Intellectual Property Appellate Board
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OA/9/2020/PT/CHN

MONDAY, THIS THE 21ST DAY OF DECEMBER, 2020

HON'BLE SHRI JUSTICE MANMOHAN SINGH — **CHAIRMAN**
HON'BLE DR. B.P. SINGH — **TECHNICAL MEMBER (PATENTS)**

1. **KYOTO UNIVERSITY**
36-1, YOSHIDA-HONMACHI SAKYO-KU,
KYOTO-SHI KYOTO 606-8501 JAPAN

…APPLICANT/APPELLANT

(Represented by: Ms. Bharathi Viswanathan)

Versus

1. **ASSISTANT CONTROLLER OF PATENTS AND DESIGNS**
GOVERNMENT OF INDIA, PATENT OFFICE
INTELLECTUAL PROPERTY RIGHTS BUILDING
GST ROAD, GUINDY CHENNAI – 600 032

…RESPONDENT

(Represented by - None)

ORDER

Hon'ble Shri Justice Manmohan Singh, Chairman

Hon'ble Dr. B.P. Singh, Technical Member (Patents)

1. The present appeal is filed under Section 117A of the Indian Patents Act, 1970, against the order dated 03/01/2020, passed by the Respondent, being the Assistant Controller of Patents & Designs, under Section 15 of the Indian Patents Act, 1970, refusing to grant the Appellants' Indian patent application no. 1636/CHENP/2009.

2. It is the case if the appellant that

2.1 During First Examination stage no objection regarding novelty and non-patentability under Section 3(d) in respect of the original claims were raised. Also the documents relied upon for inventive step were completely different.

2.2 The objections regarding novelty and inventiveness in view of new documents and in view of Section 3(d) were raised for the first time in the hearing notice.

2.3 The appellant further submits that despite the Appellant's pleading to offer another opportunity in case of any outstanding objection, the Respondent has refused the application, on the new grounds raised for the first time only in the hearing notice.

2.4 Further, the respondent has failed to provide any reasoning whatsoever in respect of the alleged ground for refusal.

2.5 The impugned order is a non-speaking one, devoid of proper deliberation, coherent reasoning and justification to the stance adopted by the Respondent.

2.6 Hence, the Appellants submit that natural justice has been denied to the appellant by the impugned decision.

3. The Present Invention as explained by the appellant is as under:

3.1 The present invention is based on the revolutionary finding that a small number of defined factors can reprogram a somatic cell nucleus to a less differentiated state. These factors are called "nuclear reprogramming factors". The present invention addresses and fulfills a significant need for providing a process for generating induced pluripotent stem cells by reprogramming differentiated somatic cells. Particularly, the present invention address the need to provide a process for generating safe induced pluripotent stem cells having no fear of tumorigenesis in the cells or

tissues obtained by differentiation-inducing the induced pluripotent stem cells.

3.2 It may be noted that one of the inventors, Prof. Yamanaka, has been awarded with the Nobel prize in Physiology and Medicine 2012, in recognition of his outstanding achievement in this field.

3.3 The independent claims presented to the Respondent during the Hearing held on 24 October 2019 and filed at IPO on 06 November 2019 along with written submission are as below:

3.1.1 Claim 1 is directed to A process for generating induced pluripotent stem cells from somatic cells, comprising the step of introducing the following five genes: Oct family gene, Klf family gene, Sox family gene, Lin28 gene, and L-Myc gene into somatic cells.

3.1.2 Claim 6 is directed to A process for generating induced pluripotent stem cells from somatic cells, comprising the step of introducing a combination of the following two genes: Oct family gene and Sox family gene or a combination of the following two genes: Oct family gene and Klf family gene, and Lin28 gene and L-Myc gene, and at least one of genes selected from the following two genes: Sall1 and Sall4 into somatic cells.

3.1.3 Claim 8 is directed to A process for generating induced pluripotent stem cells from somatic cells, comprising the step of introducing a combination of the following five genes: Oct family gene, Sox family gene, Klf family gene, Lin28 gene, and L-Myc gene, and at least one kind of genes selected from the following two genes: Sall1 and Sall4 into somatic cells.

