United States District Court,
D. Delaware.

AMGEN, INC., Immunex Corporation, Amgen USA Inc., Amgen Manufacturing Limited, and Immunex Rhode Island Corporation,
Plaintiffs.
v.
ARIAD PHARMACEUTICALS, INC., and The Whitehead Institute For Biomedical Research,
Defendants.
Ariad Pharmaceuticals, Inc., Massachusetts Institute Of Technology, The President And Fellows Of Harvard College, And The Whitehead Institute For Biomedical Research,
Counterclaim Plaintiffs.
v.
Amgen Inc., Immunex Corporation, Amgen USA Inc., Amgen Manufacturing Limited, Immunex Rhode Island Corporation, and Wyeth,
Counterclaim Defendants.

C.A. No. 06-259-MPT

Sept. 19, 2008.

Background: Competitors brought action against owners of patent pertaining to human lymphoid-cell nuclear factors binding to gene elements seeking a judgment of invalidity and non-infringement, and patent owners counterclaimed for infringement. A claim construction hearing was conducted on several disputed terms.

Holdings: The District Court, Mary Pat Thynge, United States Magistrate Judge, held that:
(1) term "NF-kB" meant a protein having each NF-kB activity;
(2) term "cells" meant intact cells, whether in cell culture or living tissue, as opposed to cell extracts;
(3) term "reducing NF-kB activity in cells" meant taking action inside cells to directly inhibit an NF-kB activity;
(4) term "NF-kB-mediated intracellular signaling" meant molecular communication within cells effected by, or conveyed through, NF-kB;
(5) term "such that NF-kB-mediated intracellular signaling is diminished" meant such that there is a decrease of any molecular communication within cells effected by, or conveyed through, NF-kB;
(6) term "mammalian cells" meant cells that come from a species falling within the class of mammals; and
(7) term "human cells" meant cells that come from a human being.

Ordered accordingly.

6,410,516. Construed.

Melanie K. Sharp, Mary Frances Dugan, Young, Conaway, Stargatt & Taylor, Wilmington, DE, for Plaintiffs.

John G. Day, Steven J. Balick, Lauren E. Maguire, Tiffany Geyer Lydon, Ashby & Geddes, Frederick L. Cottrell, III, Anne Shea Gaza, Richards, Layton & Finger, Wilmington, DE, for Defendants.

MEMORANDUM ORDER

MARY PAT THYNGE**, United States Magistrate Judge.**

INTRODUCTION

This is a patent case. On April 20, 2006, Amgen, Inc. and related entities (collectively "Amgen") filed a declaratory judgment action asserting that each claim of U.S. Patent No. 6,410,516 ("the '516 patent") is invalid and not infringed. ARIAD Pharmaceuticals, Inc., and others, (collectively "ARIAD") counterclaimed for infringement of certain claims of the '516 patent. On June 19, 2008, the court conducted a Markman FN1 hearing on the parties' respective constructions of several disputed terms of the asserted claims. This order sets forth the court's construction of those claims.

FN1. Markman v. Westview Instruments, Inc., 52 F.3d 967 (Fed.Cir.1995).

THE COURT'S CLAIM CONSTRUCTION

At Wilmington, this 19th day of September, 2008, having reviewed the papers submitted with the parties' proposed claim constructions, heard oral argument, and having considered all of the parties arguments;

IT IS ORDERED, ADJUDGED, and DECREED that the disputed claim language in asserted claims of the '516 patent, as identified by the parties, shall be construed consistent with the tenets of claim construction set forth by the United States Court of Appeals for the Federal Circuit in Phillips v. AWH Corp.,FN2 as follows:

FN2. 415 F.3d 1303 (Fed.Cir.2005).

1. *NF-kB*

[1] Amgen's proposed construction is "a protein having each NF-kB activity." FN3

FN3. Each of the parties' proposed constructions is found in their Joint Claim Construction Chart.

ARIAD's proposed construction is "a DNA-binding protein factor found in many eukaryotic cells that: (a) is constitutively present in the cytoplasm of unstimulated cells as an inactive complex, bound to inhibitory I-kB proteins; (b) upon dissociation from I-kB, translocates to the nucleus of the cell; and (c) once in the nucleus, mediates the transcription of certain genes by binding to specific DNA recognition sequences in

those genes."

