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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte KEVIN HADLEY, TERENCE FEALEY, and JULIAN E. BAILES

Appeal 2019-003808
Application 12/904,049
Technology Center 1600

Before JEFFREY N. FREDMAN, DEBORAH KATZ, and JOHN G. NEW, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal[1,2] under 35 U.S.C. § 134(a) involving claims to a method for reducing the risk of pathological effects of traumatic brain injury. The Examiner rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

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[1] We use the word "Appellant" to refer to "applicant" as defined in 37 C.F.R. § 1.42. Appellant identifies the Real Party in Interest as DSM IP Assets, B.V. (*see* Appeal Br. 3).

[2] We have considered and herein refer to the Specification of Oct. 13, 2010 ("Spec."); Final Office Action of Sep. 13, 2017 ("Final Act."); Appeal Brief of Oct. 15, 2018 ("Appeal Br."); and Examiner's Answer of Feb. 12, 2019 ("Ans.").

Statement of the Case

Background

"Traumatic brain injury (TBI) is a head injury caused by trauma to the brain" (Spec. ¶ 2). "Following a traumatic injury to the central nervous system (CNS), a cascade of physiological events can lead to neuronal loss including, for example, an inflammatory immune response and excitotoxicity resulting from the initial impact disrupting the glutamate, acetylcholine, cholinergic, [γ-aminobutyric acid ($GABA_A$)], and [N-methyl-D-aspartate (NMDA)] receptor systems" (Spec. ¶ 3). "Treatment[s] of traumatic brain injury have included diuretics, anti-convulsants, and [α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA)]/NMDA receptor antagonists. However, it is desirable to have treatments that can provide a prophylactic neuroprotective effect that can reduce the risk of neurological damage associated with traumatic brain injury" (Spec. ¶ 7).

"The present disclosure provides a method for prophylactic treatment that reduces the risk of pathological effects associated with traumatic brain injury" (Spec. ¶ 8). The method involves administering "a composition comprising [docosahexaenoate (DHA)] . . . to a subject at risk for traumatic brain injury prior to the subject engaging in an activity associated with a risk of traumatic brain injury" (*id.*). DHA "refers to (all-Z)-4,7,10,13,16,19-docosahexaenoic acid, as well as any salts or derivatives thereof. Thus, the term [DHA] encompasses the free acid DHA as well as DHA alkyl esters and triglycerides containing DHA" (Spec. ¶ 40).

The Claims

Claims 1, 3–7, 18, 22–27, 29, 33–35, and 37–40 are on appeal.[3]

Independent claim 1 is representative and reads as follows:

> 1. A method for reducing the risk of pathological effects of traumatic brain injury in a human subject, the method comprising:
>
> administering to the subject who is engaged in an activity associated with a known risk of traumatic brain injury,
>
> wherein the activity is selected from the group consisting of boxing, football, soccer, hockey, armed conflict, or brain surgery,
>
> a composition comprising docosahexaenoate (DHA) in an amount of at least about 65 wt% and less than 99 wt.% of the total fatty acid content of the composition,
>
> wherein the composition is administered prior to engagement in the activity associated with a risk of traumatic brain injury to reduce the risk of pathological effects of traumatic brain injury,
>
> wherein the composition has an eicosapentaenoate (EPA) content of less than about 2 wt% of the total fatty acid content of the composition, and the DHA to EPA ratio is at least 100:1.

(Appeal Br. 11).

[3] Claims 2, 8–17, 19–21, 28, 30–32, and 36 were cancelled (*See* Appeal Br. 11–13).

The issues

A. The Examiner rejected claims 1, 18, 22, 23, 25, and 39 under 35 U.S.C. § 103(a) as obvious over Wu,[4] Farooqui,[5] Lyden,[6] and Romano,[7] (Final Act. 4–7).

