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Filed by: Trial Section Motions Panel
Box Interference
Washington, D.C. 20231
Tel: 703-308-9797
Fax: 703-305-0942

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

RANDOLPH NOELLE
(08/742,480),
Junior Party,

v.

SETH LEDERMAN, LEONARD CHESS,
and MICHAEL J. YELLIN
(5,474,771),
Senior Party.

Patent Interference No. 104,415

Before: TORCZON, GARDNER-LANE and TIERNEY, Administrative Patent Judges.

TIERNEY, Administrative Patent Judge.

FINAL DECISION
(Decision on Lederman Preliminary Motion 8)

This interference is before a motions panel for a decision on preliminary motions. Oral argument took place on September 26, 2001. Representing Junior Party Noelle at oral argument was E. Anthony Figg and Robin L. Teskin. Senior Party Lederman was represented by James F. Haley, Jr., Margaret A. Pierri, Jane Gunnison and Stanley D. Liang. A transcript of the oral argument appears in the record. (Paper No. 134).

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I. Summary of the Opinion

This is an interference between Junior Party Noelle (real party in interest, IDEC Pharmaceuticals, Inc.) and Senior Party Lederman (real party in interest, Biogen, Inc.). The sole issue before this panel is the question of whether or not there exists an interference-in-fact between Noelle s remaining patentable claims and Lederman s claims. More particularly, there is a dispute as to whether, at the relevant time, a person of ordinary skill in the art having either the anti-mouse or anti-human CD40 counter-receptor antibodies would have had a reasonable expectation of success of obtaining the other.

Noelle has demonstrated that one skilled in the art, given the anti-mouse or anti-human antibodies, would have expected its human or mouse counterpart to exist. Moreover, Noelle has sufficiently demonstrated that screening techniques for antibodies were well known in the art at the relevant date. Nevertheless, Lederman has demonstrated that one skilled in the art, provided with Noelle s mouse claims and the prior art, would not have had a reasonable expectation of success of obtaining the anti-human antibodies. Accordingly, we hold that Lederman has sufficiently established that its human claims are not obvious or anticipated by Noelle s mouse claims. As such, no interference-in-fact exists between Noelle s remaining patentable claims and Lederman s claims.

II. Previous Decisions in the Interference

As set forth in the Memorandum, Opinion and Order (Memorandum, Paper No. 108), this interference concerns CD40 counter-receptors for the CD40 B-cell antigen and monoclonal

antibodies for these CD40 counter-receptors. CD40 counter-receptors are expressed on activated T cells and are also known as CD40CRs or CD40Ls.

This interference was declared with a single count having three alternative embodiments.[1] To simplify the terminology in this interference, the first alternative can be generally referred to as the human antibody to human CD40CR, the second alternative as mouse antibody to mouse CD40CR and the third alternative as the genus of antibodies to CD40CRs. Noelle s involved application had claims directed to all three alternative embodiments whereas Lederman s involved patent presents claims directed to only the human embodiment.

For each of its three claimed embodiments, Noelle sought 35 U.S.C. § 120 benefit of U.S. Application No. 08/338,975, filed November 14, 1994, as well as U.S. Application No. 07/835,799, filed February 14, 1992. During the course of the interference, it was determined that Noelle s genus and human embodiments lacked written descriptive support in Noelle s 799 application as of the February 14, 1992 filing date. (Paper No. 108, pages 23-33). Lacking benefit of its 1992 filing date, an Administrative Patent Judge became aware of reasons why Noelle s genus and human claims were unpatentable under 35 U.S.C. § 102(b).

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[1] The interference was declared on September 3, 1999, (Paper No. 1), with Count 1 which reads as follows:

> The monoclonal antibody of claim 1 of 5,474,771 [Lederman] or the monoclonal antibody of claim 42 or claim 51 of 08/742,480 [Noelle].

(Paper No. 1, p. 46). Claim 1 of Lederman 771 is directed to a monoclonal antibody that specifically binds and forms a complex with a 5c8 antigen (CD40CR)(human embodiment) whereas claim 42 of Noelle is directed to a monoclonal antibody or fragment thereof which specifically binds a mouse CD40CR (mouse embodiment) and Noelle claim 51 is directed to a monoclonal antibody or fragment thereof that specifically binds CD40CR (genus embodiment). (See, Paper No. 108, facts 4-7).

Accordingly, the Judge issued an Order under 37 CFR § 1.641 rejecting Noelle s genus and human claims as anticipated by the disclosures of Lederman WO 93/09812 and/or Armitage WO 93/08207. (Paper No. 109). Although reserving the right to appeal, Noelle did not contest the finding that Noelle s genus and human claims lacked written descriptive support as of the February 14, 1992 filing date and did not contest the unpatentability of these claims under 35 U.S.C. §102(b). (Lederman Preliminary Motion 8, Paper No. 116, pages 2-3, facts 4, 5, Noelle Opposition 8, Paper No. 118, p. 3, admitted facts 4 and 5).[2]

Lederman Preliminary Motions 6 and 7 sought to redefine the interfering subject matter. As noted during the oral argument of April 12, 2001, Lederman s motions were defective. Specifically, Lederman proposed counts that did not correspond to any of Lederman claims. Yet, as apparent from the motions and as noted at the oral argument of April 12, 2001, for all practical purposes Lederman Preliminary Motions 6 and 7 requested a finding of no interference-in-fact. (Order, Paper No. 109, pages 10-12).

