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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte SHI-LUNG LIN and DAVID TS WU¹

Appeal 2014-003499
Application 12/318,806
Technology Center 1600


NEW, Administrative Patent Judge.

DECISION ON APPEAL

¹Appellants state the real parties-in-interest are the inventors named above. App. Br. 2.
SUMMARY


We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

NATURE OF THE CLAIMED INVENTION

Appellants invention is directed to a method for developing, generating, and selecting tumor-free embryonic stem (ES)-like pluripotent cells using electroporation delivery of an inducible tumor suppressor mir-302 agent into mammalian cells. Specifically, the present invention relates to a method and composition for generating a Tet-On/Off recombinant

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2 Referred to in Appellants’ Brief as “Lin B.”
transgene capable of expressing a manually re-designed mir-302 microRNA (miRNA)/shRNA agent under the control of doxycyclin (Dox) in human somatic/cancer cells and thus inducing certain specific gene silencing effects on the differentiation-associated genes and oncogenes of the cells, resulting in reprogramming the cells into an ES-like pluripotent state. Abstract.

REPRESENTATIVE CLAIM

Appellants argue the claims together. App. Br. 8–11. Claim 1 is representative and recites:

1. A method for preventing stem cell tumorigenicity, said method comprising these steps of:

   (a) providing at least a cell substrate expressing a plurality of CDK2 and the associated cell-cycle-related genes targeted by mir-302;

   (b) providing at least a recombinant nucleic acid composition capable of being delivered and processed into at least an intronic microRNA-like gene silencing effector targeting said CDK2 and the associated cell-cycle-related genes in said cell substrate, wherein said intronic microRNA contains at least a nucleic acid sequence homologous to SEQ.ID.N0.3; and

   (c) treating said cell substrate with said recombinant nucleic acid composition under a condition that the concentration of said intronic microRNA-like gene silencing effector is sufficient to suppress said CDK2 and the associated cell-cycle-related genes, wherein said concentration is similar to or higher than the mir-302 level found in human embryonic stem cells.

App. Br. 15.
ISSUES AND ANALYSES

We agree with, and adopt, the Examiner’s findings and conclusion that the appealed claims are *prima facie* obvious over the cited prior art references. We address the arguments raised by Appellants on appeal below.

A. Denial of Priority to Appellants ’262 Application

*Issue*


*Analysis*

Appellants argue their ’262 application teaches a method for expressing intronic microRNA and contend mir-302, as disclosed in their Specification in the instant appeal, is a bona fide natural intronic microRNA expressed in humans. App. Br. 6. Appellants assert that it would have been reasonable for a person of ordinary skill in the art to use the method of the’262 application for expressing mir-302. *Id.*

Appellants contend that, as of 2004, 90 intronic microRNAs in Humans were known in the art, and that mir-302 was one of these. App. Br. 6 (citing A. Rodriguez et al., *Identification of Mammalian microRNA Host Genes and Transcription Units*, 14 Genome Research 1902–1910 (2004) (“Rodriguez”)Tables 1 and 4). Appellants point to Table 4 of Rodriguez, which explicitly lists mir-302 as one of the 26 intronic microRNAs as “Non-
coding Transcription Units.” *Id.* Appellants argue Rodriguez further suggests that the mechanisms of biogenesis for exonic and introic microRNA expression may be different. *Id.* (citing Rodriguez, Abstract). Appellants contend testing 26 microRNAs would not require unreasonable effort for any person of ordinary skill in the art at the time of the ’262 application. *Id.* Appellants further argue that, since the transcription unit of mir-302 does not encode any protein, a person of ordinary skill in the art would be strongly motivated to use the method disclosed in the ’262 application for expressing mir-302 in human cells and studying its function and mechanism as research in this area has been important since at least 2000. *Id.* Consequently, Appellants argue, a person of ordinary skill in the art would have been strongly motivated to, and capable of, enabling the method taught by the ’262 application for expressing mir-302. *Id.* at 7.

