

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 10,093,899; 9,993,501; 9,950,010)

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. 106,118
(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)

Interference 106,118

1 A decision granting Jantz Motion 3 of has been entered. (Decision,
2 Paper 206). As a result of this Decision, the only involved claim of senior party
3 Galetto is unpatentable and Galetto lacks standing to continue in the interference.
4 Bd. R. 201. Accordingly, we enter judgment against Galetto.

5

6

Order

7

It is

8

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

10

FURTHER ORDERED that claim 31 of Galetto application 16/027,629,
11 which corresponds to Count 1, is FINALLY REFUSED. (Declaration, Paper 1, 5);
12 35 U.S.C. § 135(a);¹

13

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

15

FURTHER ORDERED that a party seeking judicial review timely serve
16 notice on the Director of the United States Patent and Trademark Office;
17 37 C.F.R. §§ 90.1 and 104.2. *See also* Bd. R. 8(b). Attention is directed to *Biogen*
18 *Idec MA, Inc., v. Japanese Foundation for Cancer Research*, 785 F.3d 648,
19 654–57 (Fed. Cir. 2015) (determining that pre-AIA § 146 review was eliminated for
20 interference proceedings declared after September 15, 2012); and

20

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).

Interference 106,118

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

3
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5
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(APPLICATION 16/027,629).

PATENT INTERFERENCE NO. 106,118
(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

1 I. Introduction

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

8 Galetto is involved on the basis of application 16/027,629 (‘629), filed
9 July 5, 2018. (‘629 Application, Ex. 2004).⁴ Jantz is involved on the basis of three
10 of its patents: (1)10,093,899, issued October 09, 2018, application 15/964,423,
11 filed April 27, 2018 (Ex. 1018); (2) 9,993,501, issued June 12, 2018, application
12 15/864,947, filed January 08, 2018 (Ex. 1019); (3) 9,950,010, issued
13 April 24, 2018, application 15/864,984, filed January 08, 2018 (Ex. 2010).
14 (Declaration, Paper 1).

15 Jantz filed two substantive motions as did Galetto.⁵ One of the motions
16 before us, Jantz Motion 3 seeking judgment against Galetto on the basis that all the
17 involved Galetto claims are unpatentable for failure to comply with the written

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 Collectis 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 Exhibit 2004 is the published application, US 2018/0360883 A1, published December 20, 2018.

⁵ The panel decided that no oral argument was necessary and none was ordered.

1 description requirement of the first paragraph of 35 U.S.C. §112, raises a threshold
2 issue under Bd. R. 201. (Jantz Motion 3, Paper 86). Galetto opposed this motion
3 and Jantz replied. (Galetto Opposition 3, Paper 167; Jantz Reply 3, Paper 184).
4 Because Jantz Motion 3 raises a threshold issue under Bd. R. 201, i.e., an issue
5 that, if resolved in favor of the movant, would deprive the opponent of standing in
6 the interference, we first consider this motion.⁶

7 We grant the motion.

8

9 II. Discussion

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

14

15 A. Jantz Motion 3

16 *Subject matter of the interference*

17 T cells provoke an immune response through T cell receptors (“TCRs”),
18 which detect antigens expressed by pathogens or mutant cells. Cancer cells do not
19 always express antigens that can be detected by the TCRs sufficiently to mediate
20 killing of these cells. (Fry Declaration, Ex. 2003, ¶ 31, citing ’629 Application,
21 Ex. 2004, ¶ 8). The invention claimed by Galetto is directed generally to T cells
22 that have been genetically modified through the introduction of a gene encoding a
23 chimeric antigen receptor (“CAR”). CARs are synthetic receptors that are

⁶ 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 23, 1:15-2:11). As discussed further within this decision, we do not find the Galetto motion to raise a threshold issue.

1 designed to detect a target antigen (e.g., tumor antigen) to generate an immune
2 response against the antigen. CARs can be introduced to T cells ex vivo in either
3 autologous cells (cells that are taken from the patient's own body) or allogeneic
4 cells (cells that are taken from a donor that is not the intended patient). (Fry
5 Declaration, Ex. 2003, ¶ 32, citing '629 Application, Ex. 2004, ¶¶ 4-6, 216). TCR
6 from a donor may be recognized by a patient as foreign tissue, resulting in graft
7 versus host disease (GvHD). (Fry Declaration, Ex. 2003, ¶ 41, citing
8 '629 Application, Ex. 2004, ¶ 6).

9 The claimed invention calls for integration of a CAR sequence into the T
10 cell receptor alpha gene ("TCR α ") in a single genetic modification step using
11 homologous recombination ("HR").⁷ (Fry Declaration, Ex. 2003, ¶¶ 73; 96; Galetto
12 Clean Copy of Claims, Paper 6). This results in modified T cells having reduced
13 TCR expression on the cell surface as well as CAR expression for antigen
14 detection. The modified T cells may provide a better treatment option since the
15 reduction of TCR expression decreases the possibility of GvHD making the use of
16 donor cells safer for a patient. ('629 Application, Ex. 2004, ¶¶ 2, 11, 16; Galetto
17 Opposition 3, Paper 167, 18:2-4).⁸

⁷ Homologous recombination is a DNA repair process by which homologous sequences are incorporated. (Galetto Opposition 3, Paper 16, 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).

⁸ 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.

Galetto involved claim

1
2 According to the '629 specification, in an embodiment of the invention
3 where TCR α is inactivated, T cells are engineered to allow their proliferation while
4 the TCR α gene is inactivated and where the engineered T cells are then further
5 transformed with a CAR sequence. ('629 Application, Ex. 2004, ¶¶ 15, 16).

6
7 Galetto claim 31 is the only involved Galetto claim. (Declaration, Paper 1,
8 5). The claim is:

9 31. A method of immunotherapy for treating a patient with
10 cancer comprising administering the pharmaceutical composition of
11 claim 28.

12
13 Claim 28,⁹ upon which claim 31 depends, is directed to “[a] pharmaceutical
14 composition comprising the isolated genetically-modified human T cell of claim
15 26”. Claim 26 is as follows:

16
17 26. An isolated genetically modified human T cell in which a
18 T cell receptor (TCR) alpha gene has been modified by cleavage with
19 a TALEN encoded by electroporated RNAs and integration by
20 homologous recombination into the TCR alpha constant chain region
21 of an exogenous nucleic acid successively comprising:

22 a first region of homology to sequences upstream of said
23 cleavage with the TALEN, an exogenous polynucleotide sequence
24 encoding a Chimeric Antigen Receptor,

25 and a second region of homology to sequences downstream of
26 said cleavage with the TALEN,

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

⁹ Claim 28, as well as other Galetto claims, are involved in related interference 106,117 which involves the same Galetto application but different Jantz patents.