Our Memorandum (Paper No. 108) deferred resolution of Lederman Preliminary Motions 6 and 7 as they were contingent upon Lederman s prior art patentability motions 1 and 2, which were deferred. As we determined that Noelle s human and genus claims were unpatentable to Noelle, the issue of no interference-in-fact was ripe for consideration. Counsel for both Noelle and Lederman agreed to rebrief the issue of no interference-in-fact. Specifically, times were set

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[2]Lederman filed a revised Lederman Preliminary Motion 8 (Paper No. 116) to correct what it termed typographical errors in its originally filed Lederman Preliminary Motion 8 (Paper No. 113). Lederman s revised motion was entered into the record. Accordingly, this opinion refers to the revised Lederman Preliminary Motion 8 (Paper No. 116) as Lederman Preliminary Motion 8.

for Lederman to withdraw its motions 6 and 7 and to file a new motion, Lederman Preliminary Motion 8, to correct the procedural defects noted in Lederman Preliminary Motions 6 and 7. Likewise, times were set to allow for Noelle to oppose this motion and for Lederman to reply to Noelle s opposition. (Order Setting Times, Paper No. 111, Order Setting Times, Paper No. 117, and Decision on Miscellaneous Motion, Paper No. 127).

In response to Lederman Preliminary Motion 8, Noelle has filed Noelle Opposition 8 (Paper No. 118) which identifies and relies upon exhibits 2084-2095, as well as earlier-filed exhibits. In the Order Setting Times (Paper No. 111) and in the Communication of September 10, 2001 (Paper No. 122), the parties were informed that a party wishing to submit new evidence in this interference was to submit a miscellaneous motion under 37 CFR § 1.635, which was to show good cause as to why the new evidence could not have been previously presented in the interference. Seeking to have the new evidence entered into the record, Noelle filed Noelle Miscellaneous Motion 1 (Paper No. 125) which, *inter alia*, requested: 1) entry of Noelle exhibits NX 2086, 2088, 2089, 2090-2091; and 2) withdrawal of Noelle exhibits NX 2084 and 2092-2095. (Paper No. 125, p. 2). As set forth in the Decision on Miscellaneous Motion (Paper No. 127), Noelle Exhibits NX 2086, 2088, 2090 and 2091 were entered into the record whereas Noelle Exhibits NX 2084, NX 2089 and NX 2092-2095 were ***not*** entered into the record.[3]

[3]Noelle Miscellaneous Motion 1 noted that Noelle Exhibits NX 2085 and 2087 were already in evidence as Lederman Exhibits LX 1052 and 1095, respectively. (Paper No. 125, p. 2).

III. Findings of Fact

A. Previous Findings

We reaffirm our previous findings of fact and conclusions of law made in this interference. As background information on the issue of reasonable expectation of success, we reiterate findings of fact 32, 33, 35 and 36 from our Memorandum, Paper No. 108:

> Fact 32. As of February 14, 1992, the isolation and purification of CD40 counter receptors (CD40CR) was ***not*** a predictable art. As of this date, the skilled artisan could not have predicted with any reasonable degree of certainty from Noelle s disclosure whether particular CD40CRs and the antibodies specific to the CD40CRs could be generated and isolated other than Noelle s disclosed mouse CD40CR and the antibodies specific to the mouse CD40CR. Indeed, it would have been difficult for the skilled artisan to generate and isolate the CD40CRs and antibodies specific to the CD40CRs beyond those disclosed by Noelle s application. (See generally, LX 1006, LX1007, LX 1092 and LX 1093).
>
> Fact 33. As of February 14, 1992, the construction of CD40-Ig fusion protein, such as Noelle s CD40-Ig, would have been extremely difficult. (LX 1092, ¶ 16, LX1093, ¶ 10). During the prosecution history of Noelle s parent U.S. Application No. 07/835,799, Dr. Sandro Aruffo submitted a declaration stating that:
>
> > Prior to the actual construction of the CD40-immunoglobin fusion protein disclosed and claimed in the above-identified patent application [07/835,799], I and my co-inventors could not predict whether this approach would result in a biologically active fusion protein.
>
> (Declaration of Aruffo under 37 C.F.R. 1.132 dated July 7, 1994, LX 1009, p. 2). Dr. Aruffo further stated that:
>
> > [E]ach individual fusion protein must be constructed independently, and whether a particular fusion protein can be successfully generated is often not determinable until the experiment is performed. In view of this lack of predictability, there is not a reasonable expectation of success prior to the actual

> production of a recombinant immunoglobin fusion molecule.

(Declaration of Aruffo under 37 C.F.R. 1.132 dated July 7, 1994, LX 1009, p. 3).

Fact 35. One skilled in the art reviewing the Noelle 480 application would have doubts regarding the validity of Section 7 [which discusses the binding of a CD40Ig fusion protein to human T-cell lines]. Specifically, a control should have been included in Section 7 to confirm that the reported binding is due to the CD40 moiety, rather than the Ig moiety, of the CD40-Ig fusion protein. (LX1007, ¶ 39, LX 1006, ¶ 30). Absent the proper control, one skilled in the art could not have known whether the CD40-Ig fusion protein was binding to a cell surface protein on Jurkat and HSB2 cells via the CD40 portion of the CD40-Ig molecule. (LX1007, ¶ 39, LX 1006, ¶ 30). At best, Noelle s expert, Dr. Clark, states that:

> In my opinion, ***it is more plausible than not to assume that the results in Section 7 and Figure 7 are valid***, e.g., attributable to the CD40 portion of the fusion protein as the Noelle application describes several other experiments (described in Section 6.2.3 of Noelle Application), wherein an appropriate control, i.e., CD7E-Ig was utilized and confirmed that the observed binding of the CD40-Ig to activated mouse T helper cells and CD40, and not the Ig moiety of the fusion protein.

(NX 2012, ¶ 14, emphasis added).

