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Entered: October 13, 2020

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEALS BOARD

DEREK **JANTZ**,
JAMES JEFFERSON SMITH, MICHAEL G. NICHOLSON,
DANIEL T. MACLEOD,
JEYARAJ ANTONY, AND VICTOR BARTSEVICH,
JUNIOR PARTY
(PATENTS 10,093,900; 9,993,502; 9,969,975; 9,950,011; 9,889,161; 9,889,160)

V.

ROMAN **GALETTO**,
AGNES GOUBLE, STEPHANIE GROSSE, CECILE MANNIOUI,
LAURENT POIROT, ANDREW SCHARENBERG,
AND
JULIANNE SMITH
SENIOR PARTY
(APPLICATION 16/027,629).

PATENT INTERFERENCE NO. 106,117
(TECHNOLOGY CENTER 1600)

Before: SALLY GARDNER LANE, JAMES T. MOORE, and DEBORAH KATZ, *Administrative Patent Judges*.

LANE, *Administrative Patent Judge.*

JUDGMENT - Bd. R. 127(a)

A decision granting Jantz Motion 3 of has been entered. (Decision, Paper 215). As a result of this Decision, the involved claims of senior party Galetto are unpatentable and Galetto lacks standing to continue in the interference. Bd. R. 201. Accordingly, we enter judgment against Galetto.

Order

It is

ORDERED that judgment on priority is entered against senior party Galetto as to Count 1, the sole Count of the interference (Declaration, Paper 1, 5);

FURTHER ORDERED that claims 26, 28-30, 32, and 33 of Galetto application 16/027,629, which correspond to Count 1, are FINALLY REFUSED. (Declaration, Paper 1, 5); 35 U.S.C. § 135(a);[1]

FURTHER ORDERED that the parties are directed to 35 USC § 135(c) and Bd. R. 205 regarding the filing of settlement agreements;

FURTHER ORDERED that a party seeking judicial review timely serve notice on the Director of the United States Patent and Trademark Office; 37 C.F.R. §§ 90.1 and 104.2. *See also* Bd. R. 8(b). Attention is directed to *Biogen Idec MA, Inc., v. Japanese Foundation for Cancer Research*, 785 F.3d 648, 654–57 (Fed. Cir. 2015) (determining that pre-AIA § 146 review was eliminated for interference proceedings declared after September 15, 2012); and

[1] Any reference to a statute in this Judgment is to the statute that was in effect on March 15, 2013 unless otherwise indicated. *See* Pub. L. 112-29, § 3(n), 125 Stat. 284, 293 (2011).

FURTHER ORDERED that a copy of this judgment be entered into the administrative records of the involved Jantz patents and Galetto application.

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

DEREK **JANTZ**,
JAMES JEFFERSON SMITH, MICHAEL G. NICHOLSON,
DANIEL T. MACLEOD,
JEYARAJ ANTONY, AND VICTOR BARTSEVICH,
Junior Party
(Patents 10,093,900; 9,993,502; 9,969,975; 9,950,011; 9,889,161; 9,889,160)

v.

ROMAN **GALETTO**,
AGNES GOUBLE, STEPHANIE GROSSE, CECILE MANNIOUI,
LAURENT POIROT, ANDREW SCHARENBERG,
and
JULIANNE SMITH
Senior Party
(Application 16/027,629).

Patent Interference No. 106,117
(Technology Center 1600)

Before: SALLY GARDNER LANE, JAMES T. MOORE, and DEBORAH KATZ, *Administrative Patent Judges*.

LANE, *Administrative Patent Judge.*

Decision - Motions - 37 C.F.R. § 41.125

I. Introduction

The interference was declared under 35 U.S.C. § 135(a)[1] on August 19, 2019 between junior party Derek Jantz, James Jefferson Smith, Michael G. Nicholson, Daniel T. MacLeod, Jeyaraj Antony, and Victor Bartsevich ("Jantz")[2] and senior party Roman Galetto, Agnes Gouble, Stephanie Grosse, Cecile Mannioui, Laurent Poirot, Andrew Scharenberg, and Julianne Smith ("Galetto").[3][4] (Declaration, Paper 1).

Galetto is involved on the basis of application 16/027,629 ('629), filed July 5, 2018. ('629 Application, Ex. 2004).[5] Jantz is involved on the basis of the following six patents:

(1) 10,093,900, issued October 09, 2018, application 15/964,446, filed April 27, 2018;
(2) 9,993,502, issued June 12, 2018, application 15/865,055, filed January 08, 2018;
(3) 9,969,975, issued May 15, 2018, application 15/865,089, filed January 08, 2018;
(4) 9,950,011, issued April 24, 2018, application 15/865,075, filed January 08, 2018;

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[1] Any reference to a statute in this decision is to the statute that was in effect on March 15, 2013 unless otherwise indicated. *See* Pub. L. 112-29, § 3(n), 125 Stat. 284, 293 (2011).

[2] Jantz identifies Precision BioSciences, Inc. as the real party in interest of its involved patents. (Jantz Real Party Notice, Paper 9).

[3] Galetto identifies Cellectis as the real party in interest, and Allogene Therapeutics, Inc., Les Laboratoires Servier, and Institut de Recherches Internationales Servier as licensees, of its involved application. (Galetto Real Party Notice, Paper 4).

[4] The parties are involved in related interference 106,118, involving the same Galetto application but different Jantz patents. Judgment was entered against Galetto on September 30, 2020 in that interference. ('118, Judgment, Paper 207).

[5] Exhibit 2004 is the published application, US 2018/0360883 A1, published December 20, 2018.

(5) 9,889,161, issued February 13, 2018, application 15/607,059, filed May 26, 2017; and
(6) 9,889,160, issued February 13, 2018, application 15/606,995, filed May 26, 2017.

Jantz filed two substantive motions as did Galetto.[6] One of the motions before us, Jantz Motion 3 seeking judgment against Galetto on the basis that all the involved Galetto claims are unpatentable for failure to comply with the written description requirement of the first paragraph of 35 U.S.C. §112, raises a threshold issue under Bd. R. 201. (Jantz Motion 3, Paper 96). Galetto opposed this motion. (Galetto Opposition 3, Paper 176). Jantz replied. (Jantz Reply 3, Paper 193). Because Jantz Motion 3 raises a threshold issue under Bd. R. 201, i.e., an issue that, if resolved in favor of the movant, would deprive the opponent of standing in the interference, we first consider this motion.[7]

We grant the motion.

II. Discussion

The evidence supports any findings of fact in this Decision by a preponderance of the evidence. The moving party has the burden of proof and must support its motion with appropriate evidence such that, if unrebutted, it would justify the relief sought. Bd. R. 208(b).

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[6] The panel decided that no oral argument was necessary and none was ordered.

[7] Galetto does not contest that Jantz Motion 3 raises a threshold issue and urges that its Motion 1 also raises a threshold issue. (Galetto Motion 1, Paper 24, 1:15-2:11). As discussed further within this decision, we do not find the Galetto motion to raise a threshold issue.

A. Jantz Motion 3

Subject matter of the interference

T cells provoke an immune response through T cell receptors ("TCRs"), which detect antigens expressed by pathogens or mutant cells. Cancer cells do not always express antigens that can be detected by the TCRs sufficiently to mediate killing of these cells. (Fry Declaration, Ex. 2003, ¶ 31, citing '629 Application, Ex. 2004, ¶ 8). The invention claimed by Galetto is directed generally to T cells that have been genetically modified through the introduction of a gene encoding a chimeric antigen receptor ("CAR"). CARs are synthetic receptors that are designed to detect a target antigen (e.g., tumor antigen) to generate an immune response against the antigen. CARs can be introduced to T cells ex vivo in either autologous cells (cells that are taken from the patient's own body) or allogeneic cells (cells that are taken from a donor that is not the intended patient). (Fry Declaration, Ex. 2003, ¶ 32, citing '629 Application, Ex. 2004, ¶¶ 4-6, 216). TCR from a donor may be recognized by a patient as foreign tissue, resulting in graft versus host disease (GvHD). (Fry Declaration, Ex. 2003, ¶ 41, citing '629 Application, Ex. 2004, ¶ 6).