1 description of that portion of claim 31 requiring modified T cells having a CAR
2 sequence that is integrated specifically into the TCR α gene by homologous
3 recombination thus inactivating the gene. (“contested limitation”). (Fry
4 Declaration, Ex. 2003, ¶ 96).

5 As discussed in the Jantz motion, on July 6, 2018, one day after filing its
6 involved ’629 application, Galetto filed a paper requesting an interference with,
7 *inter alia*, two of the three Jantz involved patents. In that request Galetto cancelled
8 its previous claims and presented new claims, including current claim 31, that
9 appears to be substantially the same as, but not identical to, claim 1 of Jantz
10 involved patent 9,993,501. (Galetto Amendment and Suggestion of Interference,
11 Ex. 2012).

12 The new claims were rejected for lacking written description of the “specific
13 concept of inserting an exogenous CAR coding sequence into the TCR alpha gene,
14 particularly the TCR alpha constant region.” (Examiner Action, Ex. 2013, 2).¹⁰
15 While the claims were later amended, a requirement that a CAR sequence be
16 integrated, by homologous replication, into the TCR α gene remained. (Galetto
17 Amendment, Ex. 2014, 2-5).

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

¹⁰ USPTO records indicate that claim 31 was withdrawn from consideration (and later rejoined prior to allowance) based on a restriction requirement. (*See* ’629 Office Action dated August 16, 2018; Office Action dated August 09, 2019). Because claim 31 depends from rejected claims 26 and 28 and thus contains the “specific concept” referred to by the Examiner, the Examiner’s finding also applies to claim 31. (Examiner’s Action, Ex. 2013, 2).

1 Jantz asserts that the Examiner was correct in rejecting Galetto's copied
2 claims for not having written description support for the concept of inserting a
3 CAR coding sequence into the TCR α gene, particularly the TCR alpha constant
4 region at the cleavage site that inactivates the TCR α gene. Jantz urges that it
5 disagrees with Galetto's position, taken during ex parte prosecution of the
6 '629 application, that "a CAR and pTalpha are two interchangeable species" and
7 that therefore paragraphs 103 ("¶ 103") and 124 ("¶ 124") of the Galetto
8 specification considered together provide sufficient description."

9 Jantz argues that, because a CAR and pT α are not two interchangeable
10 species for the purposes of paragraph 124, one skilled in the art would not have
11 read paragraphs 103 and 124 together nor have understood these paragraphs to
12 disclose the concept of inserting a CAR coding sequence into the TCR α
13 inactivating the TCR α gene. (Jantz Motion 3, Paper 86, 2:8-3:3, citing Galetto
14 Amendment and Response filed July 26, 2019, Ex. 2013, 2). Further, Jantz argues,
15 nowhere else does the '629 specification provide descriptive support for the
16 concept such that one skilled in the art would have understood Galetto to have
17 possessed the claim 31 invention. (Jantz Motion 3, Paper 86, 4:1-12; 20:11-13).

18 Galetto argues that its involved specification describes the claimed invention
19 and specifically that portion in dispute. According to Galetto its specification
20 describes genetically modified human T cells where the T cell's TCR α gene is
21 inactivated by integrating, using HR, a sequence encoding a CAR into the TCR α
22 gene and as required by claim 31. (Galetto Opposition 3, Paper 167, 3:1-5).
23 Galetto argues that sufficient description is provided where its specification
24 discusses introducing an exogenous sequence encoding at least one recombinant
25 protein of interest into the TCR α gene. According to Galetto, one skilled in the art
26 would have understood that a "recombinant protein of interest" referred to in the
27 '629 specification could be a CAR given the disclosure of CAR as a protein of

1 interest and the numerous references to CARs elsewhere within the Galetto
2 specification. (Galetto Opposition, Paper 167, 6:23-7:15, citing Osborn
3 Declaration, Ex. 1041, ¶¶ 35, 37, 38; Fry Deposition, Ex. 1040, 21:12-22; '629
4 application, ¶¶ 102, 118).

5 Galetto argues that the '629 specification also describes that the genome
6 modification of a T cell can be performed through homologous recombination such
7 that one skilled in the art would have understood that an exogenous polynucleotide
8 sequence could be introduced through homologous recombination into the TCR α
9 gene. (Galetto Opposition, Paper 167, 7:17-20, citing Osborn Declaration, Ex.
10 1041, ¶¶ 39, 40).

11 12 *Summary of Decision*

13 We find that the '629 specification does not provide sufficient “blaze marks”
14 pointing to integrating a CAR sequence into the TCR α gene by homologous
15 recombination resulting in inactivation of the gene. While individual elements of
16 the contested limitation can be found within the '629 specification, we find, based
17 on the evidence before us, that one skilled in the art would not have been led to a
18 modified T cell having a CAR sequence that is integrated specifically into the
19 TCR α gene by homologous recombination thus inactivating the TCR α .

20 21 *Legal Principles*

22 We give claims their broadest reasonable interpretation by considering not
23 only the claim language but also how one skilled in the art would understand the
24 claim in view of the specification. *Phillips v. AWH*, 415 F.3d 1303, 1316, (Fed.
25 Cir. 2005). As explained in *Agilent Techs., Inc. v. Affymetrix, Inc.*, claims copied
26 from another are construed in view of the originating specification for purposes of
27 evaluating written description support. *Agilent v. Affymetrix, Inc.*, 567 F.3d 1366,

1 1375 (Fed. Cir. 2009). In the present circumstances there appears to be no dispute
2 that Galetto presented claims in the '629 application that are substantially the same
3 as, but not identical to, Jantz patent claims. (Galetto Amendment and Suggestion
4 of Interference, Ex. 2012, 7, 8).¹¹ To the extent we must construe Galetto
5 claim 31 in view of the Jantz patent specification, such construction does not
6 appear to result in any meaningful difference in how the claim terms are construed.
7 The parties do not argue that the construction of claim 31 differs according to
8 which of the parties' specifications is consulted.

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

15 *In haec verba* support is not necessary. *Fujikawa v. Wattanasin*, 93 F.3d
16 1559, 1570, (Fed. Cir. 1996). Whether the inventor has provided adequate written
17 description, either explicitly or inherently, must be determined from the disclosure
18 considered as a whole. *Reiffin v. Microsoft Corp.*, 214 F.3d 1342 (1346 Fed. Cir.
19 2000).