Fact 36. As of February 14, 1992, it would have been difficult for one of ***ordinary*** skill in the art to conduct the expression cloning methodology recited in the Noelle 480 application. (Amendment and Response filed October 1, 1993 in support of Armitage, U.S. Application No. 07/969,703, LX 1083, p. 7, LX 1092, ¶ 45 on p. 17, LX 1093, ¶ 33).

B. Additional Findings

We make the following additional findings of fact:

37. The claims of the parties are as follows:

(i) The claims of the parties were:

Noelle 480 :	42, 43, 45-48, 50-57, 59 and 60[4]
Lederman 771:	1-14

(ii) The claims of the parties which corresponded to Count 1 were:

Noelle 480 :	42, 43, 46-48, 50-54, 56, 57, 59 and 60
Lederman 771:	1-7 and 10-13

(iii) The claims of the parties which did not correspond to Count 1 are:

Noelle 480 :	45 and 55
Lederman 771:	8, 9 and 14

(Paper No. 1, p. 46). Noelle claims 51, 52, 53, 56, 59 and 60 are directed to the genus and human embodiment of Count 1. These claims have been determined unpatentable to Noelle. Accordingly, Noelle s corresponding claims are 42, 43, 46-48, 50, 54, and 57.

38. At the relevant time, one skilled in the art believed that the induction of B lymphocyte responses was a complex process. Specifically, one skilled in the art believed:

> The induction of B lymphocyte responses is a complex process that is initiated and regulated by T lymphocytes. T cells effect B cell responses via direct cell-cell contact or by means of soluble cytokines. Although early studies focused on the role of surface Ig in the activation of B cells, more recent studies have suggested that surface Ig facilitates the capacity of B cells to take up specific Ag and present it to T cells in a MHC-restricted manner, but may not otherwise be involved in T cell-B cell collaboration. ***The precise mechanisms by which T cells stimulate B cells remains unclear***.

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[4]Noelle originally cited claim 58 as a pending claim. (Noelle s Clean Copy of Pending Claims, Paper No. 7). Claim 58, however, was cancelled by Examiner s Amendment during the prosecution of the 480 application. (Noelle Clarification of Status of Claim 58, Paper No. 45, 480 Prosecution History, Examiner s Amendment, Paper No. 10, mailed August 12, 1998).

(LX 1095, p. 2544, right col., lines 8-18, emphasis added).

39. At the relevant time, one skilled in the art understood that:

> [A] variety of receptor ligand interactions appeared to be involved in the collaboration with activated T cells inducing B cell proliferation and differentiation.

(LX 1095, p. 2545, left col., lines 7-10).

40. Prior to the earliest application filing dates of Lederman and Noelle, it was known that both human and mouse B cells expressed CD40, an antigen involved in B cell differentiation. (LX 1079, p. 35, last ¶, Paper No. 118, p. 5, fact 32, Paper No. 129, p. 1, admitting fact 32).

41. In April 1991, i.e., prior to the earliest application filing dates of both Lederman and Noelle, Lederman published an abstract (Lederman et al., Clin. Res. 39(2):380A, April 1991, NX 2086) regarding the mechanism of inducing B cell differentiation by a CD4- Jurkat clone, identified as Jurkat clone (D1.1). This abstract suggested that molecular features on the D1.1 human T cell line, other than a lack of CD4, accounted for a constitutive ability to induce B cell activation. (NX 2086, page 380A, last line).

42. At the relevant time, the known existence of the mouse CD40CR and the general conservation in function of immune cell molecules across species would have suggested the existence of the corresponding human CD40CR. (See generally, NX 2012, ¶¶ 17, 18).

43. One skilled in the art studying B cell responses, at the relevant time, would have found it difficult to extrapolate the results obtained from anti-mouse CD40CR antibodies to anti-human CD40CR antibodies. Specifically:

> [D]ifferences between the regulation of human and murine B cells make it additionally difficult to extrapolate the results obtained from one system to another.

(LX 1095, p. 2544, right col., lines 39-42).

44. Immunization with activated human T cells or activated or non-activated cell lines, such as Jurkat and HSB2, would raise a number of known and unknown T cell proteins such as CD4, OX40 receptor, CD25, MHC class II and ICAM-1. (LX 1093, Second Kelsoe Declaration, ¶ 26).

IV. Lederman Preliminary Motion 8

Lederman Preliminary Motion 8 moves for judgment, and termination of this interference on the grounds that there is no interference-in-fact between Lederman s human claims and Noelle s mouse claims. (Lederman Preliminary Motion 8, Paper No. 116, p. 1). Noelle opposes this motion.

A. No Interference-In-Fact is a One-Way Distinctiveness Test

The question of whether there is no interference-in-fact is a one-way distinctiveness test. Specifically, a movant can establish that no interference-in-fact exists by showing that its claimed

invention is patentably distinct from the opponents claimed invention. See Example 20[5], Notice of Final Rule, Patent Interference Proceedings, 49 Fed. Reg. 48416, 48424 (col. 1) (Dec. 12, 1984). Thus, for Lederman to succeed in its motion for no interference-in-fact, Lederman need only demonstrate that: (i) Lederman s claims are not anticipated or rendered obvious by Noelle s remaining mouse claims; ***or*** (ii) Noelle s remaining mouse claims are not anticipated or rendered obvious by Lederman s claims.

1. Anticipation is Not an Issue in this Interference

Both Noelle and Lederman agree that their corresponding claims, read in light of the prior art, do not anticipate each others claims. (Noelle Opposition 8, Paper No. 118, p. 21, Lederman Reply 8, Paper No. 129, p. 4).