3.1.4 Claim 12 is directed to A process for generating induced pluripotent stem cells from somatic cells, comprising

the step of introducing the following six genes: Oct family gene, Klf family gene, Sox family gene, L-Myc gene, Lin28 and Nanog into somatic cells.

3.4 The objective technical problem addressed by the present invention is that of provision of means for production of iPS cells with improved efficiency.

4. The learned counsel of the appellant submitted the distinguishing features of the present invention over cited prior art D1: CA2632142A1 as follows:

4.1 D1: CA2632142A1 belongs to the patent family of WO2007/069666, which has been relied upon in Background of the present application as Patent Publication 1.

4.2 D1 describes preparation of iPS cells that are ES-like cells using nuclear reprogramming factors such as Oct3/4, Sox2, Klf4, and c-Myc. D1 discusses using alternate members of the Oct, Myc and Klf4 families, in particular c-Myc, for inducing iPS. D1 does not teach the use of Lin28 to induce iPS. Further, D1 does not provide any pointers that Sall1 or Sall4 in combination with Lin28 and the other factors would result in effective and safe production of iPS cells.

4.3 Thus D1 does not disclose generating iPS using a combination of reprogramming genes which comprises an Oct family gene, a Sox family gene, a Klf family gene, Lin28 and L-Myc.

4.4 Accordingly, the claimed process is novel over the disclosure of D1.

4.5 Further, D1 does not provide any pointers that the use of a combination of L-Myc and Lin28 would improve iPS cell

production efficiencies compared to the use of c-Myc and Lin28.

4.6 In fact, regarding L-Myc, Example 6 of D1 states "Further, each of N-Myc and L-Myc (each wild type) was almost the same as c-Myc in both of the number of G418-resistant colonies formed and iPS cell establishment efficiency."

4.7 Moreover, in working examples of D1, C-Myc or its variant is consistently used, except example 6. It is understood that that N-Myc and L-Myc are just comparisons or references.

4.8 Thus, D1 teaches that L-Myc is almost the same a c-myc and hence a skilled person would have had no motivation, let alone any reasonable expectation of success for using the factor combination of the present claim in order to provide means for production of iPS cells with improved efficiency. Hence, D1 can only be construed to teach away from the present invention.

4.9 On the other hand, as demonstrated in Table 14, the use of Lin28 in combination with L-myc instead of c-Myc resulted in approximately a 3.7 times higher number of iPS colonies (366 Vs 98 hiPS colonies). Thus, the use of L-Myc is critical to successful generation of safe induced pluripotent stem cells.

4.10 Additionally, Table 14 also demonstrates that use of Lin28 in combination with L-Myc improvise the efficiency of iPS cell production compared to the respective use of c-Myc.

4.11 Thus use of L-myc, as employed by the claimed process is a non-obvious departure from use of c-Myc in the prior art.

4.12 In this regard, it may be noted that c-Myc is NOT ideal for generation of iPS because c-Myc is a cancer associated transcription factor, which when introduced to somatic cells

for reprogramming along with other factors gives rise to the possibility that the cells or tissue differentiation-induced from the obtained iPS have tumorigenicity cannot be denied.

4.13 Therefore, the presently claimed invention embodies a significant technical advancement over the results achieved in prior art which could not be realised heretofore the priority date of the present invention.

5. The learned counsel of the appellant has submitted distinguishing features of the present invention over cited prior art D2: Golan-Mashiach M et al; *"Design principle of gene expression used by human stem cells: implication for pluripotency";* Federation of American Societies for Experimental Biology; Vol19(1); Jan 2005.

5.1 D2 merely analyses the expression profile of human ESC line 9.2 and compares it to the expression profiles of adult tissues—differentiated cells (blood and keratinocytes) as well as their progenitor cells.