The claimed invention calls for integration of a CAR sequence into the T cell receptor alpha gene ("TCRα") in a single genetic modification step using, e.g., homologous recombination ("HR").[8] (Fry Declaration, Ex. 2003, ¶¶ 73; 96;

[8] Homologous recombination is a DNA repair process by which homologous sequences are incorporated. (Galetto Opposition 3, Paper 176, 8:2-3 citing Osborn Declaration, Ex. 1041, ¶ 44). Integration by HR refers to a "natural, cellular process in which a double-stranded DNA-break is repaired using a homologous DNA sequence as the repair template," where the "homologous DNA sequence may be an endogenous chromosomal sequence or an exogenous nucleic acid that was delivered to the cell." (Fry Declaration, Ex. 2003, ¶ 37, citing '975 Jantz patent, Ex. 2021, 26:49-56; '629 Application, Ex. 2004, ¶ 98).

Galetto Clean Copy of Claims, Paper 7). This results in modified T cells having reduced TCR expression on the cell surface as well as CAR expression for antigen detection. The modified T cells may provide a better treatment option since the reduction of TCR expression decreases the possibility of GvHD making the use of donor cells safer for a patient. ('629 Application, Ex. 2004, ¶¶ 2, 11, 16; Galetto Opposition 3, Paper 176, 18:2-4).[9]

Galetto involved claim

According to the '629 specification, in an embodiment of the invention where TCRα is inactivated, T cells are engineered to allow their proliferation while the TCRα gene is inactivated and where the engineered T cells are then further transformed with a CAR sequence. ('629 Application, Ex. 2004, ¶¶ 15, 16).

Galetto claims 26, 28-30, 32, and 33 are involved in the interference. Claim 26 is illustrative of the involved claims and is as follows:

> 26. An isolated genetically modified human T cell in which a T cell receptor (TCR) alpha gene has been modified by cleavage with a TALEN encoded by electroporated RNAs and integration by homologous recombination into the TCR alpha constant chain region of an exogenous nucleic acid successively comprising:
>
> a first region of homology to sequences upstream of said cleavage with the TALEN, an exogenous polynucleotide sequence encoding a Chimeric Antigen Receptor,
>
> and a second region of homology to sequences downstream of said cleavage with the TALEN,

[9] The claimed invention also includes a requirement for modification of the CD52 gene to make the T cells resistant to immunosuppressive drugs, administered to prevent a patient from rejecting donor T cells. (Fry Declaration, Ex. 2003, ¶ 58; '629 Application, Ex. 2004, ¶ 7). This limitation is not the subject of the parties' dispute.

wherein the Chimeric Antigen Receptor comprises a binding domain against a tumor antigen present on a target cell,

wherein the cell expresses the Chimeric Antigen Receptor, and

wherein the integration by homologous recombination results in reduced TCR expression on the cell surface,

wherein the integration by homologous recombination into the TCR alpha constant chain region is at a position within the sequence: TTGTCCCACA GATATCCAGACCCTGACCC TGCCGTGTAC CAGCTGAGA (SEQ ID NO: 37), wherein the TALEN is encoded by RNAs having the nucleotide sequences of SEQ ID NO:49 and SEQ ID NO: 50; and

wherein the CD52 gene in the cell has been modified by cleavage with a TALEN at a position within the sequence: TTCCTCCTAC TCACCATCAG CCTCCTGGTTATGGTACAGG TAAGAGCAA (SEQ ID NO: 40), wherein the TALEN is encoded by RNAs having the nucleotide sequences of SEQ ID NO:55 and SEQ ID NO:56.

(Galetto Clean Copy of Claims, Paper 7, relevant portions underlined; Fry Declaration, Ex. 2003 ¶¶ 72-77).

Claims 28-30 depend from claim 26 and therefore also require that the CAR sequence is integrated into the TCRα constant region gene by HR. Claims 32 and 33 are independent claims.

Like claim 26, claim 32 requires "an exogenous polynucleotide sequence encoding a Chimeric Antigen Receptor inserted into the T cell receptor (TCR) alpha constant chain region … by … integration by homologous recombination into the TCR alpha constant chain region…." resulting in "reduced TCR expression on the cell surface when compared to normal T lymphocytes." (Galetto Clean Copy of Claims, Paper 7; Fry Declaration, Ex. 2003 ¶ 79).

Claim 33 requires "a polynucleotide expressing a Chimeric Antigen Receptor (CAR); wherein … integration of the polynucleotide expressing the CAR

into the TCR alpha gene inactivates the TCR alpha gene". (Galetto Clean Copy of Claims, Paper 7; Fry Declaration, Ex. 2003 ¶ 80). Claim 33 differs from the other claims in that it does not contain language requiring integration of the polynucleotide expressing the CAR to be "by homologous combination."

Summary of parties' positions

Jantz asserts, and Galetto does not dispute, that the involved Galetto claims require "genetically modified human T cells wherein the endogenous T cell receptor alpha constant region gene ("TCRα gene") is inactivated by integrating, via homologous recombination ("HR"), a sequence encoding a chimeric antigen receptor ("CAR sequence") into the TCRα gene." (Jantz Motion 3, Paper 96, 1:13-16; Galetto Opposition 3, Paper 176, 2:11-14). While Jantz concedes that the '629 specification discloses (i) "a T cell having an inactivated TCRα gene" and (ii) "integrating an exogenous DNA encoding a CAR into these T cells", Jantz argues that there is no description within the '629 specification of integrating a CAR by HR into the TCRα gene specifically with the resulting inactivation of the gene. (Jantz Reply 3, Paper 193, 1:22-2:7). Thus the parties dispute centers around whether the '629 specification provides written description of that portion of the Galetto involved claims requiring modified T cells having a CAR sequence that is integrated specifically into the TCRα gene by homologous recombination thus inactivating the gene. ("contested limitation"). (Fry Declaration, Ex. 2003, ¶ 96).[10]

As discussed in the Jantz motion, on July 6, 2018, one day after filing its involved '629 application, Galetto filed a paper requesting an interference with, *inter alia*, five of the six Jantz involved patents. In that request Galetto cancelled

[10] As discussed further below, claim 33 does not contain an express requirement that the CAR to be integrated via HR.

its previous claims and presented new claims, including the currently involved claims, that appear to be substantially the same as, but not identical to, claim 1 of Jantz involved patent 9,969,975. (Galetto Amendment and Suggestion of Interference, Ex. 2012, 6, 8).

The new claims were rejected for lacking written description of the "specific concept of inserting an exogenous CAR coding sequence into the TCR alpha gene, particularly the TCR alpha constant region." (Examiner Action, Ex. 2013, 2). While the claims were later amended, a requirement that a CAR sequence be integrated into the TCRα gene remained. (Galetto Amendment, Ex. 2014, 2-5).

The Examiner initially maintained the position that the new claims lacked written description, but then later withdrew the rejection and allowed all the claims of the '629 application (Examiner's Action, Ex. 2015, 7; Office Action dated August 09, 2019).