2. Obviousness Requires Both Motivation and Reasonable Expectation of Success

As to obviousness, both parties agree that a proper analysis under § 103 requires, *inter alia*, consideration of two factors: (i) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed subject matter; and (ii) whether the

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[5]Example 20. Application AD contains patentable claim 1 (6-cylinder engine). Application AE contains patentable claim 3 (8-cylinder engine). An interference is declared with a single count (6 or 8-cylinder engine). Claim 1 of application AD and claim 3 of application AE are designated to correspond to the count. Applicant AD believes that a 6-cylinder engine is a separate patentable invention (See § 1.601(n)) from an 8-cylinder engine. Applicant AD would file a motion under § 1.633(b) for judgment on the ground of no interference-in-fact stating why a 6-cylinder engine is patentably distinct from an 8-cylinder engine. If the Board ultimately agrees with Applicant AD, a patent could issue to AD containing claim 1 of application AD and a second patent could issue to AE containing claim 3 of application AE.

prior art would also have revealed that in making the claimed subject matter, those of ordinary skill would have a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991); *In re Dow Chem.*, 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

a. Motivation is Not an Issue in this Interference

The parties agree that, at the relevant date, the skilled worker having anti-human CD40CR antibodies or anti-mouse CD40CR antibodies would have been motivated to obtain the other. (Noelle Opposition 8, Paper No. 118, p. 21, Lederman Reply 8, Paper No. 129, p. 4).

b. Reasonable Expectation of Success

The parties disagree as to whether or not a reasonable expectation of success existed at the relevant date. Specifically, the parties disagree as to whether a person of ordinary skill in the art having either the anti-mouse or anti-human CD40CR antibodies would have had a reasonable expectation of success of obtaining the other.

A reasonable expectation of success is not a requirement of absolute predictability. Only a reasonable expectation that the beneficial result will be achieved is necessary to show obviousness. *Brown & Williamson Tobacco Corp. v. Philip Morris, Inc.*, 229 F.3d 1120, 1125, 56 USPQ2d 1456, 1459 (Fed. Cir. 2000); *In re Longi*, 759 F.2d 887, 897, 225 USPQ 645, 651 (Fed. Cir. 1985). A critical step in analyzing these expectations is casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the

prior art references and the then-accepted wisdom in the field. *In re Kotzab*, 217 F.3d 1365, 1369, 55 USPQ2d 1313, 1316 (Fed. Cir. 2000).

Both parties have predominantly addressed their arguments and evidence to the issue of whether Noelle s claimed anti-mouse CD40CR antibodies would, in light of the prior art, have provided a reasonable expectation of success of obtaining Lederman s claimed anti-human CD40CR antibodies. Noelle justifies this focus by noting that its alleged prior art screening methodology works in either direction, i.e., mouse to human or human to mouse. (Transcript of Sept. 26, 2001 Oral Argument, Paper No. 134, p. 52, lines 1-10). As the parties have focused on the expectation of success for obtaining Lederman s claimed anti-human CD40CR antibodies, we adopt a similar focus.

Lederman argues that, as of the relevant date, there would not have been a reasonable expectation of success of obtaining a monoclonal antibody specific to human CD40CR antigen using a monoclonal antibody specific to mouse CD40CR antigen. (Paper No. 116, pages 16-17). Lederman further alleges that there were no processes available at that time for obtaining an anti-human CD40CR monoclonal antibody or its antigen with a reasonable expectation of success. (Paper No. 116, pages 17-19). Noelle disagrees.

According to Noelle, the parties [sic] disclosures, coupled with the high level of skill in the art at the time, provided a reasonable expectation of success in making monoclonal antibodies to both the murine and human CD40CR antigens. (Paper No. 118, p. 3). Indeed, Noelle s expert, Dr. Edward Clark, has testified that Noelle s 480 application provided at least three different methods for making anti-CD40CR antibodies. (Declaration of Edward A. Clark,

NX 2012, p. 23, ¶ 30). Generally, the three methods mentioned by Dr. Clark are:

1) Immunization of a host with CD40CR expressing cells or cell line and selection of anti-CD40CR antibody by functional or competition binding with CD40Ig fusion protein;

2) Isolation of CD40CR by Affinity Purification using CD40Ig to precipitate at least human and mouse CD40CRs; and

3) Use MR1 monoclonal antibody or CD40Ig fusion to clone CD40CR DNA and use expression product to produce anti-CD40CR antibody.

(NX 2012, pages 23-33, ¶¶ 30-47). Noelle s opposition appears to focus upon an alleged reasonable expectation of success for the first method, immunization and screening, and the second method, using CD40Ig to co-precipitate its human counterpart ligand, human CD40CR.

Noelle s opposition argues that one skilled in the art had a reasonable expectation of success of obtaining Lederman s claimed anti-human CD40CR antibodies using immunization techniques, Dr. Clark s first method, or a precipitation technique involving a soluble CD40Ig protein, Dr. Clark s second method. Specifically, Noelle s opposition alleges that monoclonal antibodies to human CD40CR could be produced without undue experimentation since it was expected that CD40CR was expressed on activated human T-cells and:

> Also, it would be obvious to produce a population of hybridomas secreting monoclonal antibodies to activated human T-cell surface antigens and screen to identify those which express antibodies specific to CD40CR using known and available techniques. For example, a skilled person would have screened the hybridomas to identify monoclonal antibodies that block T-cell activation of B-cells. (NX 2012, ¶39). Such screening would not rise to the level of invention. The Federal Circuit has held particularly that routine screening of large populations of hybridomas does not constitute undue experimentation. *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed Cir. 1988).
>
> The Noelle application teaches that monoclonal antibodies that specifically bind human CD40CR and T cells which express human CD40CR could be

> identified by use of the hCD40Ig fusion protein as a screen. On [sic] of ordinary skill would reasonably expect anti-human CD40CR antibodies to compete with soluble CD40Ig for binding to activated human T_h cells, and immunoprecipitate the same protein expressed on activated human T_h cells.