20 The written description issue requires we consider the perspective of a
21 person of ordinary skill in the art with the understanding that “the level of detail
22 required ... varies depending on the nature and scope of the claims and on the
23 complexity and predictability of the relevant technology.” *Ariad Pharms., Inc. v.*

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. Galetto claim 26 and Jantz claim 1 are involved in related interference 106,117. Involved claim 31 is directed to a method of administering the composition of claim 26.

1 *Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010). We therefore consider
2 whether the technology involved is unpredictable in determining whether the
3 claims are sufficiently described. *Capon v. Eshhar*, 418 F.3d 1349, 1359 (Fed. Cir.
4 2005). (“It is well recognized that in the ‘unpredictable’ fields of science, it is
5 appropriate to recognize the variability in the science in determining the scope of
6 the coverage to which the inventor is entitled. Such a decision usually focuses on
7 the exemplification in the specification.”).

8 Where a claimed invention is not disclosed with specificity in the underlying
9 specification, we look to see if there are “sufficient ‘blaze marks’ to guide a reader
10 through the forest of disclosed possibilities” to the specifically claimed invention.
11 *Novozymes A/S v. DuPont Nutrition Biosciences*, 723 F.3d 1336, 1346 (Fed. Cir.
12 2013), citing *In re Ruschig*, 379 F.2d 990, 994-995 (CCPA 1967). A “mere wish
13 or plan” for obtaining the claimed invention does not satisfy the written description
14 requirement. *Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1566
15 (Fed.Cir.1997).

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

21

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Discussion

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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.

1 However, we make a determination of whether the claimed invention is
2 sufficiently described by considering the disclosure as a whole. *Reiffin v.*
3 *Microsoft Corp.*, 214 F.3d at 1346.

4 Jantz directs us to, *inter alia*, the testimony of Dr. Terry Fry to support the
5 arguments made within Jantz Motion 3.¹² Dr. Fry characterizes a hypothetical
6 person of ordinary skill in the art time period as having a Ph.D., M.D. or
7 M.D./Ph.D. with specific training in the areas of molecular biology and
8 immunology or related disciplines with substantial research or industrial
9 experience in adoptive cell therapy for cancer and the use of genetically modified
10 T cells for this purpose. (Fry Declaration, Ex. 2003, ¶ 28). A person having
11 ordinary skill in the art is presumed to know the relevant prior art. *In re GPAC*, 57
12 F.3d 1573, 1579 (Fed. Cir. 1995). Galetto does not dispute Dr. Fry’s
13 characterization of such a person and we find that such a person may have the
14 education and experiences that Dr. Fry lists in his testimony.

15 Dr. Fry testified that “T cell gene editing for immunotherapy remains a
16 highly unpredictable field” (Fry Declaration, Ex. 2003, ¶¶ 127, 128, citing, e.g.,
17 Sather¹³ as describing specific challenges associated with the development and
18 optimization of targeted integration into the T cell genome”).

19 Jantz argues that the Galetto claim requires a modified T cell that results
20 from a single step modification, i.e., where a CAR sequence is integrated
21 specifically into the TCR α gene such that it is inactivated. (Jantz Motion 3,
22 Paper 86, 3:8-14; 20:16-21:2; Fry Declaration, Ex. 2003, ¶¶ 68, 73, 96). Jantz

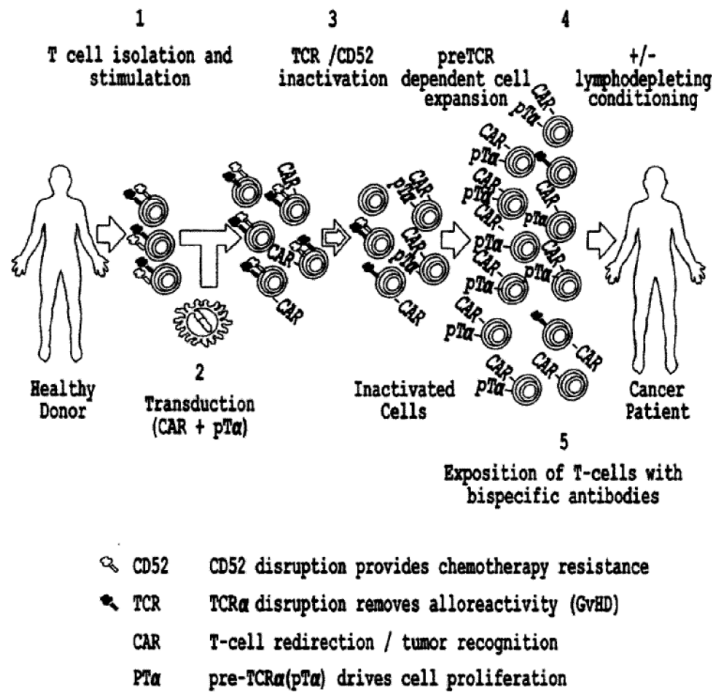
¹² We have reviewed Dr. Fry’s credentials and find Dr. Fry qualified to testify regarding the technical issues discussed in his testimony. (Fry Declaration, Ex. 2003, ¶¶ 5-16; Fry *Curriculum vitae* (Appendix A of Ex. 2003)).

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).

1 acknowledges that the '629 specification discloses inactivating four genes, of
 2 which the TCR α gene is one option, including by HR. However, Jantz argues the
 3 specification does not describe using a CAR for this purpose but only a general and
 4 undisclosed sequence. (Jantz Motion 3, Paper 86, 21:15-23:3).

5 Jantz urges that, when discussing CAR introduction, the '629 specification
 6 discloses two T cell modification steps, one to inactivate the TCR α and a second
 7 and separate step, occurring either before or after the first step, to introduce another
 8 sequence, e.g., a CAR sequence, either transiently by mRNA or by pseudo-random
 9 integration by lentiviral vector (LV). (Jantz Motion 3, Paper 86, 24:9-17, citing
 10 '629 Application, Ex. 2004, Figure 5, ¶¶ 268, 301, 202, 203; Fry Declaration, Ex.
 11 2003, ¶107).

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



Above is shown Figure 5 of the '629 disclosure.

1 As Jantz points out, the five steps of Figure 5 include: (1) “providing T
2 cells,” (2) “a) Transducing said cells with pTalpha ... b) Transducing said cells
3 with multi-chain CARs,” (3) “[e]ngineering non alloreactive and
4 immunosuppressive resistant T cells [by] ... [inactivating] TCR alpha in said cells
5 to eliminate the TCR from the surface of the cell...,” and inactivating CD52 to
6 create immunosuppressive resistance (4) “[e]xpansion in vitro, and
7 (5) “[o]ptionally expos[ing] said cells with bispecific antibodies in vivo following
8 administration to a patient.” (Jantz Motion 3, Paper 86, 9:4-11, citing,
9 ’629 specification, Ex. 2004 ¶¶ 200-209; Fry Declaration, Ex. 2003 ¶ 64).