5.2 Further, D2 only hypothesizes a strategy of expressing genes that represent various differentiation pathways. It lists only 9 genes as candidate ESC signature genes. It may be noted that Myc family in itself, let alone L_myc, is not listed as one of the signature gene. Also, Lin28 is simply listed in parallel with other genes. Therefore, a skilled person in the art reading D2 is not motivated to particularly select Lin28 from other genes. Furthermore, D2 does not provide any working examples and thus only merely indicates a selection of few genes for continuous expression upon differentiation to a particular target.

5.3 For the above reasons, it is humbly submitted that the invention claimed in the present application is not obvious over D1 & D2.

5.4 The Respondent has failed to analyze the teaching of D1 and D2 and provide the reasoning how a person skilled in the art can arrive at the claimed invention in an obvious manner.

6. The learned counsel of the appellant has submitted his arguments in respect of non-patentability of claims under section 3(d) of the Patents Act, 1970 as follows:

6.1 The restraints of Section 3(d) of the Indian Patents Act is clearly and specifically targeted to a "process" directed to mere use of a known process which does not results in a new product or employ at least one new reactant.

6.2 For reasons elaborated above, the claimed process is novel.

6.3 Also Table 14 provides a direct comparison between the use of Sox2, Oct4, Klf4, Lin28 and either c-Myc or L-Myc. The table clearly shows that the use of Lin28 in combination with L-myc instead of c-Myc resulted in approximately a 3.7 times higher number of iPS colonies.

6.4 Hence, it is submitted that the claimed 'process' cannot be construed as a "known process" under Section 3(d).

7. The appellant also submitted the details of corresponding foreign patent applications:

Country	**Application No.**	**Status**	**Patent No.**	**Date of Grant**
Australia	2008297024	**Granted**	2008297024	11/12/2014
Canada	2660123	**Granted**	2660123	09/05/2017
China	200880000834.5	**Granted**	200880000834.5	12/03/2014
Europe	08832782.0	**In order for grant**		
Japan	2009-508036	**Granted**	5349294	30/08/2013
Korea	2009-7006480	**Granted**	1564044	22/10/2015
Singapore	2009018037	**Granted**	153139	15/06/2011

7.1 In this regard, the Appellants wish to bring to the notice of the Hon'ble Board that claims on record are similar in scope with claims found in order for grant in corresponding European Application No: 08832782.0 and also been allowed as JP5349294B2. The have attached herewith a copy of the claims found to be in order for grant, the decision to allow the application in Europe and machine translated claims of JP5349294B2.

7.2 It may be noted that while EPO has relied upon D1: WO2007/069666/D1a: EP 1970446, the JPO has relied upon D1: WO2007/069666, which belong to the same family as D1: CA 2632142, that has been relied upon by the Respondent in the hearing notice.

7.3 D2, as stated above, only provides background information and is not particularly relevant to the impugned invention. Notwithstanding, even if D2 is considered, the below table highlights the features in the present invention in comparison with that in D1 and D2.

Document	**genes introduced**
D1	Oct family, Klf family, and Sox family
D2	Oct4, Lin28, TDGF1, LeftB, and Sox2
The present invention	Oct family, Klf family, Sox family, **L-Myc, and Lin28**

8. Further, in this regard, the Appellant notes that the Hon'ble Board has recently emphasized in many of its decisions, the importance of considering allowance in the corresponding applications worldwide.

8.1 In para 35 of OA/33/2015/PT/KOL the Hon'ble Board observed as follows:

" The claims are novel and also inventive in view of the cited documents and completely supported by the specification as

originally filed. Filing of additional documents, data and evidence in support of the invention, to overcome the objection raised and to attack a specific objection is something which is allowed under the Patent Law of not only India but also other foreign jurisdictions. Nothing has been discussed in the impugned order. ***We have not understood, how the respondent has taken the contrary view of the same invention which has been recognized in other countries of the world. The respondent is bound give valid reason fi contrary is taken. The said reason are missing. The reason given in the impugned order contrary to law.***

8.2 In para 29, 32, 34 of OA/3/2017/PT/CHN the Hon'ble Board observed as follows:

"29. It is also a matter of fact that the present application with similar claim scope is granted in 18 countries. Following is a compilation summarizing the countries, status of foreign applications"

"32. Hence, it is clear that amendments in the Act till 2005, was made to bring the Patents Act of India, not only in consistent with TRIPS Agreement but also to make it in consonance with international practices. In a way it would be prudent to suggest that the Act makes an attempt to consider that tests of novelty and obviousness are universal in nature."