(Paper No. 118, pages 14-15).

During the oral argument of Sept. 26, 2001, Noelle appears to have moved away from its reliance on the teachings of its own specification. During the oral argument Noelle relied more upon a combination of allegedly conventional immunization and screening techniques. For instance, at oral argument, Noelle took the position that one skilled in the art had a reasonable expectation of success of obtaining the anti-human antibodies by a combination of: (1) activating T-cells; (2) immunizing a mouse with activated mouse or human T_h-cells and preparing hybridomas that produce the resulting antibodies; (3) conducting a +/- screening using activated and resting T-cells; and, (4) conducting functional screening. (See, Paper No. 133, Noelle Hearing Visual Aids, Tabs 1-6). Noelle also argued that one skilled in the art could immunoprecipitate the human CD40CR using CD40Ig. (See, Paper No. 133, Noelle Hearing Visual Aids, Tab 7).[6] Noelle s alleged expectation of success for the three methods said to be disclosed by the Noelle application as well as the methods specifically identified in Noelle s opposition and those identified at oral argument are discussed below.

i. Noelle s Reliance on the Parties Specifications is Misplaced

At the outset, we note that Noelle s opposition relies extensively on the disclosures of the

[6]We commend both parties for the concise and informative visual aids that were provided at the oral argument of September 26, 2001.

Noelle and Lederman applications to provide one skilled in the art with a reasonable expectation of success of obtaining Lederman s claimed subject matter. For example, Noelle states:

> The parties disclosures, coupled with the high level of skill in the art at the time, provided a reasonable expectation of success in making monoclonal antibodies to both the murine and human CD40CR antigens.

(Paper No. 118, p. 3). The parties specifications, however, are not available as prior art for determining whether an interference-in-fact exists.

An interference-in-fact exists when:

> An *interference-in-fact* exists when at least one claim of a party that is designated to correspond to a count and at least one claim of an opponent that is designated to correspond to the count define the same patentable invention.

37 CFR § 1.601(j)(emphasis in original). The test for whether claims define the same or separate patentable inventions is as follows:

> Invention "A" is the *same patentable invention* as an invention "B" when invention "A" is the same as (35 U.S.C. 102) or is obvious (35 U.S.C. 103) in view of invention "B" assuming invention "B" is prior art with respect to invention "A". Invention "A" is a *separate patentable invention* with respect to invention "B" when invention "A" is new (35 U.S.C. 102) and non-obvious (35 U.S.C. 103) in view of invention "B" assuming invention "B" is prior art with respect to invention "A".

37 CFR § 1.601(n)(emphasis in original). Thus, interference-in-fact questions require an analysis of whether or not a parties corresponding ***claims*** anticipate or render obvious the opposing parties corresponding ***claims***.

In determining whether an invention is a separate patentable invention, the parties specifications underlying the respective corresponding claims are not considered prior art. The

specifications, however, could be relied upon to serve as a dictionary for the terms appearing in the claims or for admissions against interest regarding prior art.

Noelle s reliance on the parties specifications is misplaced. Specifically, Noelle has attempted to rely on the parties disclosures as evidence that the claimed monoclonal antibodies could be produced without undue experimentation. For example, Noelle states that:

> [B]oth the ***Noelle and Lederman application*** **[sic]** ***similarly teach reproducible methods*** for producing monoclonal antibodies against an antigen (CD40CR) expressed by activated T cells and selecting appropriate (anti-CD40CR) monoclonal antibodies from the population of monoclonal antibodies obtained based on function or binding characteristics (inhibition of contact-dependent T/B cell activation, binding to an antigen expressed by activated T cells involved in B cell activation and/or competition with soluble human CD40-Ig for binding to activated T cells.) The ***Noelle application provides a reagent, soluble human CD40Ig***, that was a powerful tool for the identification of human CD40CR-expressing T cells for making monoclonal antibodies against human CD40CR or to affinity purify human CD40CR with a reasonable expectation of success.

(Paper No. 118, p. 18, lines 10-13, emphasis added). The parties corresponding claims are directed to: (i) monoclonal antibodies or fragments thereof; (ii) cell lines producing the antibodies and; (iii) pharmaceutical or diagnostic compositions containing the antibodies or fragments thereof. The corresponding claims are not directed to particular methods for producing monoclonal antibodies or to Noelle s CD40Ig fusion protein. As such, Noelle s opposition does not rely upon the parties specifications to define the terms of the corresponding claims, but rather, Noelle relies upon the specifications as prior art references without showing how the specifications are admissions of, or references to, prior art. Accordingly, we discount those portions of Noelle s opposition that rely upon the parties specification as evidence of an expectation of success.

ii. Prior Art Immunization Techniques Conventional But Lacked Reasonable Expectation of Success

According to Lederman, immunization techniques, such as those described in Noelle s application, would not have provided a reasonable expectation of obtaining a monoclonal antibody specific to human CD40CR. In particular, Lederman argues that there was no available reagent that would permit the specificity of the generated antibodies to be determined. Additionally, Lederman states that a person skilled in the art would not have been able to generate antibodies to the CD40CR antigen present on activated human T cell or cell membranes of activated human T cells as the kinetics of expression of the human CD40CR antigen were unknown at the relevant time and that CD40CR is not constitutively expressed on activated human T cells. (Paper No. 116, p. 18).