10 As Jantz notes, the genetic modification step is shown as step 3, and
11 includes inactivation of existing genes where one “X” gene (TCR α) and one “Y”
12 gene (CD52) are inactivated by using rare-cutting endonucleases (TALE-
13 nucleases) to cleave the genes. Jantz points out that an exogenous polynucleotide
14 is not provided in the step, and the inactivation occurs not by HR, but by non-
15 homologous end joining (“NHEJ”), said to be an error-prone cellular repair
16 pathway that results in the insertion or deletion of nucleotides at the cleaved site.
17 (Jantz Motion 3, Paper 86, 10:1-9, citing, ’629 specification, Ex. 2004 ¶¶ 204-207;
18 Fry Declaration, Ex. 2003 ¶ 61-65). Dr. Fry testified that NHEJ is incapable of
19 integrating sequences, such as CAR, into a genome. (Fry Declaration, Ex. 2003
20 ¶ 120).

21 Jantz points to the additional genomic modification step as being shown in
22 step 2, and as including the introduction of new genes where a CAR sequence and
23 pT α sequence are introduced by way of “transduction” with lentiviral vectors that
24 randomly integrate the new genes into the genome. Jantz notes that the
25 specification states that CAR transduction can be “before or after” TCR α and
26 CD52 inactivation and is identified as an “additional genomic modification step,”
27 and shown as a separate step that does not occur simultaneously with “the genetic

1 modification step.” (Jantz Motion 3, Paper 86, 10:10-16, citing, ’629 specification,
2 Ex. 2004 ¶¶ 202, 203; Fry Declaration, Ex. 2003 ¶¶ 64, 66, 68).

3 Jantz addresses those portions of the ’629 specification that Galetto argued,
4 during ex parte prosecution, support the claim 31 contested limitation. In
5 particular, Galetto argued that paragraphs 103 and 124 of the ’629 specification,
6 when considered together, provide written description support for this limitation.

7

8 Paragraphs 103 and 124

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

11 [0100] By additional genomic modification step, can be
12 intended also the inactivation of another gene selected from the group
13 consisting of CD52, GR, TCR alpha and TCR beta. [sic] As
14 mentioned above, said additional genomic modification step can be an
15 inactivation step comprising:

16 [0101] (a) introducing into said cells at least one rare-cutting
17 endonuclease such that said rare-cutting endonuclease specifically
18 catalyzes cleavage in one targeted sequence of the genome of said
19 cell.

20 [0102] (b) Optionally introducing into said cells a exogenous
21 nucleic acid successively comprising a first region of homology to
22 sequences upstream of said cleavage, a sequence to be inserted in the
23 genome of said cell and a second region of homology to sequences
24 downstream of said cleavage,

25 wherein said introduced exogenous nucleic acid inactivates a
26 gene and integrates at least one exogenous polynucleotide sequence
27 encoding at least one recombinant protein of interest. In another
28 embodiment, said exogenous polynucleotide sequence is integrated
29 within a gene selected from the group consisting of CD52, GR, TCR
30 alpha and TCR beta.

31

1 [0103] In particular embodiment said method to engineer cell
2 *further comprises an additional genomic modification step.* By
3 additional genomic modification step, can be intended the
4 introduction into cells to engineer of one protein of interest. [sic] Said
5 protein of interest can be, as non limiting examples, pTalpha or
6 functional variant thereof, a Chimeric Antigen Receptor (CAR), a
7 multi-chain CAR, a bispecific antibody or rare-cutting endonuclease
8 targeting PDCD1 or CTLA-4 as described in the present disclosure.

9
10 ('629 specification, Ex. 2004, ¶¶100-103, emphasis added).

11
12 Paragraph 103 of the '629 specification refers to a method that “further
13 comprises an additional genomic modification step” in engineering a T cell.
14 ('629 Application, Ex. 2004 ¶ 103; Fry Declaration, Ex. 2003 ¶ 101). This
15 paragraph does not describe integrating a CAR as the exogenous nucleic acid in the
16 process described at paragraphs 100-102 but indicates that a CAR sequence, for
17 example, may be introduced in a further additional step. Nor does the paragraph
18 specify that the listed proteins of interest in paragraph 103 are integrated by HR
19 into the TCR α gene of the already modified T cell. Thus, we agree with Dr. Fry
20 that “the generic recitation in ¶ 103 of ‘the introduction^[14] into cells to engineer of
21 one protein of interest’ without any additional blaze marks does not fairly suggest
22 to a POSA that any of the listed ‘proteins of interest’ should be specifically
23 integrated into any gene, let alone the TCR α gene.” (Fry Declaration, Ex. 2003,
24 ¶¶ 102-108).

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).

1 Further, while Jantz acknowledges that paragraph 103 includes a CAR as a
2 “protein of interest”, Jantz urges that one skilled in the art would not have
3 considered the list of proteins of interest listed in paragraph 103 to be a list
4 intended for genomic integration and thus are not “interchangeable” in any method
5 of using HR disclosed by the ’629 specification, e.g., at paragraph 102. As an
6 example, Jantz asserts, one skilled in the art would not integrate the listed “rare-
7 cutting endonuclease” because its purpose is to be transiently expressed to
8 inactivate another gene and doing so would cause the nuclease to be permanently
9 expressed, causing toxicity from off-target cleavage. (Jantz Motion 3, Paper 86,
10 16:10-15, citing Fry Declaration, Ex. 2003 ¶ 108).

11 Paragraph 124 is found within a separate section of the ’629 specification
12 having the heading “Pre-Talpha”. We reproduce paragraph 124 below and include
13 the preceding paragraphs for context:

14 [0119] In another aspect, the invention relates to a method of expanding
15 TCR alpha deficient T-cell comprising introducing into said T-cell
16 pTalpha (also named preTCR.alpha.) or a functional variant thereof and
17 expanding said cells, optionally through stimulation of the CD3
18 complex. In a preferred embodiment, the method comprises:

19 [0120] a) Transforming said cells with nucleic acid encoding at
20 least a fragment of pTalpha to support CD3 surface expression

21 [0121] b) Expressing said pTalpha into said cells

22 [0122] c) Expanding said cells optionally, optionally through
23 stimulation of the CD3 complex.

24

25 [0123] The invention also relates to a method of preparing T-cells for
26 immunotherapy comprising steps of the method for expansion for T-cell.

27

28 [0124] In particular embodiment, the pTalpha polynucleotide sequence
29 can be introduced randomly or else through homologous recombination,
30

1 in particular the insertion could be associated with the inactivation of the
2 TCRalpha gene.