The court adopts Amgen's proposed construction and determines this phrase means: "a protein having each NF-kB activity." FN4

FN4. *See, e.g.,* '516 patent, 2 :26-31("As described herein, it has subsequently been shown that transcription factor NF-kB, previously thought to be limited in its cellular distribution, is, in fact, present and inducible in many, if not all, cell types and that it acts as an intracellular messenger capable of playing a broad role in gene regulation as a mediator of inducible signal transductions."); '516 patent, 2 :36-40 ("[I]it is now clear not only that NF-kB is not tissue specific in nature, but also that in the wide number of types of cells in which it is present, it serves the important function of acting as an intracellular transducer of external influences."); '516 patent, 17 :45-47 ("NF-kB is unique among transcription regulatory proteins in its role as a major intracellular transducer of a variety of external influences in many cell types.").

2. *NF-kB activity*

[2] Amgen's proposed construction is "the ability to act as an intracellular messenger by (a) being released from IkB, (b) translocating into the nucleus, and/or (c) then binding one of the DNA sequences listed in Table 2 of the '516 patent."

ARIAD's proposed construction is "the ability of NF-kB to act as an intracellular messenger that regulates the transcription of particular genes."

The court rejects both parties' proposed construction FN5 and determines this phrase means: "the ability of NF-kB to act as an intracellular messenger by being released from IkB; translocating into the nucleus; and regulating the transcription of particular genes by binding to specific DNA recognition sequences in those genes." FN6

FN5. For instance, Amgen's proposed construction improperly limits this phrase to "binding one of the DNA sequences listed in Table 2 of the ' 516 patent." The specification states that "DNA sequences known to contain NF-kB binding domains are shown in Table 2." '516 patent, 35:54-55. One of the sequences listed in Table 2 was predicted to have sequences recognized by NF-kB but had "not been tested in a binding assay." '516 patent, 37:34-35. The patent does not, however, limit the claimed invention to only those sequences. *See* Liebel-Flarsheim Co. v. Medrad, Inc., 358 F.3d 898, 906 (Fed.Cir.2004) ("[T]his court has expressly rejected the contention that if a patent describes only a single embodiment, the claims of the patent must be construed as being limited to that embodiment. Even when the specification describes only a single embodiment, the claims of the patent will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using words or expressions of manifest exclusion or restriction." (internal quotation marks omitted) (citations omitted)). The court's construction of this phrase incorporates portions of ARIAD's proposed construction of "NF-kB" and "NF-kB activity."

FN6. *See, e.g.,* '516 patent, 2 :46-64 ("[I]t has been shown that a precursor of NF-kB is present in a variety of cells, that the NF-kB precursor in cytosolic fractions is inhibited in its DNA binding activity and that inhibition can be removed by appropriate stimulation, which also results in translocation of NF-kB to the nucleus. A protein inhibitor of NF-kB, designated IkB, has been sown to be present in the cytosol and to

convert NF-kB into an inactive form in a reversible, saturable and specific reaction. Release of active NF-kB from the IkB-NF-kB complex has been shown to result from stimulation of cells by a variety of agents, such as bacterial lipopolysaccharide, extracellular polypeptides and chemical agents, such as phorbel esters, which stimulate intracellular phosphokinases. IkB and NF-kB appear to be present in a stoichiometric complex and dissociation of the two complex components results in two events: activation (appearance of NF-kB binding activity) and translocation of NF-kB to the nucleus."); '516 patent, 3 :67-4 :4 ("The present invention relates to a method of regulating or influencing transduction, by NF-kB of extracellular signals into specific patterns of gene expression and, thus, of regulating NF-kB-mediated gene expression in the cells and systems in which it occurs."); '516 patent, 12 :57-60 ("It has been shown that NF-kB participates in gene expression (e.g., cytokine gene expression) which is activated by a specific influence or extracellular signal ...."); '516 patent, 16:23-28 ("NF-kB is initially located in the cytoplasm in a form unable to bind DNA because it is complexed with I-kB. Various inducers then cause an alteration in I-kB allowing NF-kB to be released from the complex. Free NF-kB then travels to the nucleus and interacts with its DNA recognition sites to facilitate gene transcription.").

3. *cells*

[3] The parties propose that this term be construed as "intact cells, whether in cell culture or in living tissue (including in an organism), as opposed to cell extracts."

The court adopts the parties' proposed construction.

4. *reducing NF-kB activity in [the] cells*

[4] Amgen's proposed construction is "taking action inside cells to directly inhibit (interfere or block) an NF-kB activity."

ARIAD's proposed construction is "decreasing NF-kB activity in cells in which NF-kB is present by inhibiting any step along the NF-kB signal transduction pathway, in such a manner that the activity differs from the naturally occurring activity of NF-kB under the same conditions, without regard to the situs of the inhibiting agent."