In contrast, Noelle argues that one skilled in the art would have had a reasonable expectation of success in producing a monoclonal antibody to the human CD40CR antigen. First, Noelle alleges that it would have been obvious to one of ordinary skill in the art to produce a set (S1) of hybridomas that secrete monoclonal antibodies to activated human T-cell surface antigens. Once the population S1 had been generated, Noelle alleges that, using known and available techniques, one skilled in the art could then screen the population to identify those hybridomas that express antibodies specific to CD40CR. (Paper No. 118, p. 14).

Noelle s opposition cites three particular screening techniques, +/- screening, functional screening and competitive binding assay, that could be used to identify the desired hybridomas and their antibodies. (Paper No. 118, pages 14, 18 and 19). The +/- screening technique involves the testing population S1 of hybridomas to identify a subset (S1a) of hybridomas that express

antibodies that bind to activated helper T-cells and not to resting helper T-cells. (Paper No. 118, p. 20 and, Paper No. 133, Noelle Hearing Visual Aids, Tab 4). The functional screening technique involves testing a specific antibody to determine whether that antibody blocks T-cell activation of B-cells. (Paper No. 118, p. 14, Paper No. 133, Noelle Hearing Visual Aids, Tabs 5 and 6). The third screening technique, competitive binding assay, is based upon an alleged expectation that anti-human CD40CR antibodies would compete with soluble CD40Ig for binding to activated human T_h cells, and immunoprecipitate the same protein expressed on activated human T_h cells. (Paper No. 118, pages 15, 19).

At the outset, we note that Noelle has cited and relied upon the Federal Circuit s decision in *In re Wands* as evidence that screening was a known and available technique and that such screening would not rise to the level of invention. The situation in *Wands*, however, is distinguishable from the facts of the present case. Specifically, in *Wands* the starting materials, e.g., the HbsAg antigen, were available to the public whereas in the present case the CD40CR antigen was not available. 858 F.2d at 736, 8 USPQ2d at 1404.

At the relevant time, we find that the known existence of the mouse CD40CR antigen and the general conservation in function of immune cell molecules across species would have suggested the existence of the corresponding human CD40CR antigen. As such, one skilled in the art would have been motivated to identify and obtain anti-CD40CR antibodies via various conventional techniques, e.g., immunization and screening techniques. Yet, while the idea of using immunization and screening techniques to obtain anti-human CD40CR antibodies may have been obvious to try, the realization of that idea would not have been obvious. There were

many potential pitfalls. Hindsight is not a justifiable basis on which to find that ultimate achievement of a sought after and difficult scientific goal was obvious. *See, Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1209, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991).

As argued by Lederman, one skilled in the art did not have a reasonable expectation that any particular activated human T cells expressed CD40CR. (Paper No. 116, p. 6, LX 1093, ¶ 53). Moreover, Lederman argues that one skilled in the art had no reasonable expectation of identifying which activated cells produced the required antigen or of isolating the antigen itself. (Paper No. 116, pages 6-7). Yet, Noelle s alleged immunization technique requires activated human T cells as a source of human CD40CR.

Noelle argues that one skilled in the art, using Noelle s CD40Ig, could have selected the appropriate T cells. (Paper No. 118, pages 15, 18 and 20). For example, Noelle states:

> Lederman also alleges that producing a monoclonal antibody against activated human T cells or T cell lines or membranes would be complicated by the fact that CD40CR is not constitutively expressed on activated human T cells. Noelle s response is that the ordinary (constitutive) expression not only was not necessary, the availability of activated cells expressing the antigen and resting cells that did not [express the antigen] provide a useful +/- screening tool. (NX 2087). ***The ordinarily skilled artisan would have known how to select T cells that express CD40CR on their cell surface using methods disclosed in the Noelle application***, e.g., based on their reactivity with human CD40Ig using flow cytrometry and a labeled hCd40Ig fusion protein. This procedure is disclosed at page 15, line 14 to page 16, line 2 of the ***Noelle application***, and would have been readily apparent to those skilled in the art. (NX 2012, ¶ 25).

(Paper No. 118, pages 19-20, emphasis added).

As discussed above, Noelle cannot rely upon the teachings of its application as prior art evidence to demonstrate the obviousness of Lederman s corresponding claims. Moreover, as discussed below, one skilled in the art would not have possessed a reasonable expectation of

success of forming a CD40Ig fusion protein, which could then be used to obtain the claimed CD40CR antibodies. Thus, on this record, we conclude that Lederman has provided sufficient evidence to support a conclusion that, at the relevant time, one skilled in the art would not have had a reasonable expectation of success of identifying the activated T cells that produced the required CD40CR antigen or of isolating the antigen itself. Yet, we also conclude that Lederman has failed to provide sufficient evidence to convince us that this specific diminished expectation of success is, by and of itself, dispositive of the issue of whether one skilled in the art had a reasonable expectation of success of obtaining the parties claimed subject matter, i.e., the desired antibodies or fragments thereof, cell lines and pharmaceutical compositions.

Even assuming that one skilled in the art had a reasonable expectation of success of identifying activated T-cell lines that expressed CD40CR, we conclude that the screening techniques cited by Noelle lacked a reasonable expectation of success. Noelle s +/- screening technique would lead to the identification of multiple antibodies and not just the claimed anti-human CD40CR antibody. The +/- screening technique merely creates a subset of antibodies S1a that bind to activated helper T-cells and not resting T-cells. Similarly, as there are many antibodies that inhibit B cell activation, Noelle s functional screening technique would lead to the identification of a subset (S1b) of antibodies. Moreover, as discussed in detail below, one skilled in the art did not have a reasonable expectation of success of making a CD40Ig.