Jantz asserts that the Examiner was correct in rejecting Galetto's copied claims for not having written description support for the concept of inserting a CAR coding sequence into the TCRα gene, particularly the TCR alpha constant region at the cleavage site that inactivates the TCRα gene. Jantz urges that it disagrees with Galetto's position, taken during ex parte prosecution of the '629 application, that "a CAR and pTalpha are two interchangeable species" and that therefore paragraphs 103 ("¶ 103") and 124 ("¶ 124") of the Galetto specification considered together provide sufficient description. (Jantz Motion 3, Paper 96, 2:5-7; Galetto Amendment and Response, Ex. 2020, 7).

Jantz argues that, because a CAR and pTα are not two interchangeable species for the purposes of paragraph 124, one skilled in the art would not have read paragraphs 103 and 124 together nor have understood these paragraphs to disclose the concept of inserting a CAR coding sequence into the TCRα inactivating the TCRα gene. (Jantz Motion 3, Paper 96, 2:8-3:3, citing Galetto

Amendment and Response filed July 26, 2019, Ex. 2013, 2). Further, Jantz argues, nowhere else does the '629 specification provide descriptive support for the concept such that one skilled in the art would have understood Galetto to have possessed invention of the Galetto involved claims. (Jantz Motion 3, Paper 96, 3:4-4:5; 20:11-13).

Galetto argues that its involved specification describes the claimed invention and specifically that portion in dispute. According to Galetto its specification describes genetically modified human T cells where the T cell's TCRα gene is inactivated by integrating, using HR, a sequence encoding a CAR into the TCRα gene and as required by the Galetto involved claims. (Galetto Opposition 3, Paper176, 3:1-5). Galetto argues that sufficient description is provided where its specification discusses introducing an exogenous sequence encoding at least one recombinant protein of interest into the TCRα gene. According to Galetto, one skilled in the art would have understood that a "recombinant protein of interest" referred to in the '629 specification could be a CAR given the disclosure of CAR as a protein of interest and the numerous references to CARs elsewhere within the Galetto specification. (Galetto Opposition, Paper 176, 6:23-7:15, citing Osborn Declaration, Ex. 1041, ¶¶ 35, 37, 38; Fry Deposition, Ex. 1040, 21:12-22; '629 application, ¶¶ 102, 118).

Galetto argues that the '629 specification also describes that the genome modification of a T cell can be performed through homologous recombination such that one skilled in the art would have understood that an exogenous polynucleotide sequence could be introduced through homologous recombination into the TCRα gene. (Galetto Opposition, Paper 176, 7:17-20, citing Osborn Declaration, Ex. 1041, ¶¶ 39, 40).

Summary of Decision

We find that the '629 specification does not provide sufficient "blaze marks" pointing to integrating a CAR sequence into the TCRα gene leading to inactivation of the gene. While individual elements of the contested limitation can be found within the '629 specification, we find, based on the evidence before us, that one skilled in the art would not have been led to a modified T cell having a CAR sequence that is integrated specifically into the TCRα gene thus inactivating the TCRα.

Legal Principles

We give claims their broadest reasonable interpretation by considering not only the claim language but also how one skilled in the art would understand the claim in view of the specification. *Phillips v. AWH*, 415 F.3d 1303, 1316, (Fed. Cir. 2005). As explained in *Agilent Techs., Inc. v. Affymetrix, Inc.*, claims copied from another are construed in view of the originating specification for purposes of evaluating written description support. *Agilent v. Affymetrix, Inc.,* 567 F.3d 1366, 1375 (Fed. Cir. 2009). In the present circumstances there appears to be no dispute that Galetto presented claims in the '629 application that are substantially the same as, but not identical to, Jantz patent claims. (Galetto Amendment and Suggestion of Interference, Ex. 2012, 7, 8).[11] To the extent we must construe Galetto the Galetto involved claims in view of the Jantz patent specification, such construction does not appear to result in any meaningful difference in how the claim terms are construed. The parties do not argue that the construction of the Galetto involved claims differs according to which of the parties' specifications is consulted.

[11] In the Request Galetto stated that claim 26 of the '629 application is substantially the same as claim 1 of Jantz patent 9,969,975.

In evaluating written description we consider whether the disclosure of the application reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date. *Vas–Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1562–63 (Fed.Cir.1991). Thus one skilled in the art, reading the original disclosure, must "immediately discern the limitation at issue." *Waldemar Link GmbH & Co. v. Osteonics Corp*., 32 F.3d 556, 558, Fed.Cir.1994).

In haec verba support is not necessary. *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1570, (Fed. Cir. 1996). Whether the inventor has provided adequate written description, either explicitly or inherently, must be determined from the disclosure considered as a whole. *Reiffin v. Microsoft Corp*., 214 F.3d 1342 (1346 Fed. Cir. 2000).

The written description issue requires we consider the perspective of a person of ordinary skill in the art with the understanding that "the level of detail required ... varies depending on the nature and scope of the claims and on the complexity and predictability of the relevant technology." *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010). We therefore consider whether the technology involved is unpredictable in determining whether the claims are sufficiently described. *Capon v. Eshhar*, 418 F.3d 1349, 1359 (Fed. Cir. 2005). ("It is well recognized that in the 'unpredictable' fields of science, it is appropriate to recognize the variability in the science in determining the scope of the coverage to which the inventor is entitled. Such a decision usually focuses on the exemplification in the specification.").

Where a claimed invention is not disclosed with specificity in the underlying specification, we look to see if there are "sufficient 'blaze marks' to guide a reader through the forest of disclosed possibilities" to the specifically claimed invention. *Novozymes A/S v. DuPont Nutrition Biosciences,* 723 F.3d 1336, 1346 (Fed. Cir. 2013), citing *In re Ruschig*, 379 F.2d 990, 994-995 (CCPA 1967). A "mere wish

or plan" for obtaining the claimed invention does not satisfy the written description requirement. *Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1566 (Fed.Cir.1997).

"[W]hile the description requirement does not demand any particular form of disclosure… a description that merely renders the invention obvious does not satisfy the requirement, *Ariad*, 698 F.3d 1352, citing *Carnegie Mellon Univ. v. Hoffmann–La Roche Inc*., 541 F.3d 1115, 1122 (Fed. Cir. 2008) and *Lockwood v. Am. Airlines*, 107 F.3d 1565, 1571–72 (Fed.Cir.1997).

Discussion

As the moving party Jantz has the burden of proving it is entitled to the requested relief. To be sufficient, the motion must provide a showing supported with appropriate evidence such that, if unrebutted, it would justify the relief sought. Bd. R. 208(b). We separately discuss those specific portions of the '629 specification pointed out and relied upon by the parties in their briefing. However, we make a determination of whether the claimed invention is sufficiently described by considering the disclosure as a whole. *Reiffin v. Microsoft Corp*., 214 F.3d at 1346.

Jantz directs us to, *inter alia*, the testimony of Dr. Terry Fry to support the arguments made within Jantz Motion 3.[12] Dr. Fry characterizes a hypothetical person of ordinary skill in the art time period as having a Ph.D., M.D. or M.D./Ph.D. with specific training in the areas of molecular biology and immunology or related disciplines with substantial research or industrial experience in adoptive cell therapy for cancer and the use of genetically modified

[12] We have reviewed Dr. Fry's credentials and find Dr. Fry qualified to testify regarding the technical issues discussed in his testimony. (Fry Declaration, Ex. 2003, ¶¶ 5-16; Fry *Curriculum vitae* (Appendix A of Ex. 2003)).

T cells for this purpose. (Fry Declaration, Ex. 2003, ¶ 28). A person having ordinary skill in the art is presumed to know the relevant prior art. *In re GPAC*, 57 F.3d 1573, 1579 (Fed. Cir. 1995). Galetto does not dispute Dr. Fry's characterization of such a person and we find that such a person may have the education and experiences that Dr. Fry lists in his testimony.