Appellants also argue that it would not have required undue experimentation for a person of ordinary skill to achieve expression of mir-302 by following the method disclosed in the ’262 application. App. Br. 7. Appellants point to Examples 2 and 3 of the ’262 application and Examples 1–3 of Appellants’ instant Specification, which, Appellants argue, disclose the required experimental steps comprising: (1) synthesizing the mir-302 DNA templates; (2) matching the DNA ends; (3) ligating the mir-302 into the insertion site of a SpRNAi-RGFP gene expression vector; and (4) delivering the vector into a cell for expression. *Id.* Appellants assert these four steps were reasonably well-known DNA recombination technics to a person of ordinary skill in the art and all materials were commercially available at the time of the ’262 application. *Id.* Appellants assert that both the ’262 application and the present invention use the same SpRNAi-RGFP
gene to carry the intronic microRNA inserts for expression, indicating that the methodology and design of these two inventions are actually continuously connected to each other. *Id.*

Appellants argue further that the method of the ’262 application has been tested in stem cells as shown in paragraphs [0024], [0025], [0038], [0040], and [0105] as well as Figures 5 and 6 of the ’262 application. App. Br. 7. The Appellants assert the Examiner has contended that preventing stem cell tumorigenicity flows naturally from mir-302 expression and argue, therefore, that a person of ordinary skill in the art, using the ’262 application for expressing mir-302, would have naturally led to the invention now claimed by Appellants. *Id.*

Finally, Appellants point to H.B. Houbaviy et al., *Embryonic Stem Cell-Specific MicroRNAs*, 5 DEVELOPMENTAL CELL 351–358 (2003) (“Houbaviy”). According to Appellants, Houbaviy teaches that mir-302 is an embryonic stem cell-specific microRNA. *Id.* (citing Houbaviy Table 1). Appellants therefore reason that a person of ordinary skill, having compared the teachings of Rodriguez and Houbaviy, would realize that mir-302, mir-15, mir-16, mir-30, mir-31, mir-93, mir-106, mir-141, and let-7d are the nine intronic microRNAs expressed in embryonic stem cells. *Id.* Therefore, argue Appellants, a person of ordinary skill in the art would have been strongly motivated to test the over-expression effects of these nine intronic microRNAs using the method of the ’262 application in embryonic stem cells, which would then have led to the invention claimed in the instant ’806 application.

The Examiner responds that 35 U.S.C. § 120 requires that, in order to receive the benefit of a priority claim, support for all aspects of the claimed
invention must be evident in the manner required by 35 U.S.C. § 112, first paragraph in the document to which the priority claim has been made.

Ans. 7. The Examiner denied priority to the ’262 application, as well as U.S. Application Serial Nos. 11/278,143 and 12/149,725 because Appellants’ claimed invention requires mir-302 and no mention of mir-302 can be found in any of these earlier applications. Id. Furthermore, the Examiner also finds no earlier application making any reference to CDK2, whose downregulation is explicitly required in the instant invention. Id.

Finally, the Examiner finds, the 61/011,333 priority document (the “’333 priority document”), filed 1/16/2008, also lacks any teaching of preventing stem cell tumorigenicity, because no reference to such mir-302-based prevention of tumorigenicity is to be found in the document. Id. at 7–8.

The Examiner finds none of the deficient earlier applications provide written description support for the presently claimed invention in the manner required by 35 U.S.C. § 112, first paragraph, because the claimed invention requires the use of a sequence-specific microRNA family, mir-302, and none of the deficient earlier applications disclose anything about mir-302 or related sequences. Ans. 9. The Examiner therefore finds there is no evidence that Appellants were in possession of mir-302 at the time the ’262 application was filed on May 15, 2003. Id.

The Examiner further finds Appellants’ claimed method cannot be practiced without mir-302; therefore, the Examiner finds, mir-302 is a critical element of the claimed invention which cannot be excluded from the claims or the Specification of the ’262 application and yet be considered to

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3 The present application is a continuation-in-part of the ’262 application and U.S. Application Serial Nos. 11/278,143 and 12/149,725.
adequately supported under 35 U.S.C. § 112, first paragraph. App. Br. 9. The Examiner is not persuaded by Appellants’ argument that the ’262 application teaches methods of using miRNA generally, and that mir-302 is typical of the miRNA species allegedly within the scope of the ’262 application, because Appellants have not demonstrated possession of mir-302 within the disclosures of the 262 application. Id. at 10. Furthermore, the Examiner finds that, although Appellants argue that mir-302 was known in the art as early as the teachings of Rodriguez and Houbaviy, the Examiner finds the ’262 application was filed prior to these earliest mir-302 disclosures. Id. The Examiner therefore finds that, although Appellants argue that they should receive the priority benefit of something that (1) they did not disclose, and (2) is not in the prior art at the time of the ’262 application’s filing, Appellants have nevertheless failed to demonstrate possession of the essential mir-302 as required by 35 U.S.C. § 112, first paragraph. Id.

