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Table with 5 columns: APPLICATION NO., FILING DATE, FIRST NAMED INVENTOR, ATTORNEY DOCKET NO., CONFIRMATION NO. Includes application details for Sai Kiang LIM and examiner BELYAVSKIY, MICHAEL A.

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UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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*Ex parte* SAI KIANG LIM

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Appeal 2019-000865  
Application 14/444,105  
Technology Center 1600

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Before FRANCISCO C. PRATS, JEFFREY N. FREDMAN, and  
TAWEN CHANG, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal<sup>1,2</sup> under 35 U.S.C. § 134 involving claims to a method of promoting wound healing. The Examiner rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

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<sup>1</sup> 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 Agency for Science, Technology and Research (*see* Appeal Br. 2).

<sup>2</sup> We have considered and refer to the Specification of July 28, 2014 (“Spec.”); Final Action of July 18, 2017 (“Final Act.”); Appeal Brief of June 7, 2018 (“Appeal Br.”); Examiner’s Answer of Sept. 13, 2018 (“Ans.”); and Reply Brief of Nov. 13, 2018 (“Reply Br.”).

*Statement of the Case*

*Background*

“Stem cells, unlike differentiated cells, have the capacity to divide and either self-renew or differentiate into phenotypically and functionally different daughter cells” (Spec. 1:15–16). “Mesenchymal stem cells (MSCs) are multipotent stem cells . . . [that] have limited but robust potential to differentiate into mesenchymal cell types, e.g[,] adipocytes, chondrocytes and osteocytes” (Spec. 1:20–24).

“The present invention is based on the demonstration that human ESC-derived mesenchymal stem cells (MSCs) mediate cardioprotective effects through secreted large complexes of ~50-100 nm in diameter. Such complexes or particles may therefore be used for therapeutic means, including for cardioprotection, in place of the cells themselves” (Spec. 11:14–17).

*The Claims*

Claims 1–4 are on appeal. Claim 1 is representative and reads as follows:

1. A method of promoting wound healing, the method comprising administering to an individual in need thereof a pharmaceutical composition comprising an exosome derived from a mesenchymal stem cell (MSC), wherein the exosome is isolated from an MSC-conditioned serum-free medium, and wherein the exosome has a size of between 50 nm and 100 nm as determined by electron microscopy.

*The issue*

The Examiner rejected claims 1–4 under 35 U.S.C. § 103(a) as obvious over Lim,<sup>3</sup> Robbins,<sup>4</sup> and Taylor<sup>5</sup> (Final Act. 2–4).

The Examiner finds Lim teaches “a method of treating [a] wound comprising administering a condition medium obtained from mesenchymal stem cells” (Final Act. 3). The Examiner finds, without citation, that “it was well know[n] that cultured mesenchymal stem cells secreted particles into the medium in the process of culturing” (*id.*). Based on this finding, the Examiner concludes “it would be obvious to one skill[ed] in the art at the time the invention was made that MSC-condition medium comprises exosomes” (*id.*). The Examiner acknowledges that Lim “does not explicitly teach[] isolation of exosome[s] from condition[ed] medium prior to administering” (*id.*).

The Examiner finds Robbins and Taylor teach “a method of treating a patient comprising administering to said patient exosomes” and teaches the “exosomes were obtained and isolated from condition medium by well known methods, including centrifugation or by size exclusion” (Final Act. 3). The Examiner finds the combination obvious because “the prior art suggests that exosomes isolated from condition media can be used for treating” (*id.*).

The issue with respect to this rejection is: Does the evidence of record support the Examiner’s finding that Lim, Robbins, and Taylor render the claims obvious?

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<sup>3</sup> Lim et al., WO 2008/020815 A1, published Feb. 21, 2008.

<sup>4</sup> Robbins et al., US 2006/0116321 A1, published June 1, 2006.

<sup>5</sup> Taylor et al., US 2013/0243820 A1, published Sept. 19, 2013.

*Findings of Fact*

1. Lim teaches that “injured or lost tissues may be regenerated or repaired through enhancement of endogenous tissue repair by applying secretions from MSCs instead of, or in addition to, MSCs themselves” (Lim 2).

2. Lim teaches “compositions comprising one or more specific biologically active compounds in the secretions of MSCs, in particular one or more of the 794 polypeptides, may be used instead of, or in addition to, the conditioned media in such treatment” (Lim 2).

3. The Examiner does not identify any teaching in Lim regarding exosomes (*see, e.g.*, Ans. 6 “it was well know[n] that cultured mesenchymal stem cells secreted particles into the medium in the process of culturing” without citation to a reference).

4. Robbins teaches “[e]xosomes are small particles of 30 to 100 nM in size . . . Many cell types have been shown to generate exosomes including dendritic cells, reticulocytes, T lymphocytes, B cells, platelets, epithelial cells and tumor cells” (Robbins ¶ 10).