Dr. Fry testified that "T cell gene editing for immunotherapy remains a highly unpredictable field" (Fry Declaration, Ex. 2003, ¶¶ 127, 128, citing, e.g., Sather[13] as describing specific challenges associated with the development and optimization of targeted integration into the T cell genome").

Jantz argues that the Galetto claim requires a modified T cell that results from a single step modification, i.e., where a CAR sequence is integrated specifically into the TCRα gene such that it is inactivated. (Jantz Motion 3, Paper 96, 3:8-14; 20:16-21:2; Fry Declaration, Ex. 2003, ¶¶ 68, 73, 96). Jantz acknowledges that the '629 specification discloses inactivating four genes, of which the TCRα gene is one option, including by HR. However, Jantz argues the specification does not describe using a CAR for this purpose but only a general and undisclosed sequence. (Jantz Motion 3, Paper 96, 21:15-23:3).

Jantz urges that, when discussing CAR introduction, the '629 specification discloses two T cell modification steps, one to inactivate the TCRα and a second and separate step, occurring either before or after the first step, to introduce another sequence, e.g., a CAR sequence, either transiently by mRNA or by pseudo-random integration by lentiviral vector (LV). (Jantz Motion 3, Paper 96, 24:9-17, citing '629 Application, Ex. 2004, Figure 5, ¶¶ 268, 301, 202, 203; Fry Declaration, Ex. 2003, ¶107).

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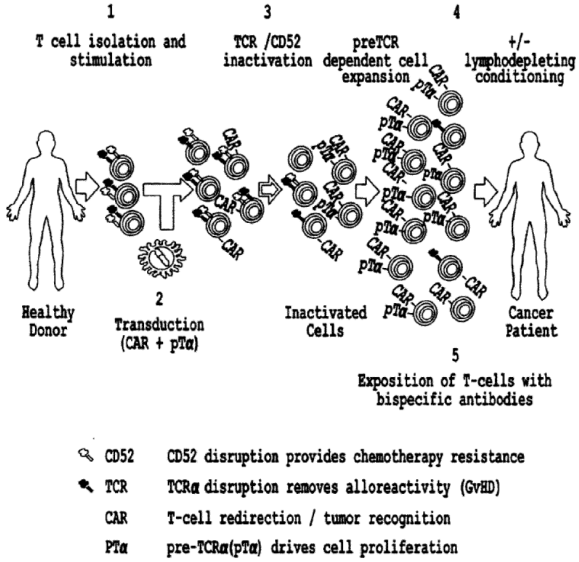
[13] Sather, B.D. et al., Efficient modification of CCR5 in primary human hematopoietic cells using a megaTAL nuclease and AAV donor template. Science Translational Medicine, Vol 7, Iss. 307, pp. 307 (September 2015). (Ex. 2022).

Jantz points to Figure 5 of the ’629 specification, reproduced below, as illustrating both the genetic modification step where a TCR gene is inactivated and the additional genomic modification step where CAR is introduced.



Above is shown Figure 5 of the ’629 disclosure.

As Jantz points out, the five steps of Figure 5 include: (1) “providing T cells,” (2) “a) Transducing said cells with pTalpha … b) Transducing said cells with multi-chain CARs,” (3) “[e]ngineering non alloreactive and immunosuppressive resistant T cells [by] … [inactivating] TCR alpha in said cells to eliminate the TCR from the surface of the cell…,” and inactivating CD52 to create immunosuppressive resistance (4) “[e]xpansion in vitro, and (5) “[o]ptionally expos[ing] said cells with bispecific antibodies in vivo following administration to a patient.” (Jantz Motion 3, Paper 96, 9:4-11, citing, ’629 specification, Ex. 2004 ¶¶ 200-209; Fry Declaration, Ex. 2003 ¶ 64).

As Jantz notes, the genetic modification step is shown as step 3, and includes inactivation of existing genes where one “X” gene (TCRα) and one “Y” gene (CD52) are inactivated by using rare-cutting endonucleases (TALE-

nucleases) to cleave the genes. Jantz points out that an exogenous polynucleotide is not provided in the step, and the inactivation occurs not by HR, but by non-homologous end joining ("NHEJ"), said to be an error-prone cellular repair pathway that results in the insertion or deletion of nucleotides at the cleaved site. (Jantz Motion 3, Paper 96, 10:1-9, citing, '629 specification, Ex. 2004 ¶¶ 204-207; Fry Declaration, Ex. 2003 ¶ 61-65). Dr. Fry testified that NHEJ is incapable of integrating sequences, such as CAR, into a genome. (Fry Declaration, Ex. 2003 ¶ 120).

Jantz points to the additional genomic modification step as being shown in step 2, and as including the introduction of new genes where a CAR sequence and pTα sequence are introduced by way of "transduction" with lentiviral vectors that randomly integrate the new genes into the genome. Jantz notes that the specification states that CAR transduction can be "before or after" TCRα and CD52 inactivation and is identified as an "additional genomic modification step," and shown as a separate step that does not occur simultaneously with "the genetic modification step." (Jantz Motion 3, Paper 96, 10:10-16, citing, '629 specification, Ex. 2004 ¶¶ 202, 203; Fry Declaration, Ex. 2003 ¶ 64, 66, 68).

Jantz addresses those portions of the '629 specification that Galetto argued, during ex parte prosecution, support the contested limitation. In particular, Galetto argued that paragraphs 103 and 124 of the '629 specification, when considered together, provide written description support for this limitation.

Paragraphs 103 and 124

We reproduce paragraph 103 below and include the preceding paragraphs for context.

> [0100] By additional genomic modification step, can be intended also the inactivation of another gene selected from the group

> consisting of CD52, GR, TCR alpha and TCR beta. [sic] As mentioned above, said additional genomic modification step can be an inactivation step comprising:
>
> [0101] (a) introducing into said cells at least one rare-cutting endonuclease such that said rare-cutting endonuclease specifically catalyzes cleavage in one targeted sequence of the genome of said cell.
>
> [0102] (b) Optionally introducing into said cells a exogenous nucleic acid successively comprising a first region of homology to sequences upstream of said cleavage, a sequence to be inserted in the genome of said cell and a second region of homology to sequences downstream of said cleavage,
>
> wherein said introduced exogenous nucleic acid inactivates a gene and integrates at least one exogenous polynucleotide sequence encoding at least one recombinant protein of interest. In another embodiment, said exogenous polynucleotide sequence is integrated within a gene selected from the group consisting of CD52, GR, TCR alpha and TCR beta.
>
> [0103] In particular embodiment said method to engineer cell *further comprises an additional genomic modification step*. By additional genomic modification step, can be intended the introduction into cells to engineer of one protein of interest. [sic] Said protein of interest can be, as non limiting examples, pTalpha or functional variant thereof, a Chimeric Antigen Receptor (CAR), a multi-chain CAR, a bispecific antibody or rare-cutting endonuclease targeting PDCD1 or CTLA-4 as described in the present disclosure.

('629 specification, Ex. 2004, ¶¶100-103, emphasis added).