We agree with the Examiner. 35 U.S.C. § 120 recites:

An application for patent for an invention disclosed in the manner provided by section 112(a) (other than the requirement to disclose the best mode) in an application previously filed in the United States, or as provided by section 363, which is filed by an inventor or inventors named in the previously filed application shall have the same effect, as to such invention, as though filed on the date of the prior application, if filed before the patenting or abandonment of or termination of proceedings on the first application or on an application similarly entitled to the benefit of the filing date of the first application and if it contains or is amended to contain a specific reference to the earlier filed application….

4 Houbaviy and Rodriguez were published in August 2003 and 2004, respectively.
We agree with the Examiner that § 120 requires that, for a later application to claim the benefit of a prior application, that prior application must meet the requirements of written description support established under 35 U.S.C. §112, first paragraph.

The first paragraph of 35 U.S.C. § 112 recites:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

It is well-established, however, that “[t]he purpose of the ‘written description’ requirement is broader than to merely explain how to ‘make and use’; the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.” Vas-Cath Inc. v. Mahurkar, 935 F.2d 1559, 1563–64 (Fed. Cir. 1991) (emphasis added). Although possession alone is not sufficient to satisfy the written description requirement of § 112’s first paragraph, it is essential to the purpose of the statute. See Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 969 (Fed. Cir. 2002). Consequently, Appellants must demonstrate that they were in possession of mir-302 in the ’262 application.

This they have not done. Appellants point to no disclosure in the ’262 application that indicates that they were in possession of mir-302 at the time of filing. Nor do they point to any prior art published prior to the filing date of the ’262 application that teaches or suggests mir-302. Appellants’ argument that it would not have required undue experimentation for a person
of ordinary skill to have arrived at mir-302 is inapposite: the first paragraph of § 112 requires a demonstration of *possession* of the invention.

Moreover, Appellants adduce no affidavits or declarations by the inventors, supported by evidence of record, indicating that they were in possession of mir-302 in May, 2003, when the ’262 application was filed.

Nor are we persuaded by Appellants’ argument that, because 90 intronic microRNAs in humans were known generally in the art, mir-302 was somehow also known and therefore falls within the scope of the ’262 application. We agree with the Examiner that mir-302 is essential and central to Appellants’ claimed invention, and therefore requires Appellants to demonstrate possession of mir-302 at the time the ’262 application was filed.

Consequently we agree with the Examiner’s conclusion that Appellants’ application on appeal cannot claim priority benefit of the ’262 application and that the references cited by the Examiner are valid prior art to Appellants’ instant application.

B. Rejection of the claims under 35 U.S.C. § 103(a)

*Issue*

Appellants argue the Examiner erred in finding the claims on appeal are obvious over the combined cited prior art. App. Br. 8.

*Analysis*

Appellants argue Kim neither teaches nor suggests “preventing stem cell tumorigenicity” as recited in claim 1. App. Br. 8. Appellants argue that, despite the Examiner’s finding Kim “teaches treating cancer,” stem cells are not cancer cells, and teaching treating cancer cells is not the same as
teaching preventing stem cell tumorigenicity. *Id.* (citing Advisory Act. 9–10 March 15, 2013). Appellants argue that stem cells, by definition, are pluripotent, whereas cancer cells are not, and that stem cells normally do not possess genetic mutations, whereas cancer cells do. *Id.* at 9. Appellants maintain that despite the Examiner’s finding “[i]n treating the process of cancer as disclosed by Kim, the miR-302 constructs would naturally prevent stem cell tumorigenicity,” the Examiner misapprehended the fact that cancer formation is due to an accumulative of mutations rather than stem cell tumorigenicity. *Id.* Furthermore, contend Appellants, the Examiner may not argue that “preventing stem cell tumorigenicity” flows naturally from mir-302 expression while denying Appellants’ priority claim to the ’262 Application because, if so, the ’262 application enables the invention of the ’806 application. *Id.*