Noelle has failed to convince us that only the desired anti-CD40CR antibody is in both the S1a and S1b sets or that one skilled in the art could specifically identify and obtain the desired antibody out of the various screened subsets. As such, we are not convinced that one

skilled in the art, at the relevant date, would have a reasonable expectation of success that the anti-CD40CR antibodies could be obtained by the functional and +/- screening techniques, whether used alone or in combination.

We hold that the combination of Noelle s anti-mouse CD40CR antibodies, the motivation to isolate the anti-human CD40CR antibodies and the conventional screening techniques of the prior art do not render Lederman s claimed anti-human CD40CR antibodies obvious, but at most simply suggested a path of inquiry for an inventor to try.[7]

iii. Prior Art Construction of CD40-Ig Fusion Protein Lacked Reasonable Expectation of Success

Lederman argues that the use of a human CD40Ig fusion protein would not have enabled the production of human CD40CR as the synthesis of such a fusion protein, at the relevant date, would have been extremely difficult. As evidence, Lederman cites our Memorandum (Paper No. 108), fact ¶ 33, which quotes from an affidavit made by Dr. Aruffo (LX 1009) during the prosecution of Noelle s parent U.S. Application No. 07/835,799. In the affidavit, Dr. Aruffo

[7] Additionally, we note Noelle has argued that the prior art to both Lederman and Noelle suggested the existence of the CD40CR antigen. (Paper No. 134, p. 38, lines 4-18). Noelle has also argued that one skilled in the art would have been motivated to obtain the antibodies to the CD40CR antigen. (Paper No. 134, p. 39, lines 6-14). Furthermore, Noelle has argued that it would have been obvious to obtain the antibodies via known and available immunization and screening techniques and that such screening would not rise to the level of invention. (Paper No. 118, p. 14). As evident from the oral argument of September 26, 2001, if we accepted Noelle s contention that the prior art provided both: (1) the motivation to obtain the claimed anti-CD40CR antibodies; and (2) conventional methods for which one skilled in the art had a reasonable expectation of success of obtaining the claimed anti-CD40CR antibodies, we could be led to a conclusion that the parties claims were obvious over the prior art. As we find that, as of the relevant date, one skilled in the art did not possess a reasonable expectation of success, we need not explore this issue.

unequivocally stated that there was not a reasonable expectation of success prior to the actual production of a recombinant immunoglobin fusion molecule. (LX 1009, p. 3).

Noelle, however, relies upon a CD40Ig fusion protein, such as that disclosed in Noelle s application, as a potential technique that could be used to immunoprecipitate CD40CR. (Paper No. 118, p. 15). Moreover, Noelle argues that the CD40Ig described in the Noelle application provides a powerful tool for the identification of human CD40CR-expressing T cells. (Paper No. 118, p. 18).

Noelle contends that whether or not the formation of a CD40Ig fusion protein was unpredictable prior to Noelle s invention is not relevant to the facts of this case. Indeed, Noelle argues that whether the synthesis of this fusion protein and the properties thereof was unpredictable is a moot issue in light of the disclosure contained in Noelle s application. (Paper No. 118, pages 20-21).

As stated above, Noelle may not rely upon the teachings of its specification as evidence of the existence of a CD40Ig fusion protein. Moreover, we credit Dr. Aruffo s undisputed testimony with regards to the unpredictability and lack of a reasonable expectation of success of forming a CD40Ig fusion protein. From this, we conclude that one skilled in the art would not have possessed a reasonable expectation of success of forming a CD40Ig fusion protein, which could then be used to obtain the claimed CD40CR antibodies.

iv. Prior Art Expression Cloning Techniques Lacked Reasonable Expectation of Success

Additionally, while not argued by Noelle in its opposition or at oral argument, we take

this opportunity to reiterate our finding from the Memorandum regarding the third method mentioned by Dr. Clark, expression cloning, and the conclusions that flow from this finding. As set forth in the Memorandum, as of February 14, 1992, it would have been difficult for one of ordinary skill in the art to conduct the expression cloning methodology recited in the Noelle 480 application. (Paper 108, p. 16, fact 36). Moreover, as stated during the prosecution of U.S. Application 07/969,703:[8]

> [A]pplicants submit that, at the time they began their efforts to clone a CD40-L [i.e., CD40CR], the skilled artisan could not have approached expression cloning with a reasonable expectation of success (this is still true today [October 1993]).

(October 1, 1993, Amendment and Response and Exhibits attached thereto, filed in U.S. Application 07/969,703, LX 1083). At the relevant time, we conclude that one of ordinary skill in the art would not have had a reasonable expectation of success of obtaining the desired anti-human CD40CR antibodies using a prior art expression cloning technique. (LX 1093 ¶¶ 32 and 33 and LX 1092, page 17, ¶ 45).

3. Lederman s Human Claims Would Not Render Obvious Noelle s Mouse Claims

Lederman argues that Noelle s mouse claims would have been unobvious over Lederman s human claims due to a lack of a reasonable expectation of success. Noelle, however, argues that one skilled in the art would have reasonably expected that a monoclonal antibody to mouse CD40CR could be generated by use of activated mouse T cells or membranes

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[8]The 07/969,703 application is assigned to Immunex Corporation. The inventors of this application are said to be Dr. Richard Armitage, William C. Fanslow and Melanie K. Spriggs. Noelle did not request cross-examination of the inventors of this application.

as an immunogen, and screening for monoclonal antibodies that inhibit B cell activation and which bind to an antigen having a similar size to human CD40CR.