Paragraph 103 of the '629 specification refers to a method that "further comprises an additional genomic modification step" in engineering a T cell. ('629 Application, Ex. 2004 ¶ 103; Fry Declaration, Ex. 2003 ¶ 101). This

paragraph does not describe integrating a CAR as the exogenous nucleic acid in the process described at paragraphs 100-102 but indicates that a CAR sequence, for example, may be introduced in a further additional step. Nor does the paragraph specify that the listed proteins of interest in paragraph 103 are integrated by HR, or other method, into the TCRα gene of the already modified T cell. Thus, we agree with Dr. Fry that "the generic recitation in ¶ 103 of 'the introduction[14] into cells to engineer of one protein of interest' without any additional blaze marks does not fairly suggest to a POSA that any of the listed 'proteins of interest' should be specifically integrated into any gene, let alone the TCRα gene." (Fry Declaration, Ex. 2003, ¶¶ 102-108).

Further, while Jantz acknowledges that paragraph 103 includes a CAR as a "protein of interest", Jantz urges that one skilled in the art would not have considered the list of proteins of interest listed in paragraph 103 to be a list intended for genomic integration and thus are not "interchangeable" in any method of using HR disclosed by the '629 specification, e.g., at paragraph 102. As an example, Jantz asserts, one skilled in the art would not integrate the listed "rare-cutting endonuclease" because its purpose is to be transiently expressed to inactivate another gene and doing so would cause the nuclease to be permanently expressed, causing toxicity from off-target cleavage. (Jantz Motion 3, Paper 96, 16:10-15, citing Fry Declaration, Ex. 2003 ¶ 108).

Paragraph 124 is found within a separate section of the '629 specification having the heading "Pre-Talpha". We reproduce paragraph 124 below and include the preceding paragraphs for context:

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[14] Dr. Fry testified that "introduction" is a broad term that include more than a dozen different methods of expressing a protein in a cell, many of which are incompatible with integration into the genome by HR. (Fry Declaration, Ex. 2003 ¶¶ 102-103).

> [0119] In another aspect, the invention relates to a method of expanding TCR alpha deficient T-cell comprising introducing into said T-cell pTalpha (also named preTCR.alpha.) or a functional variant thereof and expanding said cells, optionally through stimulation of the CD3 complex. In a preferred embodiment, the method comprises:
>
> [0120] a) Transforming said cells with nucleic acid encoding at least a fragment of pTalpha to support CD3 surface expression
>
> [0121] b) Expressing said pTalpha into said cells
>
> [0122] c) Expanding said cells optionally, optionally through stimulation of the CD3 complex.
>
> [0123] The invention also relates to a method of preparing T-cells for immunotherapy comprising steps of the method for expansion for T-cell.
>
> [0124] In particular embodiment, the pTalpha polynucleotide sequence can be introduced randomly or else through homologous recombination,
>
> in particular the insertion could be associated with the inactivation of the TCRalpha gene.

('629 Application, Ex. 2004, ¶119-124).

Paragraph 124 states that pTα may be introduced into TCRα deficient cells "randomly or else through homologous recombination." Paragraph 124 mentions HR but does not mention CAR or otherwise expressly describe integration of a CAR into the TCRα.

As Jantz notes paragraph 124 falls within a broader section of the specification that relates to a method of restoring the expansion capability of TCRα deficient T cells. ('629 Application, Ex. 2004 ¶¶ 119-133; Fry Declaration, Ex. 2003 ¶ 110).

According to Jantz inactivating TCRα in T cells eliminates a means of stimulating T cell expansion and the '629 specification discloses the introduction of the pTα sequence randomly or else through homologous recombination in order

to restore the ability to expand. In particular, according to Jantz, when pTα is introduced to T cells with an inactivated TCRα gene, it combines with the existing TCRβ to form a pre-TCR complex which restores the ability to expand the T cells. Jantz notes that the '629 specification mentions only pTα as being able to accomplish the goal of restoring expansion. Thus, argues Jantz, Galetto's argument during ex parte prosecution that "the skilled artisan would immediately recognize that a CAR and pTα are two interchangeable species of a 'protein of interest' that …can be introduced as an exogenous nucleic acid that integrates and inactivates TCR alpha" is incorrect because a CAR will not enable the formation of pre-TCR complex in TCRα deficient T cells to restore the ability of T cells to expand, the purpose of introducing pTα." (Jantz Motion 3, Paper 96, 17:9-18:6, citing Fry Declaration, Ex. 2003 ¶¶ 110-112; Galetto Amendment and Response, Ex. 2020, 7, 8).

Jantz further notes that paragraph 124 states that the pTα insertion is "in association with" inactivation of TCRα, but argues that "in association with" would be read by one skilled in the art as requiring insertion of pTα anywhere in order to remedy the deficiency associated with inactivating TCRα. Jantz notes that this understanding is consistent with paragraph 129, which describes several examples of how to create "TCR alpha deficient cells", none of which requires integrating pTα specifically into TCRα, or refer to HR. (Jantz Motion 3, Paper 96, 18:7-15, citing Fry Declaration, Ex. 2003, ¶¶ 113-117).

Jantz argues that for this reason one skilled in the art would not have been guided to select CAR from the list found in paragraph 103 and substitute it for the pTα in paragraph 124 to arrive at the claimed invention. Jantz argues that Galetto's arguments before the Examiner improperly relied upon an obviousness rationale, i.e., that it would have been obvious to integrate CAR into TCRα by HR

given paragraphs 103 and 124. (Jantz Motion 3, Paper 96, 18:18-19:1; 20:3-8 citing *Lockwood v. Am. Airlines, Inc*., 107 F.3d 1565, 1572 (Fed. Cir. 1997)).[15]

’629 specification

Jantz argues that the ’629 specification considered in its entirety fails to describe integrating a CAR sequence by HR into the TCRα gene either when discussing CARs specifically, or when CARs are in a list of proteins of interest. Jantz Motion 3, Paper 96, 20:11-13, citing Fry Declaration, Ex. 2003 ¶¶ 118-119). Jantz points out that when the ’629 specification discusses CARs specifically and not within a list, it consistently describes introducing CARs before or after, but not simultaneous with, the step of inactivating genes such as the TCRα gene. (Jantz Motion 3, Paper 96, 20:16-21, citing ’629 Application, Ex. 2004, ¶¶ 203, 268; Fry Declaration, Ex. 2003 ¶¶ 104-106).

Jantz argues that CAR introduction methods, including transient expression of a CAR sequence via electroporation of mRNA or random integration of a CAR sequence via lentiviral transduction, do not inactivate a TCRα gene and thus are described as occurring either before or after such inactivation is caused by some other process. (Jantz Motion 3, Paper 96, 20:21-25, citing ’629 Application, Ex. 2004, ¶¶ 163, 220, 301; Fry Declaration, Ex. 2003 ¶¶ 104-106). Jantz argues that since the ’629 specification discloses introducing a CAR “before or after” inactivation and does not use the term “during”, a person skilled in the art would have understood that it was not in possession of a single genetic modification step that would result in T cells having the contested limitation.

[15] Jantz does not agree that the invention found in Galetto involved claims would have been obvious in view the ’629 specification. (Jantz Motion 3, Paper 96, 18:18-20)

As pointed out by Jantz, the ’629 disclosure provides two illustrations of introducing a CAR to a T cell and both use transient introduction of a CAR sequence, not HR. (Jantz Motion 3, Paper 96, 24:9-15). One is shown at Figure 5, discussed above, and the other at Figure 2. Figure 2 is reproduced below.

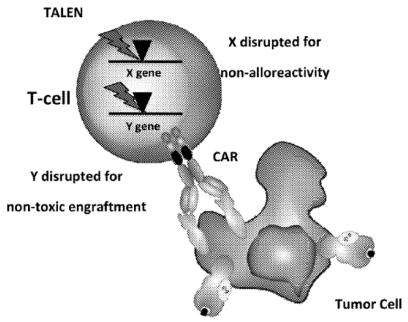

Figure 2

Above is shown Figure 2 of the ’629 disclosure.