Appellants argue further that Kim does not teach mir-302 can silence CDK2 to inhibit stem cell tumorigenicity, as required by claim 1. App. Br. 10. Appellants content that although the prior art teach mir-302 is present in embryonic stem cells, FIG. 8C of Appellants’ Specification discloses that the natural expression level of mir-302 in human embryonic stem cells (“hESCs”) is not sufficient to effectively silence CDK2. *Id.* Appellants assert their Specification discloses that, to effectively silence CDK2, mir-302 must be expressed at a higher level beyond that found normally in hESCs. Appellants point to Kim’s teaching: “[s]pecially, of miRNAs provided in the present invention, miR-200c, miR-368, miR-154*, miR-302b*-302b-302c*-302c-302a*- 302a-302d-367 cluster on chromosome 4 and miR-371-372-373*-373 cluster on chromosome 19 are expressed specifically in undifferentiated human embryonic stem cells.” *Id.*
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(quoting Kim 24, ll. 1–4). Appellants contend Kim thus teaches there should be no other differentiated human cells expressing mir-302 and, hence, the expression level of mir-302 in undifferentiated hESCs should be not only the highest but also the only observed level in humans. *Id.* Therefore this teaching of Kim can only be interpreted to show that a mir-302 level higher than that of hESCs cannot be naturally found in humans. *Id.* Appellants argue that the remaining cited prior art references do not cure the alleged deficiencies of Kim.

The Examiner responds that Kim teaches treating cancer, which involves the treatment of tumors. Ans. 13. The Examiner finds that, because tumors are well-known in the art to comprise cancer stem cells, it necessarily follows that a practitioner treating cancer according to the method of Kim will naturally inhibit the tumorigenicity of stem cells. *Id.* citing, e.g., S. Gidekel et al., *Oct-3/4 is a Dose-dependent Oncogenic Fate Determinant*, 4(5) CANCER CELL, 5, 361-370 (2003) (cited in Applicants’ IDS)). Furthermore, finds the Examiner, even if, *arguendo*, Appellants are correct that treating cancer cells is not the same as preventing stem cell tumorigenicity, any systemic administration of a mir-302-expressing vector in a human will result in that vector reaching at least some of the endogenous stem cells that humans necessarily possess. Ans. 13. The Examiner finds such a process would inhibit or prevent such stem cells from becoming tumorigenic, thereby satisfying the claim limitation. *Id.* Finally, the Examiner finds the limitation relating to “preventing stem cell tumorigenicity” occurs in the preamble, and finds the language therefore does not breathe life and meaning to the claim as a whole. *Id.* The Examiner finds this is because stem cells are ubiquitous in mammals and are
not normally tumorigenic. *Id.* The Examiner therefore places no weight on the language of the preamble requiring that a certain type of cell avoid doing what the cell would not normally do. (i.e., become tumorigenic). *Id.*

With respect to Appellants’ argument that Kim does not teach mir-302 can silence CDK2 to inhibit stem cell tumorigenicity, the Examiner finds CDK2 inhibition by mir-302 is a function that naturally occurs in response to mir-302 administration to a cell, which is the method taught by Kim. Ans. 15. The Examiner finds there is no manipulative or structural difference between the method taught by Kim in combination with the cited art and those of the presently claimed invention. *Id.* Therefore, the Examiner finds, Kim need not expressly teach this latent property (CDK2 inhibition) of mir-302 administration to a cell in order for the claim to be obvious over Kim. *Id.* (citing M.P.E.P. § 2112.02; *In re Hack*, 245 F.2d 246, 248 (C.C.P.A. 1957); *In re May*, 574 F.2d 1082, 1090 (C.C.P.A. 1978).

The Examiner finds the inhibition of CDK2 by mir-302 may be likened to a “wherein” or “whereby” clause, since its recitation in claim 1 amounts to nothing more than an intended use or purpose. App. Br. 15. The Examiner quotes M.P.E.P. § 2111.04:

In *Hoffer v. Microsoft Corp.*, 405 F.3d 1326, 1329 (Fed. Cir. 2005), the court held that when a “‘whereby’ clause states a condition that is material to patentability, it cannot be ignored in order to change the substance of the invention.” *Id.* However, the court noted (quoting *Minton v. Nat’l Ass’n of Securities Dealers, Inc.*, 336 F.3d 1373, 1381 (Fed. Cir. 2003)) that a “whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.”
Id. at 15–16. Consequently, the Examiner finds, the limitation of claim 1 reciting “treating said cell substrate with said recombinant nucleic acid composition under a condition that the concentration of said intronic microRNA-like gene silencing effector is sufficient to suppress said CDK2 and the associated cell-cycle-related genes” should not be given patentable weight.