5. Robbins teaches “exosomes of the invention may be administered to a mammalian host in order to suppress an undesirable immune response. The exosomes of the invention may be derived from a variety of different cells, including, but not limited to, antigen presenting cells such as dendritic cells and macrophages” (Robbins ¶¶ 15–16).

6. Robbins teaches that “[a]s exosomes are small particles, 30-100 nM in size, they may be recovered in serum by removing the larger cellular elements from a peripheral blood sample, for example, but not by way of limitation, by centrifugation at 1500 g for 10 minutes” (Robbins ¶ 76).

7. Taylor teaches “modified exosomes for use as vaccines. In particular, the presently disclosed subject matter relates to utilizing cell-produced exosomes modified to substantially lack one or more immunosuppressive polypeptides” (Taylor ¶ 3).

*Principles of Law*

A prima facie case for obviousness “requires a suggestion of all limitations in a claim,” *CFMT, Inc. v. Yieldup Int’l Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) and “a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007).

*Analysis*

Appellant contends

There is no indication in the art of record, or in any evidence of the general knowledge at the time, that exosomes, alone out of all of the components present in conditioned medium - the Lim reference, cited by the Examiner, teaches that MSCs secrete at least 794 unique gene products into their medium (Lim, Example 14A and 14B) - would be the fraction of MSC-conditioned medium sufficient or responsible for the wound-healing properties of such conditioned medium. Lacking such additional evidence in the art of record to indicate that exosomes, among the multitude of secreted components, could reasonably be expected to be responsible for MSC conditioned medium’s wound healing properties, there can be no reasonable expectation of success for a method of treating wound healing as instantly claimed.

(Appeal Br. 5).

The Examiner responds with two arguments. First, the Examiner contends that “when claim 1 is given its broadest reasonable interpretation it

can also read a method of promoting wound healing by administering a pharmaceutical composition COMPRISING a condition medium derived from mesenchymal stem cells (MSCs), such as serum –free conditioned medium containing an exosomes between 50 nm and 100 nm” (Ans. 4). The Examiner states, without supporting evidence, that “it was well know[n] that cultured mesenchymal stem cells secreted particles into the medium in the process of culturing” (Ans. 6).

We understand the Examiner’s first argument as based on inherency. The Examiner is contending, it appears, that administering Lim’s secretions from MSCs necessarily also results in administering exosomes because Lim’s secretions necessarily comprise exosomes.

Although we apply the broadest reasonable interpretation during examination, “[a]bove all, the broadest reasonable interpretation must be *reasonable* in light of the claims and specification.” *PPC Broadband, Inc. v. Corning Optical Commc’ns RF, LLC*, 815 F.3d 747, 755 (Fed. Cir. 2016). To the extent that the Examiner is reading the word “isolated” out of the claims, that interpretation is not reasonable.

We, therefore, find the Examiner’s inherency argument unpersuasive because claim 1 recites that “the exosome is isolated from an MSC-conditioned serum-free medium.” Lim’s secretions are, by their nature, not *isolated* exosomes but rather comprise the entirety of the conditioned medium (FF 1–2). Lim neither teaches nor suggests the use of *isolated* exosomes as required by claim 1. The Examiner also does not identify a teaching in either Robbins or Taylor to use *isolated* exosomes for wound healing (FF 3–7).

Second, the Examiner contends that Lim not only teaches “the presence of at least 794 unique gene products in MSC-condition[ed] media, it also provide[s] evidence[] of reasonable expectation of success of using just one specific biologically active compound i.e.[,] **exosomes** present in condition medium” (Ans. 10).

We find this second argument unpersuasive because Lim neither teaches nor suggests exosomes are the effective agent within the MSC conditioned media (FF 1–2). Indeed, the Examiner does not identify, and we do not find, a single mention of the term “exosome” within Lim. As the Examiner does point out, Lim teaches the presence of 794 polypeptides, along with the presence of other biologically active compounds, in MSC conditioned media (FF 2). However, Lim does not identify which, if any, of these 794 polypeptides or other active compounds have the activity necessary to improve wound healing. More importantly in the present situation, Lim does not teach, or even hint, that exosomes have any role whatsoever in wound healing. In the absence of any teaching or suggestion to use isolated exosomes from MSC conditioned media as a treatment for wound healing, we conclude the Examiner has not established that the claims are obvious.

*Conclusion of Law*

The evidence of record does not support the Examiner’s finding that Lim, Robbins, and Taylor render the claims obvious.

DECISION

In summary:

<b>Claims Rejected</b>	<b>35 U.S.C. §</b>	<b>Basis</b>	<b>Affirmed</b>	<b>Reversed</b>
1-4	103(a)	Lim, Robbins, Taylor		1-4

REVERSED