3
4 ('629 Application, Ex. 2004, ¶119-124).

5 Paragraph 124 states that pT α may be introduced into TCR α deficient cells
6 “randomly or else through homologous recombination.” Paragraph 124 mentions
7 HR but does not mention CAR or otherwise expressly describe integration of a
8 CAR into the TCR α .

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

13 According to Jantz inactivating TCR α in T cells eliminates a means of
14 stimulating T cell expansion and the '629 specification discloses the introduction
15 of the pT α sequence randomly or else through homologous recombination in order
16 to restore the ability to expand. In particular, according to Jantz, when pT α is
17 introduced to T cells with an inactivated TCR α gene, it combines with the existing
18 TCR β to form a pre-TCR complex which restores the ability to expand the T cells.
19 Jantz notes that the '629 specification mentions only pT α as being able to
20 accomplish the goal of restoring expansion. Thus, argues Jantz, Galetto's
21 argument during ex parte prosecution that “the skilled artisan would immediately
22 recognize that a CAR and pT α are two interchangeable species of a ‘protein of
23 interest’ that ...can be introduced as an exogenous nucleic acid that integrates and
24 inactivates TCR alpha” is incorrect because a CAR will not enable the formation of
25 pre-TCR complex in TCR α deficient T cells to restore the ability of T cells to
26 expand, the purpose of introducing pT α .” (Jantz Motion 3, Paper 86, 16:19-17:5,

1 citing Fry Declaration, Ex. 2003 ¶¶ 110-112; Galetto Amendment and Suggestion
2 of Interference, Ex. 2020, 7, 8).

3 Jantz further notes that paragraph 124 states that the pTα insertion is “in
4 association with” inactivation of TCRα, but argues that “in association with”
5 would be read by one skilled in the art as requiring insertion of pTα anywhere in
6 order to remedy the deficiency associated with inactivating TCRα. Jantz notes that
7 this understanding is consistent with paragraph 129, which describes several
8 examples of how to create “TCR alpha deficient cells”, none of which requires
9 integrating pTα specifically into TCRα, or refer to HR. (Jantz Motion 3, Paper 86,
10 18:7-15, citing Fry Declaration, Ex. 2003, ¶¶ 113-117).

11 Jantz argues that for this reason one skilled in the art would not have been
12 guided to select CAR from the list found in paragraph 103 and substitute it for the
13 pTα in paragraph 124 to arrive at the claimed invention. Jantz argues that
14 Galetto’s arguments before the Examiner improperly relied upon an obviousness
15 rationale, i.e., that it would have been obvious to integrate CAR into TCRα by HR
16 given paragraphs 103 and 124. (Jantz Motion 3, Paper 86, 18:18-19:1; 20:3-8
17 citing *Lockwood v. Am. Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997)).¹⁵
18

19 '629 specification

20 Jantz argues that the '629 specification considered in its entirety fails to
21 describe integrating a CAR sequence by HR into the TCRα gene either when
22 discussing CARs specifically, or when CARs are in a list of proteins of interest.
23 Jantz Motion 3, Paper 86, 20, 11-13, citing Fry Declaration, Ex. 2003 ¶¶ 118-119).
24 Jantz points out that when the '629 specification discusses CARs specifically and

¹⁵ Jantz does not agree that the claim 31 invention would have been obvious in view the '629 specification. (Jantz Motion 3, Paper 86, 18:18-20)

1 not within a list, it consistently describes introducing CARs before or after, but not
2 simultaneous with, the step of inactivating genes such as the TCR α gene. (Jantz
3 Motion 3, Paper 86, 20:16-21, citing '629 Application, Ex. 2004, ¶¶ 203, 268; Fry
4 Declaration, Ex. 2003 ¶¶ 104-106).

5 Jantz argues that CAR introduction methods, including transient expression
6 of a CAR sequence via electroporation of mRNA or random integration of a CAR
7 sequence via lentiviral transduction, do not inactivate a TCR α gene and thus are
8 described as occurring either before or after such inactivation is caused by some
9 other process. (Jantz Motion 3, Paper 86, 20:21-25, citing '629 Application, Ex.
10 2004, ¶¶ 163, 220, 301; Fry Declaration, Ex. 2003 ¶¶ 104-106). Jantz argues that
11 since the '629 specification discloses introducing a CAR “before or after”
12 inactivation and does not use the term “during”, a person skilled in the art would
13 have understood that it was not in possession of a single genetic modification step
14 that would result in T cells having the contested limitation.

15 As pointed out by Jantz the '629 disclosure provides two illustrations of
16 introducing a CAR to a T cell and both use transient introduction of a CAR
17 sequence, not HR. (Jantz Motion 3, Paper 86, 24:9-13). One is shown at Figure 5,
18 discussed above, and the other at Figure 2. Figure 2 is reproduced below.
19

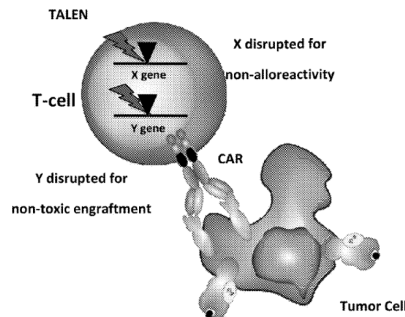


Figure 2

20

21

Above is shown Figure 2 of the '629 disclosure.

1
2 Figure 2 is identified in the '629 specification as a “[s]chematic
3 representation of the genetically modified therapeutic T-cells according to the
4 invention and the patient's tumor cells.” ('629 Application, Ex. 2004, ¶ 25). Jantz
5 urges that “[t]he core concept of the invention is shown in Figure 2, which depicts
6 the use of rare-cutting endonucleases called TALENs or TALE-nucleases to cut an
7 “X” gene that is “disrupted for non-alloreactivity” (eliminating alloreactivity or
8 GvHD associated with a donor’s TCR) and a “Y” gene that is “disrupted for non-
9 toxic engraftment” (increasing resistance to immunosuppressive drugs used to
10 deplete host T cells)”. (Jantz Motion 3, Paper 86, 7:16-20, citing '629 Application,
11 Ex. 2004 ¶¶ 21, 192, Fig. 2). According to Jantz, the '629 specification discloses
12 “inactivating an “X” gene and a “Y” gene as “the genetic modification step” and
13 identifies TCR α as one of four “X” genes and CD52 as one of two “Y” genes, that
14 can be inactivated by use of the TALEN by HR or NHEJ. ('629 specification,
15 Ex. 2004 ¶¶ 68-99; Fry Declaration, Ex. 2003 ¶ 61). Jantz asserts that the CAR
16 shown in Figure 2 is introduced in a separate, optional “additional genomic
17 modification step”, not through the use of HR, and after the T cell has been
18 modified. (Jantz Motion 2, Paper 86, 7:16-8:14).

19 Dr. Fry testified that the method shown in the two working examples of
20 introducing a CAR into a T cell use mRNA which results only in transient
21 introduction of the CAR and cannot integrate the CAR sequence into TCR α gene
22 to cause TCR inactivation. (Jantz Motion 3, Paper 86, 24:9-17; Fry Declaration,
23 Ex. 2003, ¶ 107, citing '629 Application, Ex. 2004 ¶¶ 268, 301). While an
24 applicant need not provide an example to have written description, an example
25 may indicate possession of the claimed invention. *Falkner v. Inglis*, 448 F.3d
26 1357, 1366 (Fed. Cir. 2006). We agree with Jantz that these working examples,

1 considered in view of the explanation and context of the '629 specification, do not
2 show possession of the contested limitation.

3 Jantz argues that, for the reasons it provides, and as in *Novozymes*, the
4 '629 specification provides insufficient “blaze marks” because it “provide[s]
5 formal textual support for each individual limitation recited in the claims [at
6 issue],” but “never presented [those limitations] together.” (Jantz Motion 3,
7 Paper 86, 19:6-17, citing *Novozymes*, 723 F.3d at 341).

8

9 *Galetto Opposition.*

10 In its Opposition 3, Galetto argues that the '629 specification identifies CAR
11 as a particular protein of interest and one skilled in the art would have understood
12 that CAR could have been used as an exogenous nucleotide in a single genetic
13 modification step to arrive at the claimed T cells. As Galetto notes, Jantz does not
14 dispute that the '629 specification discloses T cells having an inactivated TCR α
15 gene nor that the '629 specification describes introduction of DNA encoding a
16 CAR into these modified T cells. Jantz also agrees that CAR is said to be
17 generally “a protein of interest” in portions of the '629 specification. (Jantz
18 Reply 3, Paper 184, 2:21-3:2; citing Fry Deposition, Ex. 1040, 22:22-23:13, 65:23-
19 66:3). Galetto argues that, in view of these disclosures and within the context of
20 the entire '629 specification, the necessary blaze marks would have guided one
21 skilled in the art to the claimed invention.

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

26 Dr. Osborn testified that “[s]ince polynucleotides encoding a CAR are
27 described in the Galetto application, the skilled artisan would have further

1 understood that the integration of a polynucleotide encoding a CAR into TCR α by
2 homologous recombination could inactivate the TCR α gene.” (Osborn Declaration,
3 Ex. 1041, ¶ 63). Even accepting this testimony, a description in the
4 ’629 specification of a polynucleotide encoding CAR does not amount to
5 description sufficient to show possession of the claimed modified T cells.
6 Dr. Osborn’s testimony on this point may be relevant to obviousness under
7 35 U.S.C. § 103 in that it addresses what one skilled in the art might be motivated
8 to do or try in view of the ’629 specification. Dr. Osborn agreed that it is his
9 opinion that it would have been obvious how to get to a disclosure of a CAR
10 integrated into the TCR α from reading the ’629 specification. (Osborn Deposition,
11 Ex. 2070, 132:18-134:5-14). However, obviousness is not the issue before us.
12 *Lockwood*, 107 F.3d at 1571–72.

13 We turn to the specific portions of the ’629 specification that Galetto argues
14 support claim 31 and in particular the contested limitation.

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

23 Both Dr. Fry and Dr. Osborn seem to agree that the proteins of interest listed
24 in paragraph 103, which include rare-cutting endonucleases, are of a different
25 character than the exogenous nucleic acid to be integrated into the T cell genome
26 referred to in paragraph 102. For example, Dr. Osborn’s testimony indicates that
27 he considers inactivation of PDCD1 or CTLA-4 to be genomic modifications

1 intended in paragraph 103 and that the listed rare-cutting endonucleases are the
2 means for producing those genomic modifications, and they do so without
3 integration. (Osborn Deposition, Ex. 2070, 103:14-109:20). Dr. Fry and
4 Dr. Osborn also seem to also agree that integrating a rare-cutting endonuclease into
5 the genome would not be logical given its function. (*See, e.g.*, Fry Declaration, Ex.
6 2003, ¶ 108; Fry Deposition, Ex. 1040, 61:8-62:24, 65:23-66:3 (“The proteins of
7 interest that are included in the description of 103 include the rare cutting
8 endonuclease, and it would be, in my opinion, an odd protein that one would want
9 to stably introduce into a cell.”); Osborn Deposition, Ex. 2070, 46:2-7 (“So the
10 specific question is, why don't you integrate an endonuclease into a cell? ... I think
11 that, depending on specificity, you would have a potential concern for any off-
12 target activity”) and 108:16-109:20). Based on the evidence before us, we agree
13 with Jantz that one skilled in the art would have known not to integrate a rare-
14 cutting endonucleases to inactivate the TCR α gene because these enzymes could
15 continue their cutting function increasing the risk of off-target cutting. (Jantz
16 Motion 3, Paper 86, 23:12-24:6). It follows that one skilled in the art would not
17 have understood the unidentified proteins or sequences of interest of paragraph
18 102, as well as those similarly discussed in paragraphs 98, 99 and 118, to be the
19 same proteins of interest listed in paragraph 103 which includes, *inter alia*, rare-
20 cutting endonucleases.

21 Turning to paragraph 124, pT α is the only protein described as useful for the
22 expansion method found in paragraph 124. Galetto does not direct us to
23 convincing evidence or argument that one skilled in the art would have understood
24 CAR to be an appropriate substitution for pT α that is used for the expansion
25 method or that the paragraph 124 describes integrating pT α specifically into the
26 TCR α gene. (Galetto Opposition 3, Paper 167, 7:21-8:22; 9:3-13). Thus, we agree

1 with Jantz that this portion of the '629 considered in the context of the
2 '629 specification as a whole, does not describe the contested limitation.

3 Galetto points to other portions of the '629 specification that it urges would
4 have guided one skilled in the art to the claimed invention, including portions at
5 paragraphs 98, 99, and 118. (Galetto Opposition 3, Paper 167, 9:3-13; 10:8-11:14,
6 citing Osborn Declaration, Ex. 1041, ¶¶ 57-64). Each portion discloses
7 inactivating any one of four genes by HR, including TCR α , but does not identify
8 what exogenous sequence is to be used to affect inactivation. Galetto argues that
9 these portions encompass the possibility of “knock-ins” of the TCR α gene, i.e., the
10 introduction of new sequences or genes of interest. What is lacking though is
11 guidance to select CAR as the sequence for the “knock-in” ('629 specification,
12 Ex. 2004, ¶¶ 98, 99, 103, 118). We agree with Jantz that the '629 specification
13 “never presented [the limitations of Galetto’s involved claims] together in any
14 particular embodiment,” nor did the application provide sufficient “blaze marks” to
15 guide one toward the claimed combination among a “slew of competing
16 possibilities.” (Jantz Reply 3, Paper 184, 8:8-16, citing *Novozymes*, 723 F.3d at
17 1351).

18 Galetto argues, and Dr. Osborn testified, that the '629 specification provides
19 “blaze marks [that] point directly to a CAR as a protein of interest for introduction
20 into a TCR α -inactivated cell”, citing for example, Figures 2 and 5 (Galetto
21 Opposition 3, Paper 167, 9:16-21, 17:10-18:8, citing Osborn Declaration, Ex 1041,
22 ¶¶ 50-54). As discussed above, these Figures, while showing CAR as a protein of
23 interest, further support that the CAR sequence is introduced in a step separate,
24 either before or after, TCR α is inactivated. Dr. Osborn agreed that “introduction”
25 of CAR within the '629 specification could point to introduction of the CAR
26 sequence into TCR α that was already inactivated. (Osborn Deposition, Ex. 2070,
27 163:8-17; 90:20-91:5, 93:18-94:6). Dr. Fry, while acknowledging CAR as a

1 protein of interest, testified that the '629 specification did not suggest a CAR
2 sequence integrated into the TCR α gene. (Fry Deposition, Ex. 1040, 22:22-23:13,
3 65:23-66:3).

4 The description of introducing a CAR “before or after” TCR α inactivation in
5 relation to the Figures, as discussed above, would not lead one toward from
6 integrating a CAR sequence “during” TCR α inactivation. Thus these Figures, in
7 the context and explanation provided by the '629 specification, do not describe the
8 contested limitation.

9 Galetto argues that “nowhere does Galetto’s application indicate that [HR]
10 should NOT be used with a CAR.” (Galetto Opposition 3, Paper 167, 12:22-13:4.
11 We do not find this argument convincing. Galetto does not explain, and it is not
12 apparent to us, why one skilled in the art would have “immediately discerned” that
13 HR was to be used simply because Galetto did not expressly exclude the method.

14 Galetto argues that the portion of the '629 specification found at paragraphs
15 219 and 220 disclose non-integrative lentiviral vectors that could integrate into a
16 genome through HR. (Galetto Opposition, Paper 167, 11:15-12:21). Dr. Osborn
17 concedes though that paragraph 219 does not disclose integrating a CAR into
18 TCR α gene. (Osborn Deposition, Ex. 2070, 189:10-190:7). Further, as Jantz
19 notes, the only methods disclosed in the '629 specification for introduction of a
20 CAR specifically cannot result in integration of CAR into a TCR α gene. (Jantz
21 Motion 3, 24:9-17, citing Fry Declaration, Ex. 2003, ¶¶ 38, 105,107;
22 '629 Application, ¶¶ 202-203, 268, 301). Accordingly, we do not find these
23 portions, when considered in the context of the '629 specification as a whole, to
24 describe integrating a CAR into TCR α by HR as required by claim 31.

25 Galetto argues that Dr. Fry came to the “wrong conclusion” because he did
26 not know the legal significance of the phrase “blaze marks.” (Galetto Opposition 3,
27 Paper 167, 16:7-22, citing Fry Deposition, Ex. 1040, 59:14-23). Galetto does not

1 contend that Dr. Fry's testimony is based on a misunderstanding of the law, or
2 otherwise explain why we should not credit his testimony based on his
3 unfamiliarity with this particular phrase. Dr. Fry's testimony indicates that he
4 based his testimony upon an adequate understanding of the written description
5 issue. (Fry Declaration, Ex. 2003, ¶¶ 22-25).

6 As Galetto notes, Jantz points to references by a Galetto inventor to Jantz's
7 work of "integrating the TCR α gene by integrating a CAR sequence by HR into
8 that gene" in a Galetto patent application as well as a scientific article. Jantz argues
9 that this crediting of Jantz amounts to an acknowledgement that Jantz was the first
10 to invent the claimed subject matter. (Jantz Motion 3, Paper 86, 12:1-22). We
11 agree with Galetto though that these references to Jantz's work have no bearing on
12 whether Galetto's involved application provides adequate written description.
13 (Galetto Opposition 3, Paper 167, 18:18-19:4).

14 We find that Jantz has met its burden of showing a lack of written
15 description for the claim 31 contested limitation. We note that much of the
16 testimony before us is in agreement. The disagreement appears to lie, primarily, in
17 whether the '629 specification provided sufficient guidance or blaze marks to
18 direct one skilled in the art to what is claimed. Here, where there is conflict
19 between Dr. Fry's and Dr. Osborn's testimony, we credit the testimony of Dr. Fry
20 over that of Dr. Osborn. We find that the testimony of the latter relies more on
21 what the '629 application might have suggested to one skilled in the art than what
22 was conveyed to have been in the possession of the inventors.

23 The evidence before us is convincing to show that one skilled in the art
24 would have understood the '629 specification to disclose CAR introduction as a
25 "further" additional step that occurs separate from the TCR inactivation step.
26 While it could have done so, the '629 specification does not identify the exogenous
27 nucleic acid sequence that may be used in the inactivation step as a CAR instead

1 only identifying CAR specifically as one option to be used in further modifying
2 T cells where the TCR α or other gene has already been, or later would be,
3 inactivated. The individual components of the limitation can be found within the
4 '629 specification and one may have been able to piece together what is now
5 claimed but lacking is sufficient guidance to show that the inventors possessed
6 what is claimed. “Were we to extend *Ruschig* 's metaphor to this case, we would
7 say that it is easy to bypass a tree in the forest, even one that lies close to the trail,
8 unless the point at which one must leave the trail to find the tree is well marked.”
9 *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571 (Fed. Cir. 1996).

10 In a separate portion of its Motion 3, Jantz argues that the Galetto claim is
11 unpatentable “for the independent reason that the '629 Application does not
12 teach a POSA how to integrate a CAR sequence into the TCR α gene.” (Jantz
13 Motion 3, Paper 86, 25:4-21).

14 Galetto relies upon the testimony of Dr. Pietro Genovese¹⁶ only in the
15 portion of its briefing addressing this argument. (Galetto Opposition 3, Paper 176,
16 21:25-24:2, citing Genovese Declaration, Ex. 1042; *Genovese Curriculum Vitae*.
17 Ex. 1044). As explained below, we do not find it necessary to consider this
18 argument or to consider Dr. Genovese’s testimony addressing it to decide the
19 motion before us. However, we have considered Dr. Genovese’s testimony to the
20 extent it is relevant to the predictability of the technology involved. Dr. Genovese
21 testified that it is his opinion that, e.g., vectors and methods provided by
22 experimental results known in the art could readily be modified for inserting a
23 CAR to an endogenous TCR gene. (Genovese Declaration, Ex. 1042, ¶ 33).

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

1 As we noted above, Dr. Fry testified that “T cell gene editing for
2 immunotherapy remains a highly unpredictable field.” (Fry Declaration, Ex. 2003,
3 ¶¶ 127, 128). Dr. Fry later modified his testimony to acknowledge that
4 investigators had achieved targeted integration in T cells earlier than his initial
5 testimony had indicated. (Galetto Opposition 3, Paper 167, 20:27-36, citing Fry
6 Deposition, Ex. 1040, 66:12-67:2). Dr. Fry went on to testify that, while there was
7 mention of integrating into T cells in some earlier publications, this fact “certainly
8 does not change the challenges associated with modifying primary cells” and did
9 not change his opinion regarding written description. (Fry Deposition, Ex. 1040,
10 67:14-68:8).

11 As discussed above we find that the ’629 specification does not describe the
12 integration of a CAR sequence into the TCR α gene. Accordingly we need not, and
13 do not, consider this “independent reason.” Further our decision would not change
14 even accepting Galetto’s position that “[w]hen the scientific and technological
15 knowledge available at that time is appropriately considered, the POSA would
16 have known how to integrate a CAR sequence into the TCR α gene by HR”, since
17 we find that the claimed invention does not appear in the specification regardless
18 of whether one of skill in the art could make the claimed invention. (Galetto
19 Opposition 3, Paper 167, 19:18-20) *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598
20 F.3d at 1348 (“In either case the analysis compares the claims with the invention
21 disclosed in the specification, and if the claimed invention does not appear in the
22 specification....the claim...fails regardless whether one of skill in the art could
23 make or use the claimed invention.”)

24 We GRANT Jantz Motion 3.

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

1 B. Remaining Motions

2 Jantz filed two additional motions as did Galetto.

3 Jantz Motion 2 challenges the benefit accorded to Galetto in the declaration
4 of the interference. (Jantz Motion 2, Paper 85). Jantz also filed a miscellaneous
5 motion seeking exclusion of certain evidence. (Jantz Motion 5, Paper 195).

6 Galetto Motion 1 seeks judgment against Galetto on the basis that all the
7 involved Jantz claims are unpatentable for failure to comply with the written
8 description requirement of the first paragraph of 35 U.S.C. §112. (Galetto
9 Motion 1, Paper 23). Galetto Motion 2 seeks judgment against Galetto on the basis
10 that all the involved Jantz claims are unpatentable for failure to comply with the
11 second first paragraph of 35 U.S.C. §112.

12

13 1. Galetto Motion 1

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

17 A threshold issue is an issue that, if resolved in favor of the movant, would
18 deprive the opponent of standing in the interference. Threshold issues may
19 include, but are not expressly limited to, “in the case of an involved application
20 claim first made after the publication of the movant’s application or the movant’s
21 patent.....unpatentability for lack of written description under 35 U.S.C. 112(a) of
22 the involved application claim where the applicant suggested, or could have
23 suggested, an interference under” Bd. R. 202(a). Bd. R. 201.¹⁷ Addressing this
24 threshold issue requires a determination of whether a party presenting a claim that
25 interferes with a claim of an already published application or patent has adequate

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

1 basis to challenge priority of invention, a question that turns on whether that
2 party's specification adequately supports subject matter that was first claimed by
3 another party. *Cf. Agilent Techs., Inc. v. Affymetrix, Inc.*, 567 F.3d at 1375 (Fed.
4 Cir. 2009), citing *Rowe v. Dror*, 112 F.3d 474, 479 (Fed. Cir. 1997).

5 Galetto concedes that its Motion 1 does not “directly fall[] within the
6 explicitly described ‘threshold issues,’” of Bd. R. 201. However, Galetto urges
7 that its motion “should be included with such issues due to the pre- and post-AIA
8 status of Galetto’s application and Jantz’s involved patents, respectively”. In
9 particular, Galetto urges that Jantz could not have requested an interference due to
10 its post AIA status and, given this restriction, we should consider the Galetto
11 motion to raise a threshold issue. (Galetto Motion 1, Paper 23, 2:5-11).

12 Regardless of whether or not Jantz could have properly suggested
13 interference,¹⁸ it was Galetto that substantially copied Jantz patent claims and
14 requested the interference. Thus we consider whether Galetto had adequate
15 support for the subject matter that was first claimed by Jantz to see if Galetto has
16 standing to contest priority of invention. *Agilent Techs.*, 567 F.3d at 1375 (Fed.
17 Cir. 2009). Galetto does not provide a convincing reason why Jantz, who first
18 claimed the interfering subject matter, should be deprived of standing to contest
19 priority of invention even were we to grant Galetto Motion 1.

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

23

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.

1 2. Jantz Motion 2 and Galetto Motion and 2

2 Jantz Motion 2 challenges the benefit accorded to Galetto in the declaration
3 of the interference. (Jantz Motion 2, Paper 85). Galetto Motion 2 seeks judgment
4 against Galetto on the basis that all the involved Jantz claims are unpatentable for
5 failure to comply with the second first paragraph of 35 U.S.C. §112. (Galetto
6 Motion 2, Paper 24).

7 Because we grant Jantz Motion 3 and find Galetto claim 31 to lack written
8 description support, Galetto lacks standing to continue in this interference. Bd. R.
9 201. We need not, and do not, consider Jantz Motion 2 or Galetto Motion 2.

10 We DISMISS these motions as moot.

11
12 3. Jantz Motion 5

13 In its Motion 5, Jantz moves to exclude certain testimonial evidence Galetto
14 relies upon in Galetto Motions 1 and 2. (Jantz Motion 5, Paper 195). Because we
15 need not, and do not, consider Galetto Motions 1 and 2, we need not, and do not,
16 consider Jantz Motion 5 nor the evidence cited in the motion.

17 We DISMISS Jantz Motion 5 as moot.

18
19 C. Conclusion

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

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1 III. Order

2 It is

3 ORDERED that Jantz Motion 3 is GRANTED;

4 FURTHER ORDERED that Jantz Motions 1 and 5, and Galetto

5 Motions 1 and 2, are DISMISSED as moot; and

6 FURTHER ORDERED that judgment shall be entered against Galetto

7 in a separate paper.

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