Figure 2 is identified in the ’629 specification as a “[s]chematic representation of the genetically modified therapeutic T-cells according to the invention and the patient's tumor cells.” (’629 Application, Ex. 2004, ¶ 25). Jantz urges that “[t]he core concept of the invention is shown in Figure 2, which depicts the use of rare-cutting endonucleases called TALENs or TALE-nucleases to cut an “X” gene that is “disrupted for non-alloreactivity” (eliminating alloreactivity or GvHD associated with a donor’s TCR) and a “Y” gene that is “disrupted for non-toxic engraftment” (increasing resistance to immunosuppressive drugs used to deplete host T cells)”. (Jantz Motion 3, Paper 96, 7:19-24, citing ‘629 Application, Ex. 2004 ¶21, 192, Fig. 2). According to Jantz, the ’629 specification discloses “inactivating an “X” gene and a “Y” gene as “the genetic modification step” and identifies TCRα as one of four “X” genes and CD52 as one of two “Y” genes, that can be inactivated by use of the TALEN by HR or NHEJ. (’629 specification,

Ex. 2004 ¶¶ 68-99; Fry Declaration, Ex. 2003 ¶ 61). Jantz asserts that the CAR shown in Figure 2 is introduced in a separate, optional "additional genomic modification step", not through the use of HR, and after the T cell has been modified. (Jantz Motion 3, Paper 96, 8:8-8:14).

Dr. Fry testified that the method shown in the two working examples of introducing a CAR into a T cell use mRNA which results only in transient introduction of the CAR and cannot integrate the CAR sequence into TCRα gene to cause TCR inactivation. (Jantz Motion 3, Paper 96, 24:9-17; Fry Declaration, Ex. 2003, ¶¶ 38, 105,107; '629 Application, Ex. 2004 ¶¶ 268, 301). While an applicant need not provide an example to have written description, an example may indicate possession of the claimed invention. *Falkner v. Inglis*, 448 F.3d 1357, 1366 (Fed. Cir. 2006). We agree with Jantz that these working examples, considered in view of the explanation and context of the '629 specification, do not show possession of the contested limitation.

As noted above, claim 33 differs from the other claims because it does not contain language requiring integration of the CAR polynucleotide to be by HR. Like the other Galetto involved claims, claim 33 requires that the CAR polynucleotide be integrated into the TCRα gene specifically. Jantz argues, and Dr. Fry testified, that the '629 specification does not describe the integration into the TCRα gene specifically. Jantz argues, and Dr. Fry's testimony supports the argument, that the only methods disclosed in the '629 specification for introduction of a CAR specifically cannot result in integration of a CAR into a TCRα gene. (Jantz Motion 3, Paper 96, 24:9-17, citing Fry Declaration, Ex. 2003, ¶¶ 38, 105,107; '629 Application, ¶¶ 202-203, 268, 301).

Jantz argues that, for the reasons it provides, and as in *Novozymes*, the '629 specification provides insufficient "blaze marks" because it "provide[s] formal textual support for each individual limitation recited in the claims [at

issue]," but "never presented [those limitations] together." (Jantz Motion 3, Paper 96, 19:6-17, citing *Novozymes*, 723 F.3d at 341).

Galetto Opposition.

In its Opposition 3, Galetto argues that the '629 specification identifies CAR as a particular protein of interest and one skilled in the art would have understood that CAR could have been used as an exogenous nucleotide in a single genetic modification step to arrive at the claimed T cells. As Galetto notes, Jantz does not dispute that the '629 specification discloses T cells having an inactivated TCRα gene nor that the '629 specification describes introduction of DNA encoding a CAR into these modified T cells. Jantz also agrees that CAR is said to be generally "a protein of interest" in portions of the '629 specification. (Jantz Reply 3, Paper 193, 1:22-2:23; citing Fry Deposition, Ex. 1040, 22:22-23:13, 65:23-66:3). Galetto argues that, in view of these disclosures and within the context of the entire '629 specification, the necessary blaze marks would have guided one skilled in the art to the claimed invention.

In support of its position, Galetto directs us to the testimony of Dr. Mark Osborn. We have reviewed Dr. Osborn's credentials and find Dr. Osborn qualified to testify regarding the technical issues discussed in his testimony. (Osborn Declaration, Ex. 1041; Osborn *Curriculum vitae.* Ex. 1043).

Dr. Osborn testified that "[s]ince polynucleotides encoding a CAR are described in the Galetto application, the skilled artisan would have further understood that the integration of a polynucleotide encoding a CAR into TCRα by homologous recombination could inactivate the TCRα gene." (Osborn Declaration, Ex. 1041, ¶ 63). Even accepting this testimony, a description in the '629 specification of a polynucleotide encoding CAR does not amount to description sufficient to show possession of the claimed modified T cells.

Dr. Osborn's testimony on this point may be relevant to obviousness under 35 U.S.C. § 103 in that it addresses what one skilled in the art might be motivated to do or try in view of the '629 specification. Dr. Osborn agreed that it is his opinion that it would have been obvious how to get to a disclosure of a CAR integrated into the TCRα from reading the '629 specification. (Osborn Deposition, Ex. 2070, 132:18-134:5-14). However, obviousness is not the issue before us. *Lockwood*, 107 F.3d at 1571–72.

We turn to the specific portions of the '629 specification that Galetto argues support the Galetto involved claims and in particular the contested limitation.

As we discussed above the proteins of interest recited in paragraph 103 are recited only in connection with the further "additional genomic modification step" in which a protein is introduced into the modified cell, but not in connection with inactivating the TCRα gene as described in paragraph 102. Regarding paragraph 103, Dr. Osborn asserts there are known techniques for accomplishing simultaneous inactivation and modification, but agrees that paragraph 103 describes a separate action from the inactivation described in paragraph 102. (Osborn Deposition, Ex. 2070, 168:12-169:11).

Both Dr. Fry and Dr. Osborn seem to agree that the proteins of interest listed in paragraph 103, which include rare-cutting endonucleases, are of a different character than the exogenous nucleic acid to be integrated into the T cell genome referred to in paragraph 102. For example, Dr. Osborn's testimony indicates that he considers inactivation of PDCD1 or CTLA-4 to be genomic modifications intended in paragraph 103 and that the listed rare-cutting endonucleases are the means for producing those genomic modifications, and they do so without integration. (Osborn Deposition, Ex. 2070, 103:14-109:20). Dr. Fry and Dr. Osborn also seem to also agree that integrating a rare-cutting endonuclease into the genome would not be logical given its function. (*See*, *e.g.,* Fry Declaration,

Ex. 2003, ¶ 108; Fry Deposition, Ex. 1040, 61:8-62:24, 65:23-66:3 ("The proteins of interest that are included in the description of 103 include the rare cutting endonuclease, and it would be, in my opinion, an odd protein that one would want to stably introduce into a cell."); Osborn Deposition, Ex. 2070, 46:2-7 ("So the specific question is, why don't you integrate an endonuclease into a cell? ... I think that, depending on specificity, you would have a potential concern for any off-target activity") and 108:16-109:20).

Based on the evidence before us, we agree with Jantz that one skilled in the art would have known not to integrate a rare-cutting endonucleases to inactivate the TCRα gene because these enzymes could continue their cutting function increasing the risk of off-target cutting. (Jantz Motion 3, Paper 96, 23:12-24:6). It follows that one skilled in the art would not have understood the unidentified proteins or sequences of interest of paragraph 102, as well as those similarly discussed in paragraphs 98, 99 and 118, to be the same proteins of interest listed in paragraph 103 which includes, *inter alia*, rare-cutting endonucleases.