Finally, with respect to the amount of mir-302 required to be administered to be effective, the Examiner finds the optimization of the method taught by Kim for using mir-302 for treating cancer via a vector would establish the concentration that would result in expression sufficient to inhibit CDK2, because CDK2 is known to be fundamentally involved in cell replication. App. Br. 16. The Examiner finds that a person of ordinary skill in the art, seeking to treat cancer using mir-302 following the method of Kim, would find a level of expression of mir-302 sufficient to stop cell replication, and by extension, sufficiently suppress CDK2. Id.

We agree with the Examiner. The language of claim 1 reciting “A method for preventing stem cell tumorigenicity,” is in the preamble of the claim. Our reviewing court has held:

In general, a preamble limits the invention if it recites essential structure or steps, or if it is “necessary to give life, meaning, and vitality” to the claim. Conversely, a preamble is not limiting “where a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention.

Catalina Marketing International, Inc. v. Coolsavings.com, Inc., 289 F.3d 801, 808 (Fed. Cir. 2002) (internal citations omitted). The Federal Circuit has since enlarged upon this subject:
Whether to treat a preamble term as a claim limitation is “determined on the facts of each case in light of the claim as a whole and the invention described in the patent.” While there is no simple test for determining when a preamble limits claim scope, we have set forth some general principles to guide that inquiry. “Generally,” we have said, “the preamble does not limit the claims.” Nonetheless, the preamble may be construed as limiting “if it recites essential structure or steps, or if it is ‘necessary to give life, meaning, and vitality’ to the claim.” A preamble is not regarded as limiting, however, “when the claim body describes a structurally complete invention such that deletion of the preamble phrase does not affect the structure or steps of the claimed invention.


In the appeal presently before us, we agree with the Examiner that the language of the preamble does not limit the claim. The language preamble states the overall purpose of the method of the claim, viz., “preventing stem cell tumorigenicity,” but we find that that all of the steps of that method could be practiced, when viewed in light of the Specification, by following the subsequent steps recited in the body of the claim without reference to the preamble. We therefore find that the preamble does not limit the claim and we uphold the Examiner’s finding on this ground.

Furthermore, we agree with the Examiner that the method of Kim, which teaches treating cancer cells with mir-302, inherently teaches suppression of CDK2, because treatment of the cells with a sufficiently high expression of mir-302 to stop cell proliferation necessarily would result in the suppression of CDK2. To establish inherency, “the limitation at issue necessarily must be present, or the natural result of the combination of elements explicitly disclosed by the prior art.” *Par Pharmaceutical, Inc.*, 356 F.3d 1376, 1381 (Fed. Cir. 2004) (internal citations omitted).
and Alkermes Pharma Ireland Limited, v. Twi Pharmaceuticals, Inc., 773 F.3d 1186, 1195-96 (Fed. Cir. 2014). We agree with the Examiner that Kim teaches suppression of cancer cell proliferation via treatment with mir-302, and that CDK2 was known in the art to be fundamentally involved in cell proliferation. Moreover, we agree that suppression of CDK2 is the natural result of the treatment of cancer cells with mir-302, as taught by Kim.

Furthermore, we agree with the Examiner that a person of ordinary skill in the art, upon learning the teachings of Kim, would be motivated to optimize the expression of mir-302 in the treatment of cancer cells to suppress cancer cell proliferation. And because it was well-known in the art that CDK2 is fundamental to cell proliferation, we further agree with the Examiner that a person of skill in the art would optimize the “concentration of said intronic microRNA-like gene silencing effector is sufficient to suppress said CDK2 and the associated cell-cycle-related genes, wherein said concentration is similar to or higher than the mir-302 level found in human embryonic stem cells,” as required by claim 1. We consequently affirm the Examiner’s rejection of claims 1–12, 14–15, 17–18, 20, 22, 25–28, 30–36, 38–39 and 43–45.

C. Rejection under the Nonstatutory Doctrine of Obviousness-Type Double Patenting

Issue

Appellants argue the Examiner erred in finding claims 1–12, 14–15, 17–18, 20, 22, 25–28, 30–36, 38–39 and 43–45 are unpatentable unpatentable under the nonstatutory doctrine of obviousness-type double
patenting over the combination of Appellants’ US Application Serial No. 12/149,725 (the “‘725 application”) and Kim.

Analysis

Appellants point to claim 1 of the ‘725 application, which recites:

A method for reprogramming mammalian cells to pluripotent stem cells, comprising the steps of:

(a) constructing a recombinant nucleic acid composition that contains at least an intron encoding a mir-302-like microRNA effector;

(b) introducing said recombinant nucleic acid composition into a plurality of mammalian cells, wherein said plurality of mammalian cells generate a plurality of mir-302-like microRNA effectors derived from said intron to a level that is sufficient to induce DNA demethylation of Oct3/4 promoter and activate Oct3/4 expression, which consequently results in reprogramming the cells to a plurality of stem cell-like pluripotent cells.

