representative of the claims on appeal, and reads as follows:

> 20. A method for *promoting hepatic regeneration and/or hepatic function recovery after hepatectomy*, the method comprising administering to a mammal in need thereof a polypeptide derivative capable of binding to growth hormone secretagogue receptor and elevating intracellular calcium ion concentration, or a salt thereof, the derivative consisting of an amino acid sequence selected from SEQ ID NOS: 1 to 16, 19 to 22, or combinations thereof, wherein the second or third amino acid residue from the amino-terminus of the amino acid sequence comprises a serine or a group represented by the formula (2),



(2),

> wherein R^3 is $-T^2-P^2-Q^2$, T^2 is methylene, P^2 is -CO-O, and Q^2 is an optionally substituted $C_{1–20}$ alkyl group.

Appeal Br. 10 (Claims Appendix)(emphasis added).

Appellant requests review of Examiner's rejection of claims 20, 27, 32, and 48–53 under pre-AIA 35 U.S.C. § 103(a) over Bednarek[2] and/or Kangawa[3] in view of Matsumoto,[4] Tacke,[5] Skakkebaek,[6] and Wonke.[7]

Examiner finds that Bednarek and Kangawa teach the polypeptide derivative as claimed, but recognizes that Kangawa "does not teach the use of Ghrelin for the treatment of hepatopathy." Final Act. 5. Examiner relies on Matsumoto and Tacke to teach that ghrelin peptides are potent ligands for the growth hormone secretagogue receptor. *Id.* Examiner relies on Skakkebaek and Wonke to teach that administration of growth hormone provides a benefit to patients with chronic liver disease. *Id.* at 6. Based on the beneficial effect of growth hormone in patients with chronic liver disease and the knowledge the ghrelin stimulates growth hormone secretion, Examiner concludes that "[t]here is no reason to believe that [by administering ghrelin to stimulate growth hormone secretion] there would not be a benefit to liver function in general, or to patients in need of hepatic regeneration or after a liver transplant. The instant invention is beneficial for the liver." *Id.* at 7.

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[2] Bednarek, WO 01/92292 A2, published December 6, 2001.
[3] Kangawa et al., US 7,385,026 B1, issued June 10, 2008 ("Kangawa").
[4] Matsumoto et al., *Structure-Activity Relationship of Ghrelin: Pharmacological Study of Ghrelin Peptides*, 287 Biochem. Biophys. Research Comm. 142–46 (2001)("Matsumoto").
[5] Tacke et al., *Ghrelin is a parameter of catabolism in patients with chronic liver disease*, Hepatology AASID Abstracts, 530A (2002)("Tacke").
[6] Skakkebaek et al. US 5,492,891, issued February 20, 1996 ("Skakkebaek").
[7] Wonke et al., *New Approaches to the Management of Hepatitis and Endocrine Disorders in Cooley's Anemia*, 850 Annals New York Academy of Science, 232–41 (1998)("Wonke").

Appellant contends that the Examiner has failed to articulate a rationale that would lead one of ordinary skill in the art to select patients based on the need for supporting hepatic regeneration. *See* Appeal Br. 3; *see also* Reply Br. 5 (the present claims are directed to "'promoting hepatic regeneration and/or hepatic function recovery after hepatectomy,' while the previously appealed claims were directed to the broader scope of 'treating hepatopathy.'").

The issue is, does the preponderance of evidence of record support Examiner's conclusion that the combination of references renders the claims directed to recovery after hepatectomy obvious?

We begin with claim interpretation in order to determine the scope of the claim so that we can then compare the claimed subject matter to the prior art. "[D]uring examination proceedings, claims are given their broadest reasonable interpretation consistent with the specification." *In re Hyatt*, 211 F.3d 1367, 1372 (Fed. Cir. 2000). The current claims are directed to "hepatic regeneration and/or hepatic function recovery after hepatectomy." Here, the limitation "after hepatectomy" modifies both "hepatic regeneration" and "hepatic function recovery." This interpretation is reasonable given that the Specification discloses that a ghrelin polypeptide derivative "has hepatocyte proliferation promoting activity, and is also useful as an agent for promoting hepatic regeneration/hepatic function recovery after liver operation, particularly, hepatectomy." Spec. 63: 20–23. "After hepatectomy in liver cirrhosis or liver cancer, or in liver transplantation or liver regeneration drug, it is shown that ghrelin promotes hepatocyte regeneration, and is useful for prevention of disorder or early curing." *Id.* 61:2–4. Additionally, the Specification describes that "in the

case of living-donor liver transplantation, reduction or abnormality in hepatic function is frequently seen after transplantation operation in both of a donor and a recipient." *Id.* 2:23–25.

The dispute lies with the selection of the particular patient population for the administration of the ghrelin peptides. Here, Examiner is relying on references that suggest treating hepatopathy[8] by administering ghrelin peptides. *See* Final Act. 3–8; *see* Ans. 3–8. In *Perricone*, the Federal Circuit distinguished between the topical application of a lotion to skin generally to prevent sunburn, and the topical application of a lotion to treat sunburned skin, finding that the "issue is not . . . whether [the prior art] lotion if applied to skin sunburn would inherently treat that damage, but whether [the prior art] discloses the application of its composition to skin sunburn. It does not." *Perricone v. Medicis Pharm. Corp*., 432 F.3d 1368, 1378 (Fed. Cir. 2005).

Similar to *Perricone*, a patient population having hepatopathy is different from a patient population having undergone a hepatectomy. In our prior Decision, the claims were directed to treating patients suffering from hepatopathy using ghrelin peptides. In the Decision, we concluded that if a patient population, i.e. those having cirrhosis of the liver, is treated with the ghrelin peptides and that same cirrhosis patient population is in need of hepatic regeneration, then the administration of ghrelin peptides to that cirrhotic patient population would inherently achieve hepatic regeneration. *See* Decision 9–10 ("The limitation that the 'polypeptide promotes hepatic regeneration and/or recovery of hepatic function' is a property that is

[8] Hepatopathy encompasses patients having "hepatitis, liver cirrhosis and hepatic insufficiency." Spec. 1:25–26.

associated with the structure of the ghrelin analog compound. 'Newly discovered results of known processes directed to the same purpose are not patentable because such results are inherent.' *Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1376 (Fed. Cir. 2001)."). This rationale no longer applies in the present appeal because the claims are now directed to a different patient population.

Given our interpretation that the method applies to a patient population that has undergone a hepatectomy, we find that the evidence of record does not support Examiner's conclusion that the combination of references teaches administering ghrelin peptides to a patient population recovering from a hepatectomy. Accordingly, we reverse the rejection for obviousness.

CONCLUSION

In summary:

Claims Rejected	Basis	Affirmed	Reversed
20, 27, 32, 48–53	pre-AIA 35 U.S.C. § 103(a) Bednarek/Kangawa, Matsumoto, Tacke, Skakkebaek, Wonke		20, 27, 32, 48–53

REVERSED