The court adopts Amgen's proposed construction, and determines this phrase means: "taking action inside cells to directly inhibit (interfere or block) an NF-kB activity." FN7

FN7. *See, e.g.,* '516 patent, 3 :59-64 ("[i]t is now possible to alter or modify the activity of NF-kB as an *intracellular messenger* and, as a result, to alter or modify the *effect* of a variety of external influences, referred to as inducing substances whose messages are transduced *within* cells through NF-kB activity.") (emphasis added); *see also,* '516 patent, 16 :47-49 ("An important feature of this second messenger or mediator model is that the hormone (first messenger) need not enter to the cell."); '516 patent, 35 :42-43 ("methods and composition of the present invention are based on the use of the role of NF-kB as a *second messenger,* or mediator, in the expression of genes ....") (emphasis added). The court agrees with Amgen's statement that, in claim 18, "the cells" are "mammalian cells" and that the construction of this limitation in claims other than claim 18 may incorporate antecedent bases for cell types other than mammalian cells, but otherwise is consistent across all claims.

5. ***NF-kB-mediated intracellular signaling***

[5] Amgen's proposed construction is "molecular interactions within cells effected by, or conveyed through, NF-kB."

ARIAD's proposed construction is "the intracellular steps of the NF-kB signal transduction pathway."

The court adopts Amgen's proposed construction and determines this phrase means: "molecular communication within cells effected by, or conveyed through, NF-kB." FN8

FN8. *See, e.g.,* '516 patent, 2 :26-31 ("As described herein, it has subsequently been shown that transcription factor NF-kB, previously thought to be limited in its cellular distribution, is, in fact, present and inducible in many, if not all, cell types and that it acts as an intracellular messenger capable of playing a broad role in gene regulation as a mediator of inducible signal transductions."); '516 patent, 2 :36-40 ("[I]it is now clear not only that NF-kB is not tissue specific in nature, but also that in the wide number of types of cells in which it is present, it serves the important function of acting as an intracellular transducer of external influences."); '516 patent, 10 :45-46 (describing NF-kB as acting "as an intracellular transducer or mediator of a variety of external influences"); '516 patent, 17:45-47 ("NF-kB is unique among transcription regulatory proteins in its role as a major intracellular transducer of a variety of external influences in many cell types.") The construction adopted by the court recites "molecular communication," rather than "molecular interaction." At oral argument, Amgen stated it was not opposed to substituting "communication" for "interaction" in this definition. The court notes that the construction adopted here is the construction for this phrase ARIAD proposed in a separate litigation. *See* D.I. 582, Ex. 6 at 4 (ARIAD's opening claim construction brief in *Ariad Pharmaceuticals, Inc., et al. v. Eli Lilly and Co.,* 02 CV 11280 RWZ, D. Mass). Further, ARIAD states that its "definitions in both cases are substantively similar."

6. ***diminishing induced NF-kB-mediated intracellular signaling***

[6] Amgen argues that this phrase of the preamble does not limit the claim. It states that if the court determines that it is limiting and requires construction, its proposed construction is "decreasing any existing molecular interaction within cells effected by, or conveyed through, NF-kB."

ARIAD's proposed construction is "inhibiting the intracellular steps of the NF-kB signal transduction pathway, performed after the pathway has been initiated in response to application of a stimulus prior to the performance of the claimed method."

The court determines that this preamble phrase is not limiting and, therefore, does not require construction.FN9

FN9. *See* Catalina Marketing Int'l, Inc. v. Coolsavings.com, Inc., 289 F.3d 801, 808 (Fed.Cir.2002) ("In general, a preamble limits the invention if it recites essential structure or steps, or if it is 'necessary to give life, meaning, and vitality' to the claim. Conversely, a preamble is not limiting 'where a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention.' ") (quoting Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1305 (Fed.Cir.1999) and Rowe v. Dror, 112 F.3d 473, 478 (Fed.Cir.1997)); *see also* Symantec Corp. v. Computer Assoc., 522 F.3d 1279, 1288-89 (Fed.Cir.2008) ("[I]n general, the purpose of a claim preamble is to give context for what is being described in the body of the claim; if it is reasonably susceptible to being

construed to be merely duplicative of the limitations in the body of the claim (and was not clearly added to overcome a rejection), we do not construe it to be a separate limitation.").

7. such that NF-kB-mediated intracellular *signaling is diminished*

[7] Amgen's proposed construction is "such that there is a decrease of any molecular interaction within cells effected by, or conveyed through, NF-kB."

ARIAD's proposed construction is "[such that NF-kB-mediated] signaling is reduced from an existing induced state to a lower state."