Turning to paragraph 124, pTα is the only protein described as useful for the expansion method found in paragraph 124. Galetto does not direct us to convincing evidence or argument that one skilled in the art would have understood CAR to be an appropriate substitution for pTα that is used for the expansion method or that the paragraph 124 describes integrating pTα specifically into the TCRα gene. (Galetto Opposition 3, Paper 176, 7:21-8:22; 9:3-13). Thus, we agree with Jantz that this portion of the '629 considered in the context of the '629 specification as a whole, does not describe the contested limitation.

Galetto points to other portions of the '629 specification that it urges would have guided one skilled in the art to the claimed invention, including portions at paragraphs 98, 99, and 118. (Galetto Opposition 3, Paper 176, 9:3-13; 10:8-11:14, citing Osborn Declaration, Ex. 1041, ¶¶ 57-64). Each portion discloses

inactivating any one of four genes by HR, including TCRα, but does not identify what exogenous sequence is to be used to affect inactivation. Galetto argues that these portions encompass the possibility of "knock-ins" of the TCRα gene, i.e., the introduction of new sequences or genes of interest. What is lacking though is guidance to select CAR as the sequence for the "knock-in" ('629 specification, Ex. 2004, ¶¶ 98, 99, 103, 118). We agree with Jantz that the '629 specification "never presented [the limitations of Galetto's involved claims] together in any particular embodiment," nor did the application provide sufficient "blaze marks" to guide one toward the claimed combination among a "slew of competing possibilities." (Jantz Reply 3, Paper 193, 8:8-16, citing *Novozymes*, 723 F.3d at 1351).

Galetto argues, and Dr. Osborn testified, that the '629 specification provides "blaze marks [that] point directly to a CAR as a protein of interest for introduction into a TCRα-inactivated cell", citing for example, Figures 2 and 5 (Galetto Opposition 3, Paper 176, 9:21-22, 17:10-18:8, citing Osborn Declaration, Ex 1041, ¶¶ 50-54). As discussed above, these Figures, while showing CAR as a protein of interest, further support that the CAR sequence is introduced in a step separate, either before or after, TCRα is inactivated. Dr. Osborn agreed that "introduction" of CAR within the '629 specification could point to introduction of the CAR sequence into TCRα that was already inactivated. (Osborn Deposition, Ex. 2070, 163:8-17; 90:20-91:5, 93:18-94:6). Dr. Fry, while acknowledging CAR as a protein of interest, testified that the '629 specification did not suggest a CAR sequence integrated into the TCRα gene. (Fry Deposition, Ex. 1040, 22:22-23:13, 65:23-66:3).

The description of introducing a CAR "before or after" TCRα inactivation in relation to the Figures, as discussed above, would not lead one toward integrating a CAR sequence "during" TCRα inactivation. Thus these Figures, in the context and

explanation provided by the ’629 specification, do not describe the contested limitation.

Galetto argues that “nowhere does Galetto’s application indicate that [HR] should NOT be used with a CAR.” (Galetto Opposition 3, Paper 176, 11:15-12:2. We do not find this argument convincing. Galetto does not explain, and it is not apparent to us, why one skilled in the art would have “immediately discerned” that HR was to be used simply because Galetto did not expressly exclude the method.

Galetto argues that the portion of the ’629 specification found at paragraphs 219 and 220 disclose non-integrative lentiviral vectors that could integrate into a genome through HR. (Galetto Opposition, Paper 176, 11:15-12:21). Dr. Osborn concedes though that paragraph 219 does not disclose integrating a CAR into TCRα gene. (Osborn Deposition, Ex. 2070, 189:10-190:7).

As Jantz notes, the only methods disclosed in the ’629 specification for introduction of a CAR specifically cannot result in integration of CAR into a TCRα gene. (Jantz Motion 3, Paper 96, 24:9-17, citing Fry Declaration, Ex. 2003, ¶¶ 38, 105,107; ’629 Application, ¶¶ 202-203, 268, 301). Accordingly, we do not find these portions, when considered in the context of the ’629 specification as a whole, to describe integrating a CAR into the TCRα gene as required by the Galetto involved claims.

Galetto does not separately present arguments directed to either independent claim 32 or 33. Like the other involved Galetto claims, both claims 32 and 33 require integrating a CAR into the TCRα gene specifically. Claim 32 contains language specifying that integration is through HR but claim 33 does not. Jantz argues that the ‘629 specification “never discloses or suggests- [] any description of a CAR sequence integrated specifically into the TCRα gene.” (Jantz Reply 3, Paper 193, 2:6-7). Dr. Fry testified that none of the ’629 methods where CAR introduction is discussed specifically would result in the required specific

integration. (Jantz Motion 3, Paper 96, 24:9-17, citing Fry Declaration, Ex. 2003, ¶¶ 38, 105, 107; '629 Application, ¶¶ 202-203, 268, 301). Galetto does not dispute that these methods would not result in the specific integration required by its claims. We agree with Jantz that the requirement for specific integration, found in both claims 32 and 33, is not described.

Galetto argues that Dr. Fry came to the "wrong conclusion" because he did not know the legal significance of the phrase "blaze marks." (Galetto Opposition 3, Paper 176, 16:7-22, citing Fry Deposition, Ex. 1040, 59:14-23). Galetto does not contend that Dr. Fry's testimony is based on a misunderstanding of the law, or otherwise explain why we should not credit his testimony based on his unfamiliarity with this particular phrase. Dr. Fry's testimony indicates that he based his testimony upon an adequate understanding of the written description issue. (Fry Declaration, Ex. 2003, ¶¶ 22-25).

As Galetto notes, Jantz points to references by a Galetto inventor to Jantz's work of "inactivating the TCRα gene by integrating a CAR sequence by HR into that gene" in a Galetto patent application as well as a scientific article. Jantz argues that this crediting of Jantz amounts to an acknowledgement that Jantz was the first to invent the claimed subject matter. (Jantz Motion 3, Paper 96, 12:1-22). We agree with Galetto though that these references to Jantz's work have no bearing on whether Galetto's involved application provides adequate written description. (Galetto Opposition 3, Paper 176, 18:18-19:4).

We find that Jantz has met its burden of showing a lack of written description for the contested limitation. We note that much of the testimony before us is in agreement. The disagreement appears to lie, primarily, in whether the '629 specification provided sufficient guidance or blaze marks to direct one skilled in the art to what is claimed. Here, where there is conflict between Dr. Fry's and Dr. Osborn's testimony, we credit the testimony of Dr. Fry over that

of Dr. Osborn. We find that the testimony of the latter relies more on what the '629 application might have suggested to one skilled in the art than what was conveyed to have been in the possession of the inventors, and give it less weight accordingly.

The evidence before us is convincing to show that one skilled in the art would have understood the '629 specification to disclose CAR introduction as a "further" additional step that occurs separate from the TCR inactivation step. While it could have done so, the '629 specification does not identify the exogenous nucleic acid sequence that may be used in the inactivation step as a CAR instead only identifying CAR specifically as one option to be used in further modifying T cells where the TCRα or other gene has already been, or later would be, inactivated. The individual components of the limitation can be found within the '629 specification and one may have been able to piece together what is now claimed but lacking is sufficient guidance to show that the inventors possessed what is claimed. "Were we to extend *Ruschig* 's metaphor to this case, we would say that it is easy to bypass a tree in the forest, even one that lies close to the trail, unless the point at which one must leave the trail to find the tree is well marked." *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571 (Fed. Cir. 1996).

In a separate portion of its Motion 3, Jantz argues that the Galetto claim is unpatententable "for the independent reason that the '629 Application does not teach a POSA how to integrate a CAR sequence into the TCRα gene." (Jantz Motion 3, Paper 96, 25:4-21).