App. Br. 13. Appellants contend that the differences between claim 1 of the ‘725 application and claim 1 of the instant appeal render the subject matter claimed in each claim patentably distinct. Id. at 12. Specifically, Appellants argue: (1) claim 1 of the current application is a method for “preventing stem cell tumorigenicity,” whereas claim 1 of the ‘725 application is a method for “reprogramming mammalian cells to pluripotent stem cells”; (2) claim 1 of

5 Appellants state claim 1 of the ‘725 application is a method for: “inducing intronic mir-302-mediated gene silencing effects in mammalian cells.” We find no such language in claim 1 of the ‘725 application, but we find this language of the preamble to be equivalent.
the current application has a step requiring “expressing a plurality of CDK2,” whereas claim 1 of the ’725 application contains no such limitation; (3) claim 1 of the current application also has a step requiring “an intronic microRNA-like gene silencing effector targeting said CDK2,” whereas claim 1 of the ’725 application contains no such limitation; and (4) claim 1 of the current application has a further step requiring “a condition that the concentration of said intronic microRNA-like gene silencing effector is sufficient to suppress said CDK2” while the claim 1 of the ’725 application contains no such specification. App. Br. 18. Appellants contend that, for these reasons, the differences in the language of the claims render the methods claimed in each patentably distinct. Id.

The Examiner finds that, although the conflicting claims are not identical, they are not patentably distinct, because the claims of the both applications teach methods of expressing gene silencing elements comprising the use of an intron-encoded gene silencing effector. Non-Final Act. 14. The Examiner finds that, whereas the competing claims do not teach the expression of mir-302, nor the production of stem cells that result from the use of mir-302, the use of mir-302 in such a method is obvious over Kim. Id. The Examiner finds Kim teaches expressing mir-302 from expression vectors and, for the reasons cited supra, in the Examiner’s §103 analysis, it would have been obvious to one of ordinary skill in the art to substitute mir-302 in place of the gene silencing elements of claim 1 of the ’725 application, because Kim teaches expressing such elements would

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6 The Examiner relies upon these findings in the Answer. See Ans. 17.
allow for greater study of how stem cells maintain pluripotency, and that such elements may be useful in treating cancer. *Id.*

We agree with the Examiner. As an initial matter, Appellants compare claim 1 of the current application with claim 1 of the ’725 application without reference to the teachings of Kim. “[O]ne cannot show non-obviousness by attacking references individually where … the rejections are based on combinations of references.” *In re Keller,* 642 F.2d 413, 426 (C.C.P.A. 1981).

With respect to Appellants’ argument (1) we have already found that the claim language “preventing stem cell tumorigenicity” in the current claim 1 is preamble language which does not limit the claim. The language of claim 1 of the ’725 application recites “reprogramming mammalian cells to pluripotent stem cells,” which, for similar reasons, is not limiting on that claim.

With respect to (2) we agree with the Examiner’s conclusion that the teachings of Kim, when combined with those of the ’725 application would render claim 1 of the current application obvious based upon the fact that Kim teaches using mir-302 in the treatment of proliferating cancer cells and CDK2 is essential to the regulation of the cell cycle and proliferation.

With respect to (3) and (4), we have related *supra* the reasons why we agree with the Examiner that these limitations flow naturally from the teachings of Kim. Therefore, despite Appellants’ argument that certain limitations present in the current claim 1 are absent from claim 1 of the ’725 application, we agree with the Examiner’s conclusion that the claim 1 of the current application is obvious over the combination of claim 1 of the ’725

CONCLUSION

We agree with the Examiner’s findings and conclusions establishing a 
prima facie case of obviousness and we do not find Appellant’s arguments to the contrary persuasive. We consequently affirm the Examiner’s rejection of the claims.

DECISION

The Examiner’s rejection of claims 1–3, 5–10, 12, 14–15, 17–21, 26–29, 35–36, 39 and 42 as unpatentable under 35 U.S.C. § 103(a) is affirmed.

The Examiner’s rejection of 1–12, 14–15, 17–18, 20, 22, 25–28, 30–36, 38–39 and 43–45 as unpatentable under the nonstatutory doctrine of obviousness-type double patenting is 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). See 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED