

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

JOHN H. GRIFFIN and JUDITH GREENGARD
(08/410,488),

Junior Party,

v.

ROGIER M. BERTINA and PIETER H. REITSMA
(08/454,353),

Senior Party.

Interference No. 104,021

Before SCHAFER, LEE, and TORCZON, Administrative Patent Judges.

TORCZON, Administrative Patent Judge.

JUDGMENT

(PURSUANT TO 37 CFR § 1.658)

INTRODUCTION

After consideration of the briefs, the evidence, and the oral argument on priority, we conclude from the preponderance of the facts before us that junior party Griffin has failed to establish a reduction to practice before senior party Bertina's effective filing date.

BACKGROUND

The count and involved claims

After decision on preliminary motions (Paper No. 70), the interference was redeclared (Paper No. 71) with the following count:

A method according to claim 62 of the Bertina application

OR

A kit according to claim 81 of the Bertina application.¹

Claims 62 and 81 of the Bertina application are as follows

62. A method for diagnosing an increased risk for thrombosis of a genetic defect causing thrombosis comprising the steps of:

- (A) obtaining, from a test subject, test nucleic acid comprising codon 506 within EXON 10 of the human Factor V gene; and
- (B) assaying for the presence of a point mutation in the nucleotides of codon 506 within EXON 10 of the human Factor V gene, wherein said point mutation correlates to a decrease in the degree of inactivation of human Factor V and/or human Factor Va by activated protein C, wherein the presence of said point mutation in said test nucleic acid indicates an increased risk for thrombosis or a genetic defect causing thrombosis.

81. The kit of claim 80,^[2] wherein said forward primer is selected from the group consisting of SEQ ID NO:4, SEQ ID NO:9, and SEQ ID NO:11, and said reverse primer is selected from the group consisting of SEQ ID NO:5, SEQ ID NO:10 and SEQ ID NO:14.

¹ No evidence was presented regarding the kit alternative in the count, so this opinion will focus on the method alternative.

² Claim 80, which the examiner has deemed to be unpatentable, is:

A kit for diagnosing an increased risk from thrombosis or a genetic defect causing thrombosis comprising a forward and a reverse primer that are capable of amplifying codon 506 within EXON 10 of the human Factor V gene.

The count requires an appreciation of the significance of a mutation at codon 506 within exon 10 of the human Factor V gene to the diagnosis of an increased risk of thrombosis due to a genetic defect.

Priority cases

Junior party Griffin filed a principal brief on priority (Paper No. 94), a reply brief (Paper No. 99), and supporting exhibits. Bertina filed an opposition brief (Paper No. 97) and supporting exhibits, but elected to rely on its accorded benefit date rather than put on a separate priority case (Paper No. 96).³

Counsel for each party appeared for oral argument and ably presented the views of his client.

DISCUSSION

The only issue presented for decision is whether junior party Griffin successfully reduced to practice the invention of the count before senior party Bertina's earliest accorded benefit date (Paper No. 94 at 4; Paper No. 97 at 4 & 5). Reduction to practice requires the production and recognition of an embodiment meeting all limitations of the count and the recognition of a specific practical utility for the invention. Estee Lauder Inc. v. L'Oreal, S.A., 129 F.3d 588, 593, 44 USPQ2d 1610, 1614 (Fed. Cir. 1997). Recognition of the invention in the count cannot be established retroactively: it must be contemporaneous with the alleged priority date. E.g., Estee

³ The Griffin record is paginated as "Gxxx", where "xxx" is a three-digit number. Griffin exhibits are numbered starting with "1001". The Bertina record is paginated "Bxxxx", where "xxxx" is a four-digit number. Bertina exhibits are numbered starting with "2001".

Lauder, 129 F.3d at 593-94, 44 USPQ2d at 1614 (citing Breen v. Henshaw, 472 F.2d 1398, 1401, 176 USPQ 519, 521 (CCPA 1973)).