B. The Examiner rejected claims 3–7, 26, 27, and 35 under 35 U.S.C. § 103(a) as obvious over Wu, Farooqui, Lyden, Romano, and Groenendijk[8] (Final Act. 7–8).

C. The Examiner rejected claims 24, 29, 33, 34, and 40 under 35 U.S.C. § 103(a) as obvious over Wu, Farooqui, Lyden, Romano, and Barnes[9] (Final Act. 8–12).

D. The Examiner rejected claims 37 and 38 under 35 U.S.C. § 103(a) as obvious over Wu, Farooqui, Lyden, Romano, Barnes, and Groenendijk (Final Act. 12–13).

A. 35 U.S.C. § 103(a) over Wu, Farooqui, Lyden, and Romano

The Examiner finds Wu teaches that orally administering a fish oil composition containing equal amounts DHA and eicosapentaenoic acid (EPA) to rats for 28 days before subjecting the rats to traumatic brain injury was effective in reducing the risk of pathological effects of traumatic brain injury (Final Act. 4). The Examiner finds that one skilled in the art would

[4] Wu, A. et al., *Dietary Omega-3 Fatty Acids Normalize BDNF Levels, Reduce Oxidative Damage, and Counteract Learning Disability after Traumatic Brain Injury in Rats*, 21 J. NEUROTRAUMA 1457–1467 (2004).
[5] Farooqui, A. A. et al., *Modulation of inflammation in brain: a matter of fat*, 101 J. NEUROCHEMISTRY 577–599 (2007).
[6] Lyden, US 2002/0188997 A1, published Dec. 19, 2002.
[7] Romano, US 2005/0215571 A1, published Sept. 29, 2005.
[8] Groenendijk et al., WO 2009/057994 A1, published May 7, 2009.
[9] Barnes et al., US 5,506,211, issued Apr. 9, 1996.

have been able "to optimize this period of time in order to attain the best treatment for a particular human patient," including 6 weeks of pre-treatment (*id.* at 6–7). The Examiner finds Wu teaches "it is likely that the beneficial effects of fish oil supplementation are attributable to DHA" (*id.* at 4). The Examiner finds Farooqui teaches "based on recent literature, the dietary intake of food rich DHA can decrease or prevent inflammatory processes in the brain tissue and can be beneficial for the neuroinflammation associated with acute neural trauma and neurodegenerative diseases" (*id.* at 5).

The Examiner acknowledges that neither Wu nor Farooqui teach "that the subjects who are engaged in an activity that is associated with a risk of TBI are selected from the group consisting of boxing, football, soccer, etc." (*id.*). The Examiner finds Lyden and Romano teach traumatic brain injury may be caused by sports injuries, including repeated heading of the soccer ball (*id.*). The Examiner determines

> [I]t would have been prima facie obvious for a person of ordinary skill in the art to administer pure DHA or almost pure DHA, instead of a mixture of DHA and EPA, to individuals at risk of suffering TBI, like individuals engaged in sports like soccer, before they engage in such activity that is associated with a risk of TBI, since the prior art teaches that the activity observed with the mixture of DHA and EPA is more likely to be concentrated in DHA and not EPA.

(*id.* at 5–6).

The issue with respect to this rejection is: Does the evidence of record support the Examiner's conclusion that Wu, Farooqui, Lyden, Romano, Barnes, and Groenendijk render the claims obvious?

Findings of Fact ("FF")

1. Wu teaches that "[t]raumatic brain injury (TBI) is a major cause of disability such that a great concern exists to develop means to decrease its short- and long term effects" (Wu 1457).

2. Wu teaches an experiment to assess "whether omega-3 fatty acids in the diet can provide protection against learning impairment [in rats] after TBI" (Wu 1460).

3. Wu teaches feeding rats a diet containing 8% fish oil (12.4% DHA and 13.5% EPA) for a total of 4 weeks. The rats were exposed to TBI by "mild fluid percussion injury (FPI)." The rats were given the same diet for 1 week post injury (Wu 1458).