Galetto relies upon the testimony of Dr. Pietro Genovese[16] only in the portion of its briefing addressing this argument. (Galetto Opposition 3, Paper 176,

[16] We have reviewed Dr. Genovese's credentials and find Dr. Genovese qualified to testify regarding the technical issues discussed in his testimony.

21:25-25:2, citing Genovese Declaration, Ex. 1042; *Genvoves Curriculum Vitae.* Ex. 1044). As explained below, we do not find it necessary to consider this argument or to consider Dr. Genovese's testimony addressing it to decide the motion before us. However, we have considered Dr. Genovese's testimony to the extent it is relevant to the predictability of the technology involved. Dr. Genovese testified that it is his opinion that, e.g., vectors and methods provided by experimental results known in the art could readily be modified for inserting a CAR to an endogenous TCR gene. (Genovese Declaration, Ex. 1042, ¶ 33).

As we noted above, Dr. Fry testified that "T cell gene editing for immunotherapy remains a highly unpredictable field." (Fry Declaration, Ex. 2003, ¶¶ 127, 128). Dr. Fry later modified his testimony to acknowledge that investigators had achieved targeted integration in T cells earlier than his initial testimony had indicated. (Galetto Opposition 3, Paper 176, 20:27-36, citing Fry Deposition, Ex. 1040, 66:12-67:2). Dr. Fry went on to testify that, while there was mention of integrating into T cells in some earlier publications, this fact "certainly does not change the challenges associated with modifying primary cells" and did not change his opinion regarding written description. (Fry Deposition, Ex. 1040, 67:14-68:8).

As discussed above we find that the '629 specification does not describe the integration of a CAR sequence into the TCRα gene. Accordingly we need not, and do not, consider this "independent reason." Further our decision would not change even accepting Galetto's position that "[w]hen the scientific and technological knowledge available at that time is appropriately considered, the POSA would have known how to integrate a CAR sequence into the TCRα gene by HR", since we find that the claimed invention does not appear in the specification regardless of whether one of skill in the art could make the claimed invention. (Galetto Opposition 3, Paper 176, 19:18-20) *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598

F.3d at 1348 ("In either case the analysis compares the claims with the invention disclosed in the specification, and if the claimed invention does not appear in the specification….the claim…fails regardless whether one of skill in the art could make or use the claimed invention.")

We GRANT Jantz Motion 3.

As noted above, Jantz Motion 3 presents a threshold issue under Bd. R. 201. Because we grant Jantz Motion 3 and find the Galetto claim to lack written description support, Galetto lacks standing to continue in this interference.

B. Remaining Motions

Jantz filed two additional motions as did Galetto.

Jantz Motion 2 challenges the benefit accorded to Galetto in the declaration of the interference. (Jantz Motion 2, Paper 95). Jantz also filed a miscellaneous motion seeking exclusion of certain evidence. (Jantz Motion 5, Paper 204).

Galetto Motion 1 seeks judgment against Jantz on the basis that all the involved Jantz claims are unpatentable for failure to comply with the written description requirement of the first paragraph of 35 U.S.C. §112. (Galetto Motion 1, Paper 24). Galetto Motion 2 seeks judgment against Jantz on the basis that all the involved Jantz claims are unpatentable for failure to comply with the second first paragraph of 35 U.S.C. §112. (Galetto Motion 2, Paper 25).

1. Galetto Motion 1

Galetto argues that we also should consider its Motion 1 as a threshold motion. (Galetto Motion 1, Paper 24, 1:20-23). Galetto Motion 1 seeks judgment against Jantz on the basis that the Jantz claims lack written description support.

A threshold issue is an issue that, if resolved in favor of the movant, would deprive the opponent of standing in the interference. Threshold issues may

include, but are not expressly limited to, "in the case of an involved application claim first made after the publication of the movant's application or the movant's patent…..unpatentability for lack of written description under 35 U.S.C. 112(a) of the involved application claim where the applicant suggested, or could have suggested, an interference under" Bd. R. 202(a). Bd. R. 201.[17] Addressing this threshold issue requires a determination of whether a party presenting a claim that interferes with a claim of an already published application or patent has adequate basis to challenge priority of invention, a question that turns on whether that party's specification adequately supports subject matter that was first claimed by another party. *Cf. Agilent Techs., Inc. v. Affymetrix, Inc*, 567 F.3d at 1375 (Fed. Cir. 2009), citing *Rowe v. Dror*, 112 F.3d 474, 479 (Fed. Cir. 1997).

Galetto concedes that its Motion 1 does not "directly fall[] within the explicitly described 'threshold issues,'" of Bd. R. 201. However, Galetto urges that its motion "should be included with such issues due to the pre- and post-AIA status of Galetto's application and Jantz's involved patents, respectively". In particular, Galetto urges that Jantz could not have requested an interference due to its post AIA status and, given this restriction, we should consider the Galetto motion to raise a threshold issue. (Galetto Motion 1, Paper 24, 1:16-23).

Regardless of whether or not Jantz could have properly suggested interference,[18] it was Galetto that substantially copied Jantz patent claims and requested the interference. Thus we consider whether Galetto had adequate support for the subject matter that was first claimed by Jantz to see if Galetto has

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[17] Bd. R. 201 does not limit threshold issues to those listed.

[18] It would seem that Jantz would have had no reason to do so until it was aware Galetto had presented interfering claims in the '629 application. The '629 application did not publish until December 20, 2018, well after all the Jantz patents had issued.

standing to contest priority of invention. *Agilent Techs,* 567 F.3d at 1375 (Fed. Cir. 2009). Galetto does not provide a convincing reason why Jantz, who first claimed the interfering subject matter, should be deprived of standing to contest priority of invention even were we to grant Galetto Motion 1.

Because our grant of Jantz Motion 3 deprives Galetto of standing and Galetto has not shown that its Motion 1 raises a threshold issue, we do not further consider Galetto Motion 1. We DISMISS as moot Galetto Motion 1.

2. Jantz Motion 2 and Galetto Motion and 2

Jantz Motion 2 challenges the benefit accorded to Galetto in the declaration of the interference. (Jantz Motion 2, Paper 95). Galetto Motion 2 seeks judgment against Jantz on the basis that all the involved Jantz claims are unpatentable for failure to comply with the second first paragraph of 35 U.S.C. §112. (Galetto Motion 2, Paper 25).

Because we grant Jantz Motion 3 and find the Galetto involved claims to lack written description support, Galetto lacks standing to continue in this interference. Bd. R. 201. We need not, and do not, consider Jantz Motion 2 or Galetto Motion 2.

We DISMISS these motions as moot.

3. Jantz Motion 5

In its Motion 5, Jantz moves to exclude certain testimonial evidence Galetto relies upon in Galetto Motions 1 and 2. (Jantz Motion 5, Paper 204). Because we need not, and do not, consider Galetto Motions 1 and 2, we need not, and do not, consider Jantz Motion 5 nor the evidence cited in the motion.

We DISMISS Jantz Motion 5 as moot.

C. Conclusion

Because we grant Jantz Motion 3 and find the Galetto claim to lack written description support, Galetto lacks standing to continue in this interference. Bd. R. 201. Accordingly, we enter judgment against Galetto in a separate paper and do not consider, except to the extent discussed in this decision, the remaining motions filed by the parties.

III. Order

It is

ORDERED that Jantz Motion 3 is GRANTED;

FURTHER ORDERED that Jantz Motions 1 and 5, and Galetto Motions 1 and 2, are DISMISSED as moot; and

FURTHER ORDERED that judgment shall be entered against Galetto in a separate paper.

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