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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte SHANTA DHAR and SEAN M. MARRACHE
(APPLICANT: University of Georgia Research Foundation, Inc.)

Appeal 2018-002932
Application 14/378,813[1]
Technology Center 1600

Before DONALD E. ADAMS, RACHEL H. TOWNSEND, and DAVID COTTA, *Administrative Patent Judges*.

ADAMS, *Administrative Patent Judge*.

DECISION ON APPEAL

This Appeal under 35 U.S.C. § 134(a) involves claims 1, 3–24, and 28 (App. Br. 2). Examiner entered rejections under 35 U.S.C. § 103(a). We have jurisdiction under 35 U.S.C. § 6(b).

We REVERSE.

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[1] Appellants identify "University of Georgia Research Foundation, Inc." as the real party in interest (Appellants' June 26, 2017 Appeal Brief (App. Br.) 2).

STATEMENT OF THE CASE

Appellants' disclosure "relates to nanoparticles configured to traffic agents to mitochondria and methods of use thereof, including diagnostic and therapeutic uses" (Spec. ¶ 3). Claim 1 is representative and reproduced below:

> 1. A nanoparticle, comprising:
>
> a hydrophobic nanoparticle core;
>
> a hydrophilic layer surrounding the core; and
>
> *a mitochondria targeting moiety tethered to the core*,
>
> wherein the nanoparticle has a diameter of from about 10 nanometers to about 200 nanometers or less and has a zeta potential of about 0 mV or greater.

(Appellants' August 16, 2017 Claims Appendix (Claims App.) (emphasis added).)

Grounds of rejection before this Panel for review:

Claims 1, 3–8, 10–23, and 28 stand rejected under 35 U.S.C. § 103(a) as unpatentable over the combination of Sung[2] and Levy.[3]

Claims 9 and 24 stand rejected under 35 U.S.C. § 103(a) as unpatentable over the combination of Sung, Levy, and Skulachev.[4]

ISSUE

Does the preponderance of evidence relied upon by Examiner support a conclusion of obviousness?

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[2] Sung et al., US 8,449,915 B1, issued May 28, 2013.
[3] Levy et al., US 2007/0292353 A1, published Dec. 20, 2007.
[4] Skulachev et al., US 2011/0245207 A1, published Oct. 6, 2011.

FACTUAL FINDINGS (FF)

FF 1. Sung discloses a "nanoparticle system for topical transcutaneous or transdermal delivery or targeted epidermal delivery of the biodegradable nanoparticles that encapsulate at least one bioactive agent of protein/peptides, nucleic acid (for example pDNA, RNA, or siRNA) via nanoparticle projectile bombardment or other transcutaneous/transdermal means" (Sung 2: 54–60).

FF 2. Sung's "nanoparticles for transcutaneous or transdermal bombardment delivery processes hav[e] a mean particle size between about 50 and 500 nanometers" (*id.* at 13:36–39; *see* Ans. 3).

FF 3. Examiner finds that Sung discloses a nanoparticle having "zeta potentials ranging from -34.6 to 27.6" (Ans. 3).

FF 4. Sung's nanoparticles comprise: (1) "a core portion comprised of [(a)] hydrophobic poly (D,L-lactic-co-glycolic acid) (PLGA) and [(b)] a detection-enhancing substance, and [(2)] a shell portion comprised of positively charged chitosan adapted to cause no aggregation of nanoparticles due to electrostatic repulsion between the positively charged nanoparticles" (Sung, Abstract; *see* Ans. 3).

FF 5. Sung discloses that "[b]y modifying the chitosan structure to alter its charge characteristics, such as grafting the chitosan with . . . polyethylene glycol (PEG) . . . the surface charge density (zeta potential) of the . . . nanoparticles may become more pH resistant or more hydrophilic" (Sung 21:62–22:2).

FF 6. Sung discloses the *encapsulation* of "rhodamine 6G . . . in the PLGA hydrophobic core of [the nanoparticles] as a fluorescent probe" to track the nanoparticle "internalization pathway" (Sung 44:9–11; *see* Ans. 3).

FF 7. Although Examiner asserts that "rhodamine 6G reads on 'a mitochondrial targeting moiety'," Examiner recognizes that Sung fails to disclose a "mitrochondrial targeting moiety. . . [] attached to the [nanoparticle's] core" (Ans. 4). Examiner, therefore, relies on Levy to make up for this deficiency in Sung (*see id.* at 4–5).

FF 8. Levy "relates to biocompatible composite nanoparticles, comprising: [(1)] a nucleus comprising at least one inorganic or organic compound activatable by excitation, [(2)] optionally, a biocompatible coating, and [(3)] at least one targeting molecule, preferably exposed at the particle surface, displaying affinity for an intracellular molecule or structure" (Levy ¶¶ 12–15; *id.* ¶ 1 (Levy "relates to composite particles comprising an intracellular targeting element, which can generate a response when excited, and to the uses thereof in the health field, particular in relation to human health").

FF 9. Levy's "particles comprise a nucleus comprising at least one inorganic or organic compound which can be activated, in order to label or alter cells, tissues or organs" (*id.* ¶ 1)

FF 10. Levy's "nanoparticles . . . can additionally comprise a coating . . . [that] preferably comprises one or more compounds selected [from] the group consisting of slica (SiO_2), alumina, metals (Au, etc.), polyethylene glycol (PEG) or dextran, optionally in mixture(s)" (*id.* ¶¶ 46,49; *see* Ans. 4–5).

FF 11. Levy's "targeting molecule is grafted to the optional coating *or* to the nucleus of [Levy's] nanoparticle," wherein the "grafting can be achieved for example via molecular hydrocarbon chains of variable length but also via other types of molecules such as polysaccharides, polypeptides, DNA, etc." (Levy ¶ 61 (emphasis added)).