4. Wu teaches the experimental results demonstrated that "TBI rats fed the FO supplemented diet showed significant improvement in their learning ability," similar to that of rats which did not receive TBI, and unlike rats with a regular diet that received TBI (Wu 1460).

5. Wu teaches that the findings "suggest that omega-3 fatty acid-enriched dietary supplements can be a potent therapeutic agent for reducing the deleterious effects of TBI on synaptic plasticity and cognition" (Wu 1461).

6. Wu teaches "[a]lthough the major components of FO in our study are DHA and EPA, it is likely that the beneficial effects of FO supplementation are attributable to DHA. . . . However, a direct link between DHA and the observed findings in our study need to be further investigated by using pure DHA in the diet" (Wu 1463–1464).

7. Farooqui teaches that fish oil supplements containing EPA and DHA can reduce neuroinflammation (Farooqui 589–590).

8. Farooqui teaches "[n]euroinflammation is an active defensive process against diverse insults [including] metabolic and traumatic injuries" (Farooqui 592).

9. Lyden teaches "soccer players are at risk of chronic traumatic brain injury due to repeated heading of the soccer ball. The cumulative trauma has a degenerative effect similar to that which has been observed in boxers" (Lyden ¶ 5).

10. Romano teaches "cognitive impairments caused by traumatic brain injuries" include "traumas to the head, such as, for example, traumas caused by accidents and/or sports injuries" (Romano ¶ 49).

Principles of Law

"Obviousness does not require absolute predictability of success . . . all that is required is a reasonable expectation of success." *In re Kubin*, 561 F.3d 1351, 1360 (Fed. Cir. 2009).

Analysis

We adopt the Examiner's findings of fact and reasoning regarding the scope and content of the prior art (Final Act. 4–7; FF 1–10) and agree that the claims are rendered obvious by Wu, Farooqui, Lyden, and Romano. We address Appellant's arguments below.

Appellant contends "Wu does not teach or suggest DHA in an amount of at least about 65 wt.% and less than 99 wt.% of the total fatty acid composition" (Appeal Br. 5). Appellant contends Wu does not teach or suggest "a pure or 100% DHA mixture" (*id.*). Rather, "[t]he DHA in the diet of Wu is in an amount of 12.4%, which is a percentage of the fish oil"

(*id.*). Appellant contends therefore, that "[t]here was no expectation that the use of DHA alone would be successful based on Wu" (*id.* at 6).

We are not persuaded. Wu suggests that "it is likely that the beneficial effects of fish oil supplementation are attributable to DHA" (FF 6). We agree with the Examiner that "the prior art offers a very strong motivation to repeat Wu's experiments, but administering only DHA (instead of a mixture of DHA and EPA), or mainly DHA, since both Wu and Farooqui suggest and/or teach that DHA is likely responsible for the efficacy in treating or decreasing the risk of TBI" (Ans. 15). A discovery that "proved conclusively what was strongly suspected before," even though it "may have significantly advanced the state of the science," is not "inventive in nature." Therefore, inventions based on that discovery are unpatentable under § 103. *Pharmastem Therapeutics, Inc. v. Viacell, Inc.*, 491 F.3d 1342, 1363–1364 (Fed. Cir. 2007). "Scientific confirmation of what was already believed to be true may be a valuable contribution, but it does not give rise to a patentable invention." *Id. See, e.g.*, *Ariosa Diagnostics, Inc. v. Sequenom, Inc*., 809 F.3d 1282, 1293 (Fed. Cir. 2015) ("[M]erely routine optimization of drug dosage to maximize therapeutic effect.")