Facts

A junior party in an interference between co-pending applications must establish priority by a preponderance of evidence. Cooper v. Goldfarb, 154 F.3d 1321, 1327, 47 USPQ2d 1896, 1900 (Fed. Cir. 1998). Inventor testimony must be independently corroborated. Cooper, 154 F.3d at 1330, 47 USPQ2d at 1903.

F1. John H. Griffin (Dr. Griffin) and Judith S. Greengard (Dr. Greengard) are the named inventors of Griffin's involved 07/410,488 application.

F2. Griffin's involved application was filed 24 March 1995. Griffin has not been accorded benefit of any other application.

F3. Bertina's involved 08/454,353 application was filed 6 June 1995. Bertina was accorded the benefit (Paper No. 1 at 41) of Patent Cooperation Treaty (PCT) application PCT/EP95/00553, filed 14 February 1995, and of European patent application 94-200377.3, filed **14 February 1994** (the critical date).

F4. Griffin's case is that the Griffin inventors (Drs. Griffin and Greengard) identified the codon 506 mutation as a genetic cause of activated protein C (APC) resistance, which increases the risk of thrombosis, no later than **2 December 1993** (Griffin's alleged priority date) (Paper No. 94 at 15).

F5. The codon 506 point mutation is an A for G substitution at the middle nucleotide of the codon (Paper No. 94 at 15 n.2). This mutation is also identified as nucleotide 205 of

exon 10 or as nucleotide 1691 (nt 1691) of the complementary DNA (cDNA) (Paper No. 94 at 15 n.2). This mutation results in a substitution of glutamine (Q) for arginine (R) at amino acid 506 (hence, the nomenclature "R506Q" in Paper No. 70).

F6. Drs. Griffin and Greengard testified that in the summer of 1993 they were seeking mutations in Factor V protein as a cause or contributing cause of APC resistance (G019-20 & G028-29).

F7. In July 1993, Drs. Griffin and Greengard were billed for the production of the following eight twenty-base oligonucleotides (G038; Exh. 1029):

FV1 made 07-27-93
FV2 made 07-27-93
FV3 made 07-27-93
FV4 made 07-27-93
FV5 made 07-27-93
FV6 made 07-27-93
FV7 made 07-27-93
FV8A made 07-27-93

F8. The only use of such primers apparent from the record is the amplification of the DNA of Factor V cleavage sites (e.g., G028; Exh. 1001).

F9. As of 28 July 1993, Dr. Greengard intended to use the primers to examine Factor V from APC-resistant patients (Exh. 1001).

F10. By 4 August 1993, Xiao Xu, a colleague of Drs. Griffin and Greengard, had identified "best" conditions for amplifying the primers (G032; Exh. 1020).

F11. On 23 August 1993, the Centers for Disease Control and Prevention shipped to Dr. Griffin stabilized blood samples from the "S" family (G042).

F12. Jose Fernandez, another colleague of the Griffin inventors, performed a coagulation assay of the S family blood and determined that a sample from S family member "LS" exhibited APC resistance, while a sample from S family member "AS" did not (G035-36; Exhs. 1030 & 1031).

F13. On 27 August 1993, Xu amplified DNA samples from S family members, including AS and LS, using the eight primers (FV1-FV8A)⁴ as well as additional primers (FV9-FV12)⁵ (G032; Exh. 1021).

F14. On 18 October 1993, Xu prepared sequencing gels (Exh. 1023)⁶ for LS and for AS (G033; Exh. 1022) using the FV7 primer, among others. The record copy of the 18 October 1993 gel contains no indication that the nt 1691 point mutation was recognized. Exhibit 1023 indicates that AS only has a band in the G column for nucleotide 1691.

F15. On 25 October 1993, Xu again prepared sequencing gels (Exh. 1024)⁷ for LS and for AS (Exh. 1022 at 3) using the FV7 primer, among others. The record copy of the 25 October 1993 gel contains no indication that the nt 1691 point mutation was recognized. Exhibit 1024 indicates that AS only has a band in the G column for nucleotide 1691.

F16. The gels lanes are in sets of four for A, C, G, and T, respectively, running left to right. The sequence should be read up from the bottom.