We concluded above that one skilled in the art lacked a reasonable expectation of success of obtaining Lederman s claimed human subject matter when provided with Noelle s mouse subject matter and using the screening techniques cited by Noelle. Likewise, we conclude that one skilled in the art would have lacked a reasonable expectation of success of obtaining Noelle s claimed mouse subject matter when provided with Lederman s claimed human subject matter and using these same screening methods. Additionally, we find that the alleged similarity in size does not help Noelle. Specifically, as noted by Lederman, the antigen bound by Lederman s anti-human CD40CR antibody is said to have a molecular weight of 30 kilodaltons whereas Noelle s anti-mouse CD40CR antibody binds an antigen that is said to have a molecular weight of 39 kilodaltons. (Paper No. 129, p. 8). Moreover, Noelle s expert, Dr. Clark, has testified that:

> [M]olecular weight determinations made by use of SDS-PAGE electrophoresis procedures are well known to be *subject to significant variability*, dependent upon factors including the extent of glycosylation of protein, the nature of polyacrylamide SDS gel, buffer conditions, among other factors.

(NX 2012, ¶ 26, emphasis added). Thus, one skilled in the art may have had doubts regarding the accuracy of the molecular weight determinations for the antigens. Furthermore, even if one skilled in the art were informed that Lederman s antigen had a molecular weight of 30 kilodaltons, it is unclear whether the person of ordinary skill in the art would have had a reasonable expectation of success of obtaining the mouse antigen, which was reported to have a molecular weight of 39 kilodaltons.

4. Dispute over Structural and Functional Obviousness

Lederman argues that a monoclonal antibody specific to human CD40CR antigen is structurally, chemically and functionally distinct from a monoclonal antibody specific to mouse CD40CR antigen. (Paper No. 116, p. 12). According to Lederman, because the structures and functions of the mouse and human antibodies are distinct and unobvious over each other, there is no interference-in-fact between the parties. Noelle disputes this contention. As we have determined that there was no reasonable expectation of success of obtaining either party s corresponding claimed subject matter starting from the others corresponding claims, this issue is moot.

V. Decision on Deferred Motions

Our Memorandum (Paper No. 108), deferred several preliminary motions. In particular, Lederman Preliminary Motions 1 and 2 were deferred and Noelle Preliminary Motions 1-4 were deferred.[9]

Noelle Preliminary Motions 1 and 3 request that the interfering subject matter be redefined. In light of our holding that none of Noelle s remaining corresponding patentable claims interferes with any of Lederman s corresponding claims, these motions are ***denied***.

Noelle Preliminary Motions 2 and 4 are contingent upon Noelle Preliminary Motions 1 and 3 and request priority benefit of an earlier filed Noelle application. As Noelle Preliminary Motions 1 and 3 are denied, Noelle Preliminary Motions 2 and 4 are also ***denied***.

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[9]Lederman Preliminary Motions 6 and 7 were also deferred, however, Lederman has withdrawn these motions from our consideration.

Lederman Preliminary Motions 1 and 2 generally request judgment against Noelle s human and genus claims on the grounds that they are unpatentable over prior art. Noelle, however, did not contest our finding that Noelle s genus and human claims lacked written descriptive support as of the February 14, 1992 filing date and did not contest the unpatentability of these claims under 35 U.S.C. §102(b). We note, however, that Lederman Preliminary Motion 1 does allege that certain Noelle mouse claims are unpatentable over prior art. In light of our decision that there is no interference-in-fact and as Noelle s claims are present in a pending U.S. application, a determination as to the patentability of Noelle s mouse claims is best resolved outside the course of this interference. Moreover, it is our understanding that Lederman has agreed to this procedure. Thus, Lederman Preliminary Motions 1 and 2 are dismissed as ***moot***.

VI. Conclusion

Lederman has demonstrated that, as of the relevant date, one of ordinary skill in the art would not have had a reasonable expectation of success of obtaining an anti-mouse CD40CR antibody or an anti-human CD40CR antibody. Accordingly, we hold that Lederman has established that its claimed human embodiment is patentably distinct from Noelle s claimed mouse embodiment and *vice-versa.* Thus, we ***grant*** Lederman Preliminary Motion 8.

VII. Order

It is:

ORDERED that Lederman Preliminary Motion 8 is ***granted***.

FURTHER ORDERED that no interference-in-fact exists between claims 1-7 and 10-13 of Lederman, U.S. Patent No. 5,474,771 and claims 42, 43, 46-48, 50, 54, and 57 of Noelle, U.S. Application No. 08/742,480.

FURTHER ORDERED that Noelle is not entitled to a patent containing claims 51, 52, 53, 56, 59 and 60 of Noelle, U.S. Application No. 08/742,480.

FURTHER ORDERED that a copy of this final decision shall be placed and given a paper number in the file of Lederman, U.S. Patent No. 5,474,771 and Noelle, U.S. Application No. 08/742,480.

RICHARD TORCZON Administrative Patent Judge	)	
SALLY GARDNER-LANE Administrative Patent Judge	)	BOARD OF PATENT APPEALS AND INTERFERENCES
MICHAEL P. TIERNEY Administrative Patent Judge	)	

cc: (via Federal Express)

Counsel for Noelle:

Anthony Figg
ROTHWELL, FIGG, ERNST & MANBECK, PC
555 Thirteenth Street, NW
Washington DC 20004
Tel: (202) 783-6040
Fax: (202) 783-6031

Counsel for Lederman:

James F. Haley, Jr., Esq.
Margaret A. Pierri
Jane T. Gunnison
Stanley D. Liang
FISH & NEAVE
1251 Avenue of the Americas, 50th Floor
New York, New York 10020
Tel: (212) 596-9000
Fax: (212) 596-9090