Appellant contends that "Wu discloses feeding a diet having 0.9% DHA and 0.1 % EPA following injury; *see*, p. 1458, '[a]fter consumption of the same diet for 1 week post-injury'" (Appeal Br. 5–6). Appellant contends "[i]t is not possible to conclude in Wu that pre-injury treatment alone would actually be efficacious as Wu disclosed administration of a composition both pre- and post-injury" (*id.* at 6). Appellant contends:

> One of skill in the art would not look to Wu for reducing risks associated with traumatic brain injury by administration of a composition comprising DHA prior to engagement in an

> activity associated with a risk of traumatic brain injury, as Wu includes continuous feeding of DHA and EPA post-injury and neuroprotection could just as easily have been attributed to treatment post-injury w/DHA or EPA based upon the study design.

(*id.*).

We are not persuaded. Wu teaches administering omega-3 fatty acids to protect against TBI-induced learning impairment (FF 2). Therefore, Wu teaches pre-injury treatment. Moreover, we agree with the Examiner that "the instant claims do not exclude other steps to be performed like . . . the administration of DHA after the TBI occurs" (Ans. 17). *See Invitrogen Corp. v. Biocrest Mfg., L.P.*, 327 F.3d 1364, 1368 (Fed. Cir. 2003) ("The transition 'comprising' in a method claim indicates that the claim is open-ended and allows for additional steps"). Because the claims do not exclude continued treatment after TBI, Appellant's arguments do not distinguish the combination of Wu, Farooqui, Lyden, and Romano.

Appellant separately argues dependent claim 23 (Appeal Br. 7). Appellant contends that treatment for 6 weeks is distinguishable from Wu's teaching of 4 weeks, in that "6 weeks is a 50% increase over 4 weeks" (*id.*). Appellant contends "[t]he claimed amount in the present application and the amount disclosed in Wu are not close enough that one skilled in the art would have expected them to have the same properties" (*id.*).

We do not agree. "The law is replete with cases in which the difference between the claimed invention and the prior art is some range or other variable within the claims. These cases have consistently held that in such a situation, the applicant must show that the particular range is *critical*, generally by showing that the claimed range achieves unexpected results

relative to the prior art range." *In re Woodruff*, 919 F. 2d 1575, 1578, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). Appellant has provided no evidence showing the criticality of the claimed 6 week treatment. "[A]ttorney argument [is] not the kind of factual evidence that is required to rebut a prima facie case of obviousness." *In re Geisler*, 116 F.3d 1465, 1470 (Fed. Cir. 1997). Rather, the evidence in the Specification describes the same 28 day pre-treatment as the prior art (*see* Spec. ¶ 174).

Conclusion of Law

A preponderance of the evidence of record support the Examiner's conclusion that Wu, Farooqui, Lyden, and Romano render the claims obvious.

B–D. 35 U.S.C. § 103(a) over Wu, Farooqui, Lyden, Romano, Groenendijk and Barnes

Appellant does not separately argue these obviousness rejections, instead relying upon their arguments to overcome the combination of Wu, Farooqui, Lyden, and Romano (*see* Appeal Br. 7–10). Having affirmed the obviousness of claims 1, 18, 22, 23, 25, and 39 for the reasons given above over Wu, Farooqui, Lyden, and Romano, we also find that the further combinations with Groenendijk and Barnes render the rejected claims obvious for the reasons given by the Examiner (*see* Final Act. 7–17).

DECISION

In summary:

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
1, 18, 22, 23, 25, 39	103(a)	Wu, Farooqui, Lyden, Romano	1, 18, 22, 23, 25, 39	
3–7, 26, 27, 35	103(a)	Wu, Farooqui, Lyden, Romano, Groenendijk	3–7, 26, 27, 35	
24, 29, 33, 34, 40	103(a)	Wu, Farooqui, Lyden, Romano, Barnes	24, 29, 33, 34, 40	
37, 38	103(a)	Wu, Farooqui, Lyden, Romano, Groenendijk, Barnes	37, 38	
Overall Outcome			1, 3–7, 18, 22–27, 29, 33–35, 37–40	

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

AFFIRMED