⁴ Griffin's record is inconsistent in its labeling of primers. Some primers, such as FV8 variously include either an "A" or "a" designation. We assume that, for the purposes of our decision FV8, FV8A, and FV8a are the same. The critical sequencing gels in the record were made using only the FV7 primer in any case.

⁵ The primers sometimes have an "A" or "a" added to their names. If this addition indicates a different primer, then even more primers may have been tested.

⁶ Exhibit 1025 is an enlarged and labeled portion of Exhibit 1023.

⁷ Exhibit 1026 is an enlarged and labeled portion of Exhibit 1024.

F17. Whether the FV7 sequencing gels clearly show the nt 1691 point mutation for LS is a point of considerable contention.⁸ We assume, without deciding, that Drs. Griffin and Greengard could have read the sequencing gels and identified the nt 1691 point mutation with reasonable⁹ certainty.

F18. Dr. Griffin testified (G030):

15. I recall that I discussed with Dr. Judy Greengard prior to our weekly laboratory meeting on December 2, 1993, her findings of a G to A nucleotide mutation at position [1691] of [LS's] genomic DNA.

F19. Dr. Greengard testified (G023):

25. I read the sequencing films, GRIFFIN EXHIBITS 1023 and 1024, after the Thanksgiving holiday in November 1993, but before our weekly Laboratory Meeting which was held on Tuesday, December 2, 1993.

26. During my reading of these sequencing films, GRIFFIN EXHIBITS 1023 and 1024, I had noted a G to A mutation in the genomic DNA of LS at nucleotide position [1691] and discussed this finding with Dr. Griffin prior to the aforementioned weekly Laboratory Meeting on December 2, 1993.

F20. Fernandez testified (G036):

9. That prior [to] going to the American Society of Hematology meeting in St. Louis, MO held December 3 to December 7, 1993, he [Fernandez] learned from Dr. Greengard that a G to A mutation had been found at nucleotide 205 of exon 10.

⁸ In summary, Bertina's semi-independent, experienced expert (van Gemen) testified that the gels are too unclear to read with certainty. Griffin's highly experienced expert, who works for Griffin's real party-in-interest, (Sutcliffe) testified that the gels were typical of 1993 sequencing gels and were readily understandable although they might be difficult for one unskilled to read. Griffin has not pointed us to any testimony on the level of skill of the Griffin inventors at reading sequencing gels or any details about how they went about deciphering the gels.

⁹ Griffin's expert Sutcliffe distinguished between being confident that he "knew" the sequence and being sufficiently certain to publish the result (G179).

F21. While the testimony indicates that the Griffin inventors had discovered a noteworthy mutation, none of this testimony states that the inventor's recognized that they had discovered the mutation that caused the condition they were studying.

F22. A page of notes (Exh. 1032) for a lab meeting on 2 December 1993 attributed to Greengard and Xu discuss the use of the FV1-FV12 primers on eight APC functional sites in the S family. They report that "[n]ot all of these have been explored in the [S] fa[m]ily as yet." The notes show that primers FV7/8a correspond to an N-terminal APC cleavage site (Exh. 1032).

F23. The notes report (Exh. 1032) the discovery of five¹⁰ nucleotide mutations as follows:

Nucleotide	Effect on protein
2298	Silent
2325	Silent
5380	Silent
5248 (A T)	Serine Cysteine
5380 (G A)	Valine Methionine

F24. Both of the protein changes caused by mutations are in the phospholipid binding site, which is probed using primers FV3/4 (Exh. 1032).

¹⁰ The notes indicate two mutations at nucleotide 5380, one that does not change the encoded amino acid (silent) and one that does.

F25. The notes (Exh. 1032) do not report a mutation at nucleotide 1691,¹¹ a G A mutation that changes the encoded amino acid from arginine (R) to glutamine (Q), or a mutation of any sort in the N-terminal APC cleavage site probed with primers FV7 and FV8.

F26. The notes focus on the nt 5248 (Cys) mutation, indicating that Xu would sequence the phospholipid binding site where it occurs in other patients that week and that the mutation does not always show up in LS sequences and may be a "sequencing artifact" (Exh. 1032).