"34. It is true that the International Search Report (ISR) issued by World Intellectual Property Organization in respect of PCT application is not binding in view of Article 33(1) of the Patent Cooperation Treaty, which provides that the object of the International Preliminary Examination is to formulate a preliminary and non- binding opinion. Article 35(2) of the PCT

provides that the International Preliminary Examination Report shall not contain any statement on the question whether the claimed innovation is patentable or not according to any national law. But we are of the view that some importance is to be given when the similar patent in many other countries are registered after overcoming the objection of prior art, novelty, obviousness. It may not be binding effect but the Examiner must take into this aspect while examination of application and to consider also about the registration of some invention in other countries at the time of raising objection in the examiner report."

8.3 In para 45 of OA/40/2015/PT/KOL the Hon'ble Board observed as follows:

"45. It appears to us that argument addressed on behalf of appellant and written – submission filed have not been considered carefully. The impugned order is passed without application of mind. It should have been passed after considering the material on record and affidavit of export. It is also matter of fact that this similar invention of corresponding patents have been granted in all major jurisdiction. The details of such countries are given, however no provivences is given by Respondent No. 2. The same is not acceptable."

8.4 As the presently claimed subject matter has been acknowledged to be novel and inventive by EPO, JPO, to list a few, the Appellant request a similar consideration in the India too.

9. Let's have a look on the First Examination Report:

9.1 The First Examination Report (FER) issued on 30/11/2018 contained the mainly the following objections:

9.1.1 *Claims 1-19 of the instant application lack inventive step in view of documents cited below:*

Claims 1-19 of the instant application lack inventive step in view of documents cited belowD1: EP1254211A1; Nov 06 2002: Discloses method of producing neurectoderm cells, which method includes providing a source of early primitive ectoderm-like (EPL) cells; a conditioned medium as hereinbefore defined; or an extract therefrom exhibiting neural inducing properties; and contacting the EPL cells with the conditioned medium or extract, for a time sufficient to generate controlled differentiation to neurectoderm cells, wherein the conversion of EPL cells to neurectoderm cells is characterised by down regulation of expression of Oct4 relative to embryonic stem (ES) cells; and; and one or more of up regulation of expression of N-Cam and nestin; up regulation of expression of Sox1 and Sox2; and initial up regulation of expression of Gbx2; followed by down regulation thereof as neurectoderm cells persist. D2: WO2001098463A1; Dec 27, 2001: Discloses preparation of undifferentiated embryonic stem (ES) cells maintained in an undifferentiated state and wherein said cells will undergo stem cell renewal or somatic differentiation. D2 also discloses that Undifferentiated stem cells may be propagated and subcultured for multiple passages in the presence of insulin or analogue or the factor. Successful long term maintenance of stem cells in the presence of insulin or analogue or the factor

may be proven by the continued presence in the cultures of diploid cells bearing stem cell markers and expressing stem cell specific genes such as Oct-4. D3: WO2003042405A2; May 22, 2003: Discloses method for producing a population of cells enriched for pluripotent fetal stem cells, comprising selecting c-kit positive cells from a chorionic villus, amniotic fluid, or placenta sample, said methid further comprising the step of further enriching for the pluripotent fetal stem cells by additionally selecting for cells expressing markers expressed by SSAE and/or SSAE4 embryonic stem cells. D1-D3 disclose the method of production of pluripotent cell from somatic cell and role of OCT4 gene and SOX family gene in said method. Therefore in view of disclosured of D1-D3, it is obvious for a person skilled in art to generate induced pluripotent cells from somatic cell by introducing Oct family gene Sox family gene and k1f family gene into somatic cells. Therefore claims 1-19 of the instant application lack inventive step under section 2(1)(j) of The Patents Act, 1970.