The court adopts Amgen's proposed construction and determines this phrase means: "such that there is a decrease of any molecular communication within cells effected by, or conveyed through, NF-kB." FN10

FN10. As with the construction of "NF-kB mediated intracellular signaling," the court substitutes "communication" for "interaction" in this construction. Logically, when "NF-kB mediated intracellular signaling" is "diminished," there is a "decrease" in that signaling. The court also notes that during reexamination, the PTO rejected ARIAD's assertion that prior induction is required. ARIAD argued "[t]he instant claims should be interpreted to require a first activating step which excludes prophylaxis, pretreatment or simultaneous activator or inhibitor administration; and thus be limited solely to treatment of an already NF-kB-induced cell or organism." The Examiner responded: "[t]he claimed methods are drawn to 'reducing NF-kB activity' to inhibit NF-kB regulated gene expression in a ... cell. There is nothing in the independent claims compelling a person of ordinary skill in the art to include any particular steps including a 1st activation step." D.I. 571, Ex. V at 20. The Examiner also commented that "to the extent that patentee's claim construction is tantamount to rewriting the claims to insert a negative claim limitation, it is noted that a negative limitation or exclusionary proviso must have basis in the original disclosure." *Id.*, Ex. V at 21.

8. *mammalian cells*

[8] The parties propose that this term be construed as "cells that come from a species falling within the class of mammals."

The court adopts the parties' proposed construction.

9. *reducing Interleukin-1 or* Tumor Necrosis ***Factor-(alpha) activity in mammalian cells***

Amgen argues that this phrase of the preamble does not limit the claim. FN11 It states that if the court determines it is limiting and requires construction, its proposed construction is "taking action inside the cell to directly inhibit (interfere or block) any molecular interaction within mammalian cells caused by Interleukin-1 or Tumor Necrosis Factor-(alpha)."

FN11. Amgen notes that it does believe that the phrase "in mammalian cells" provides antecedent basis for the body of claim 18 and is limiting in that regard.

ARIAD's proposed construction is "decreasing intracellular NF-kB signal transduction induced by

Interleukin-1 or Tumor Necrosis Factor-(alpha) that exists in mammalian cells in which NF-kB is present and capable of acting as an intracellular messenger."

The court determines that this preamble phrase is only limiting to the extent of "in mammalian cells" providing the antecedent basis for "the cells" in the body. The remaining language of the preamble merely states the purpose of the method, "is reasonably susceptible to being construed to be merely duplicative of the limitations in the body of the claim," and, therefore, does not require construction.FN12

FN12. *See* footnote 9; *see also* ABB Automation Inc. v. Schlumberger Resource Management Services, Inc., 254 F.Supp.2d. 475, 477 (D.Del.2003) (determining preamble phrase "input voltage" was limiting as it provided antecedent basis for "said input voltage" but preamble language indicating an intended use did not operate to limit the scope of the claims).

10. ***Intracellular signaling caused by IL-1 or TNF-(alpha)***

Amgen references its proposed construction for " *so as to reduced intracellular signaling caused by Interleukin-1 or* Tumor Necrosis *Factor-(alpha) in the cells,*" below.

ARIAD's proposed construction is "signaling along the intracellular steps of the NF-kB pathway, having been induced by the binding of IL-1 or TNF-a to their receptors, prior to the performance of the claimed method."

The court determines this phase does not need to be construed separately from the following claim term.

11. ***so as to reduce intracellular signaling caused by Interleukin-1 or*** Tumor Necrosis ***Factor-(alpha) in the cells***

[9] Amgen's proposed construction is "so as to take action inside cells to directly inhibit (interfere or block) any molecular interaction within cells caused by Interleukin-1 or Tumor Necrosis Factor-(alpha)."

ARIAD's proposed construction is "so as to inhibit the intracellular steps of the NF-kB signal transduction pathway induced by Interleukin-1 or Tumor Necrosis Factor-(alpha) prior to the performance of the claimed method, applied to the mammalian cells described in the preamble of the claim."

The court adopts Amgen's proposed construction and determines this phrase means: "so as to take action inside cells to directly inhibit (interfere or block) any molecular communication within cells caused by Interleukin-1 or Tumor Necrosis Factor-(alpha)." FN13

FN13. This phrase is construed consistently with the phrase at number 4, above, with additional language to include "Interleukin-1 or Tumor Necrosis Factor-(alpha) in the cells." The court again substitutes "communication" for "interaction" in this construction.

12. ***human cells***

[10] The parties propose that this term be construed as "cells that come from a human being."

The court adopts the parties' proposed construction.

13. ***immune cells***

[11] The parties propose that this term be construed as "cells involved in the immune response."

The court adopts the parties' proposed construction.

D.Del.,2008.
Amgen, Inc. v. Ariad Pharmaceuticals, Inc.