Analysis

If we assume that Dr. Greengard could, and did, read the FV7 sequencing gels of LS and AS on or before 2 December 1993 and then discussed her finding with Drs. Griffin and Fernandez, the evidence still does not support a conclusion that Griffin had a reduction to practice. At best, the evidence Griffin has adduced indicates that the Griffin inventors had, by 2 December 1993, identified a mutation of interest at an interesting place in a gene of interest in one affected patient.¹² Even the inventors' testimony does not attest to the possession of more. It simply says, as does the corroborating testimony of Fernandez, that they had identified a mutation. Contemporaneous documentary evidence (Exh. 1032), does not reflect this identification, but does indicate that the search for the cause was on-going, with other possible sites to explore and other patients to test.

¹¹ The "S1691C (nt A5248T)" mutation is a mutation at nucleotide 5248 (A T) that corresponds to a change at amino acid 1691 (S C).

¹² Indeed, it is questionable whether there was even a conception. That issue is not before us, but the identification of a possible cause does not seem to add up to a "a definite and permanent idea of an operative invention, including every feature of the subject matter sought to be patented". Sewall v. Walters, 21 F.3d 411, 415, 30 USPQ2d 1356, 1358-59 (Fed. Cir. 1994); Burroughs Wellcome Co. v. Barr Lab., Inc., 40 F.3d 1223, 1228, 32 USPQ2d 1915, 1919 (Fed. Cir. 1994) ("An idea is definite and permanent when the inventor has a specific, settled idea, a particular solution to the problem at hand, not just a general goal or research plan he hopes to pursue.")

This is not a case that turns on whether the test results are sufficient evidence of a reduction to practice. Even if we assume that the testing was properly done and properly interpreted, and if we further accept that the test was equivalent to the diagnostic method of the count,¹³ we still have no basis for inferring that the inventors recognized the significance of the test by 2 December 1993. With hindsight, one can see that the nt 1691 mutation is in a codon that changes the coding of a critical amino acid (arginine) at a critical place (a terminal cleavage site), which might have enhanced the significance of the identification, but the testimony of Drs. Griffin, Greengard, and Fernandez does not even go that far. All they purport to have found was a point mutation in one patient, while other evidence indicates that they had also contemporaneously identified several other mutations of interest. We cannot attribute to Griffin, nunc pro tunc, the knowledge of the significance of the nt 1691 mutation absent support in the record. The portions of the record to which we have been pointed, including the testimony of the inventors, does not support a finding that the Griffin inventors had a contemporaneous understanding of the significance of their discovery.

ORDER

Upon consideration of the arguments and evidence on priority, it is

ORDERED that judgment on priority as to count 4 is awarded against junior party

Griffin;

¹³ The test used knowledge of the disease to identify the mutation, which is the mirror image of using the mutation to identify the disease. Even assuming the test could qualify as a reduction to practice, Griffin would still have to show that the inventors recognized the correlation between that mutation and the disease.

FURTHER ORDERED that Griffin is not entitled to a patent containing application 08/410,488 claims 1-4, 7-11, 14, 19-28, 30-32, and 34-40, which correspond to Count 4;

FURTHER ORDERED that, based on the record before us, senior party Bertina is entitled to a patent containing application 08/454,353 claims 62-88,¹⁴ which correspond to Count 4; and

FURTHER ORDERED that a copy of this decision be given a paper number and be entered in the administrative records of application 08/410,488 and application 08/454,353.

RICHARD E. SCHAFER
Administrative Patent Judge

JAMESON LEE
Administrative Patent Judge

RICHARD TORCZON
Administrative Patent Judge

BOARD OF PATENT
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INTERFERENCE
TRIAL SECTION

¹⁴ Note that the examiner has separately determined that claim 80-88 are not patentable although claims 81-88 may be redrafted in independent form to avoid unpatentability (Rule 609(b) statement). This judgment on priority does not bar the examiner from pursuing this rejection.

Interference No. 104,021
Griffin v. Bertina

Paper No. 112
Page 12

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