9.1.2 *Claim(s) (1-19) are statutorily non-patentable under the provision of clause (3(b), 3(j), 3(i)) of Section 3 for the following reasons:*

9.1.2.1 *The claims 1-19 relate to "method of generating induced pluripotent cells from somatic cell by introducing Oct family gene Sox family gene and k1f family gene into somatic cells". The said claims fall within the scope of*

section 3(b) of The Patents Act, 1970 as the said claims are directed towards an invention the primary or intended use or commercial exploitaion of which could be contrary public order or morality.

9.1.2.2 *Claims 1-19 recites "method of generating induced pluripotent cells from somatic cell by introducing Oct family gene Sox family gene and k1f family gene into somatic cells". Claims 1-19 fall within the scope of section 3(j) of The Patents Act, 1970, as the said claims are directed towards essential biological processes for the production of plants/animals; and use of animal in whole or any pary thereof.*

9.1.2.3 *The claims 1-16 of the instant application relate to "method of generating induced pluripotent cells from somatic cell by introducing Oct family gene Sox family gene and k1f family gene into somatic cells", therefore fall within the scope of section 3(i) of The Patents act, 1970.*

9.1.3 *As per the requirement u/s. 10(4) (ii) (D) you have to disclose the source and geographical origin of ALL THE BIOLOGICAL MATERIALS used in the invention (even if not from India). The same may be*

provided in a tabular format. (Source means the exact source from where the applicants procured the biological material(s) and Geographical origin means the actual geographical origin of the biological material(s). The source and geographical origin can be same or different.)

9.1.4 *The subject matter of claims 1-19 recite terms such as "induced pluripotent cell, somatic cell, oct family gene, sox family gene and klf family gene, tissue, organ, body fluis or individual, human somatic cell etc." said terms are very broad and do not define the scope of invention. Hence these terms shall be clearly specified.*

10. The hearing notice issued on 02/09/2019 contained mainly the following objections:

10.1 In view of applicant's submission dated 20/08/2019, claims 1-13 of the instant application lack novelty in view of the document cited below

D1: CA2632142A1; June 21, 2007: Discloses nuclear reprogramming factor for a somatic cell, which comprises a gene product of each of the following three kinds of genes: an Oct family gene, a Klf family gene, and a Myc family gene, wherein said factor further comprises a gene product or gene products of one or more kinds of genes selected from the group consisting of Fbx15, Nanog, ERas, ECAT15-2, Tcl1, and beta.-catenin. D1 also discloses method for preparing an induced pluripotent stem cell by nuclear reprogramming of a somatic cell, which comprises a step of contacting the said nuclear reprogramming factor with the somatic cell. D1 further discloses method for improving differentiation ability and/or

growth ability of a cell, which comprises the step of contacting the nuclear reprogramming factor with a somatic cell, wherein the cell is a human cell.

All the essential technical features of claims 1-13 have been disclosed in D1, hence claims 1-19 of the instant application lack novelty in view of D1.

Inventive step: Claims 1-19 of the instant application lack inventive step in view of the document cited below

D1: CA2632142A1; June 21, 2007

D2: Golan-Mashiach M et al; "Design principle of gene expression used by human stem cells: implication for pluripotency"; Federation of American Societies for Experimental Biology; Vol19(1); Jan 2005: Discloses that genes that were analyzed in various ESC systems and shown to be essential for pluripotency and self-renewal include OCT4, LIN28, TDGF1, LeftB, SOX2, and others.

D1 discloses process for generating induced pluripotent stem cells from somatic cells by a method, comprising the step of introducing the following three genes: Oct family gene, Klf family gene, and Sox family gene into somatic cells. D2 discloses that LIN28 gene is essential for the pluripotency and selfrenewal. Therefore in view of disclosure of D1 and D2, it is obvious for a person skilled in art to generate induced pluripotent stem cells from somatic cells, comprising the step of introducing the following six genes: Oct family gene, Klf family gene, Sox family gene, Myc family gene, Lin28 and Nanog into somatic cells. Therefore claims 1-19 of the instant application lack inventive step under section 2(1)(j) of The Patents Act, 1970.