FF 12. Levy discloses the use of "[r]hodamine . . . as [a] targeting molecule" to target "nanoparticles to intracellular mitochondria" (Levy ¶ 63; *see* Ans. 4–5).

FF 13. Examiner finds that the combination of Sung and Levy fails to disclose "triphenyl phosphonium . . . or 2,4-DNP" and relies on Skulachev to make up for this deficiency in the combination of Sung and Levy (Ans. 5–6).

ANALYSIS

The rejection over the combination of Sung and Levy:

Appellants' claim 1 is reproduced above and requires, *inter alia*, a mitochondrial targeting moiety tethered to the core of a nanoparticle (Claims App.). According to Appellants, "'targeting' a nanoparticle to mitochondria means that the nanoparticle accumulates in mitochondria relative to other organelles or cytoplasm at a greater concentration than [a] substantially similar non-targeted nanoparticle" (Spec. ¶ 55). In addition, Appellants' disclose that "targeting moieties may be tethered to the core or components that interact with the core" (*id.* ¶ 37; *see id.* ¶ 56 ("mitochondrial targeting moieties may be tethered to the core in any suitable manner, such as binding to a molecule that forms part of the core or to a molecule that is bound to the core")).

Examiner finds that Sung discloses nanoparticles having a diameter of from about 10 to about 200 nanometers or less and a zeta potential of about 0 mV or greater (*see* FF 2–3). Sung and Levy both suggest nanoparticles that comprise (1) a nucleus or core and (2) a shell or coating (*see* FF 3, 7). Sung and Levy both disclose a shell or coating comprising a hydrophilic layer, which surrounds the core (*see* FF 4 (Sung discloses a coating

comprising a modified chitosan structure, wherein the coating is made more hydrophilic by modifying the chitosan with PEG), FF 9 (Levy's coating may comprise PEG)). In addition, Sung and Levy both disclose nanoparticles comprising rhodamine, which Levy discloses as a targeting moiety, wherein rhodamine is encapsulated in Sung's core or grafted to Levy's optional coating or to the nucleus of Levy's nanoparticle (FF 5, 6, 10, 11).

Based on the combination of Sung and Levy, Examiner concludes that, at the time Appellants' invention was made, it would have been prima facie obvious to incorporate Levy's mitochondrial targeting moiety "into a multifunctional nanoparticle as taught by Sung" (Ans. 5). In support of Examiner conclusion, Examiner asserts that: (a) "one of ordinary skill in the art confronted with the problem of improving and diversifying targeted delivery to mitochondria," would have combined Sung and Levy, (b) such a combination is nothing more than adding "known ingredients to [a] known composition[] with the expectation of obtaining their known function," and (c) a person of ordinary skill in this "art would have had a reasonable expectation of success in the modification as Sung . . . already teaches the incorporation and/or use of rhodamine" (*id.*).

We are not persuaded that Examiner established an evidentiary basis on this record that is sufficient to support a conclusion that the combination of Sung and Levy discloses a nanoparticle, comprising a core, a layer surrounding the core, and *a mitochondria targeting moiety tethered to the core*, as is required by Appellants' claimed invention (*see* Claims App.). Notwithstanding the requirements of Appellants' claimed invention, Examiner has, at best, established that the combination of Sung and Levy suggests a nanoparticle comprising *a targeting moiety tethered to a*

component of a hydrophilic layer surrounding the nanoparticle's core not to the nanoparticle's core as required by Appellants' claimed invention (*see* Ans. 4–5 ("PEG . . . [meets] the limitation of the hydrophilic layer and hydrophilic polymer moiety being attached to the core" and "the targeting moiety would be attached to the core via hydrophilic polymer moiety"); *cf.* FF 11 (Levy's targeting molecule is attached to a nanoparticle's coating when present or, in the absence of a coating, to a nanoparticle's nucleus (i.e. core)); Spec. ¶ 34 (Appellants' disclose that "targeting moieties may be tethered to the core or components that interact with the core"); *see also id.* ¶ 56 ("mitochondrial targeting moieties may be tethered to the core in any suitable manner, such as binding to a molecule that forms part of the core or to a molecule that is bound to the core"); *see* App. Br. 9 (Appellants' "claims recite that the mitochondria targeting moiety is tethered to the core"); *see also* App. Br. 11 ("Another relevant question is whether one would consider the rhodamine to such a nanoparticle to be tethered to the core")).

The rejection over the combination of Sung, Levy, and Skulachev:

Examiner finds that the combination of Sung and Levy fails to disclose "triphenyl phosphonium . . . or 2,4-DNP" and relies on Skulachev to make up for this deficiency in the combination of Sung and Levy (FF 13). Based on the combination of Sung, Levy, and Skulachev, Examiner concludes that, at the time Appellants' invention was made, it would have been prima facie obvious "to modify the combined teachings of Sung . . . and Levy . . . with the teachings of Skulachev . . . the modification being the

simple substitution of one mitochondrial targeting moiety for another to obtain predictable results" (Ans. 6). We are not persuaded.

As Appellants' explain, Examiner failed to establish that Skulachev makes up for the deficiencies in the combination of Sung and Levy discussed above (App. Br. 13).

CONCLUSION

The preponderance of evidence relied upon by Examiner fails to support a conclusion of obviousness. The rejection of claims 1, 3–8, 10–23, and 28 under 35 U.S.C. § 103(a) as unpatentable over the combination of Sung and Levy is reversed. The rejection of claims 9 and 24 under 35 U.S.C. § 103(a) as unpatentable over the combination of Sung, Levy, and Skulachev is reversed.

REVERSED