Non-Patentability u/s 3

Claims 1-19 of the instant application relate to "process for generating induced pluripotent stem cells from somatic cells, comprising the step of introducing the following three genes: Oct family gene, Klf family gene, and Sox family gene into somatic cells". The document D1 already discloses method for preparing an induced pluripotent stem cell by nuclear reprogramming of a somatic cell which comprises a gene product of each of the following three kinds of genes: an Oct family gene, a Klf family gene, and a Myc family gene. Therefore the claims 1-19 of the instant application fall within the scope of section 3(d) of The Patents Act, 1970 as the said claims are directed towards mere use of a known process/new for a known product.

11. A look on the order of the respondent reveals that he has just narrated the objections of hearing notice and held in operating portion of his order as:

"The post-hearing proposed amendment is not allowed under section 57 read with section 59 of the Patent Act.

After carefully reading through the FER response, while hearing oral and post-hearing written submissions and in light of the specification and amended claims, it is understood that the requirements of clarity and conciseness and along with formal requirements stand complied/waived off.

The oral & written submission placed before me could not justify the objections u/s 2(1)(j) & 2(1)(ja), and 3(d).

Therefore, in view of the above discussion, this application is refused patent u/s 15 of "The Patent Act 1970" for want of compliance requirements u/s 2(1)(j) & 2(1)(ja), and 3(d). The application stands disposed off."

12. The order of the respondent is a classic example of non-speaking order. Issuance of such orders is against the principal of natural

justice and at this stage, we only express our displeasure on such orders. We expect that the respondent will be very cautious herein after and will be issuing speaking order(s) in all future cases.

13. We have reviewed the post-hearing amendments of claims, submitted by the applicants/appellant and found that they have introduced the features of *Lin28* in combination with *L-Myc* into each claim which appears an essential amendment to bring out the inventive feature(s) not only in the principal claim but in all the subsidiary claims as well. Claims 10 and 11 were consequentially amended or deleted accordingly. Further, claims 17-19 which were relating to either to 'product by process' or 'product' claims have been deleted; which were otherwise not relating to patentable subject matter. The amendments bring clarity and definitiveness to the claims and are restricting the scope of the claims. Further, the amendments are incorporating the actual facts and based on the matter disclosed in the specification prior to the amendment. Hence the amended claims 1-15 are well within the scope of section 57 read with section 59 of the Patents Act, 1970 and we allow such amendments.

14. We have also analyzed the cited documents D1 and D2 and are inclined to accept the arguments of the appellant that the invention is 'novel' and 'inventive' with respect to both the citations. The lone citation for novelty i.e. CA2632142A1 belongs to same family of ISA citation WO2007069666 a common citation in the other entire jurisdictions, where the patent stands granted.

15. Let's have a look on provisions of section 3(d)

> *(d) the mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance or the mere discovery of any new property or new use for a known substance or of the* ***mere use of a known process,*** *machine or apparatus unless such*

known process results in a new product or employs at least one new reactant.

Explanation.—For the purposes of this clause, salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations and other derivatives of known substance shall be considered to be the same substance, unless they differ significantly in properties with regard to efficacy; [Emphasis added]

16. The application of section 3(d) appears totally misplaced as Section 3 (d) is applicable only if the claimed process is a *mere use of a known process.* In the instant case, the claimed process is held to be novel in its entirety and therefore falls outside the purview of "known" process and hence does not attract the provision of section 3(d) of the Patents Act, 1970.

17. We, therefore, set aside the impugned order dated 03/01/2020 issued by the respondent, and direct the respondent to grant the patent within 3 weeks from the issuance of this order.

18. Keeping in view the above facts and circumstances, the instant appeal is allowed. No cost.

-Sd/-

(Dr. B.P. Singh)
Technical Member (Patents)

-Sd/-

(Justice Manmohan Singh)
Chairman