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UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF CALIFORNIA

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CHIRON, CORPORATION
Plaintiff,

NO. CIV. S-00-1252 WBS GGH

v.

MEMORANDUM AND ORDER RE:
ANTICIPATION, FRACKELTON 2G8
ANTIBODY

GENENTECH, INC.
Defendant.

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In a separate order, the court has determined that Genentech's product, Herceptin, infringes Chiron's U.S. Patent No. 6,054,561 ("'561 patent"). Genentech has raised various defenses and counterclaims, alleging inter alia that the '561 patent is invalid because it is anticipated by prior art. Chiron moves for summary judgment, arguing that the patent is not anticipated by the prior art references cited by Genentech, including the 2G8 antibody discovered and patented by Dr. Albert Frackelton.

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1 I. Factual and Procedural Background

2 A. Procedural Background

3 The '561 patent claims monoclonal antibodies that
4 bind to a human breast cancer antigen known as HER2. The patent
5 issued from a patent application filed in 1995, which is a
6 continuation of a long line of patent applications dating back to
7 1984 and 1985. The court addresses in a separate Memorandum and
8 Order filed concurrently herewith whether the '561 patent is
9 entitled to rely on the 1984 and 1985 applications for priority
10 so as to pre-date inventions that arose after 1985 but before
11 1995. (See Mem. and Order Re: Priority, Anticipation, Written
12 Description, Enablement, Best Mode, Utility.) This Order
13 addresses whether an invention discovered and patented before
14 1984 and 1985 anticipates, and thereby invalidates, the '561
15 patent under 35 U.S.C. § 102.¹

16 Genentech initially asserted that a number of pre-1984
17 and 1985 references invalidated the patent. After Chiron moved
18 for summary judgment, Genentech withdrew its anticipation
19 defenses based on the publications by Hapgood, Waterfield, Yuan,
20 Colcher, Sato, Papsidero, Gooi, Richert, Schreiber, Krolick,
21 Menard, Grimm, Kwamoto, Schlom, and Loop, and the patents by
22 Mendelsohn, Waterfield, Sakamoto, Bander, Fradet, Cairncross,
23 Mattes, Albino, Cardiff, Harvey, Cote, Keydar, Koprowski, and
24 Schlom that are cited in Appendix A to Chiron's motion for

25
26 ¹ A separate, but related question is whether the '561
27 patent is "obvious" under 35 U.S.C. § 103 in light of references
28 published before 1984 and 1985. The court addresses that
question in a separate Memorandum and Order regarding
inventorship, obviousness, and inequitable conduct. (See Mem.
and Order Re: Inventorship, Obviousness, Inequitable Conduct).

1 summary judgment regarding section 102 and 103 (non-drebin
2 references). Genentech also filed a non-opposition to Chiron's
3 summary judgment motions regarding two other pre-1984 references:
4 the MOPC 21 antibody and the 7.16.4 Drebin/Greene antibody.
5 Genentech, however, opposes Chiron's motion for summary judgment
6 on the ground that the 2G8 monoclonal antibody binds to the HER2
7 antigen and therefore anticipates a number of the claims of the
8 '561 patent.

9 B. The 2G8 Antibody

10 Antigens are proteins, which are made up of amino
11 acids. One amino acid found in proteins is tyrosine. Tyrosine
12 can become "phosphorylated" when enzymes called tyrosine kinases
13 add phosphate into the tyrosine residues of specific proteins.
14 (Frackelton Dep. at 70.) The phosphorylated tyrosine is referred
15 to as "phosphotyrosine." (Id.)

16 In March of 1981, Dr. Albert Frackelton created a
17 monoclonal antibody called 2G8, which binds to a phosphotyrosine
18 moiety on the cytoplasmic, or intracellular, domain of
19 phosphotyrosine-containing proteins. (Expert Report of Dr.
20 Frackelton, Emery Decl. Ex. P.) Dr. Frackelton received a patent
21 on the 2G8 antibody in 1985 after filing a patent application on
22 December 13, 1982. (Emery Decl. Ex. Q.) Claim 1 of Dr.
23 Frackelton's '439 patent covers "[a] monoclonal antibody of the
24 class IgG or IgM, derived from the fusion of a murine myeloma
25 cell and a murine antibody-producing lymphoid cell, demonstrating
26 specific reactivity to a phosphotyrosine moiety on
27 phosphotyrosine-containing proteins." (Id.)

28 The HER2 antigen contains at least four tyrosine sites

1 that can become phosphorylated, and 2G8 has been shown to bind to
2 phosphotyrosines on a phosphorylated HER2 antigen. (Frackelton
3 Dep. at 83-85; Emery Decl. Ex. P.) However, it is undisputed
4 that not all HER2 antigens contain phosphotyrosine. It is also
5 undisputed that HER2 is by no means the only protein that can
6 become phosphorylated. (Unkeless Dep. at 169). Nor are the
7 phosphotyrosines on HER2 the only phosphotyrosines to which the
8 2G8 antibody binds. In fact, the 2G8 antibody is known to bind
9 to the phosphotyrosine on at least 30 to 40 different proteins,
10 and may bind to hundreds more. (Frackelton Dep. at 244-245;
11 Unkeless Dep. at 169.)

12 II. Discussion

13 The court must grant summary judgment to a moving party
14 "if the pleadings, depositions, answers to interrogatories, and
15 admissions on file, together with the affidavits, if any, show
16 that there is no genuine issue as to any material fact and that
17 the moving party is entitled to judgment as a matter of law."
18 Fed. R. Civ. P. 56(c). The party adverse to a motion for summary
19 judgment may not simply deny generally the pleadings of the
20 movant; the adverse party must designate "specific facts showing
21 that there is a genuine issue for trial." Fed. R. Civ. P. 56(e);
22 see Celotex Corp. v. Catrett, 477 U.S. 317 (1986). Simply put,
23 "a summary judgment motion cannot be defeated by relying solely
24 on conclusory allegations unsupported by factual data." Taylor
25 v. List, 880 F.2d 1040, 1045 (9th Cir. 1989). The non-moving
26 party must show more than a mere "metaphysical doubt" as to the
27 material facts. Matsushita Elec. Indus. Co. v. Zenith Radio, 475
28 U.S. 574, 587 (1986).

1 In addition, the court must take into consideration the
2 burden of proof at trial when evaluating the sufficiency of the
3 evidence on summary judgment. Eli Lilly & Co. v. Barr Labs.,
4 Inc., 251 F.3d 955, 962 (Fed. Cir. 2001). Because a patent is
5 presumed valid, Genentech has the burden of proving invalidity by
6 clear and convincing evidence. Union Oil Co. of Cal. V. Atlantic
7 Richfield Co., 208 F.3d 989, 993 (Fed. Cir. 2000).

8 A patent is anticipated and therefore invalidated by
9 prior art if (1) the invention it claims was known or used by
10 others in this country before the patent application was filed;
11 (2) the invention was in public use or on sale in this country
12 more than one year before the application was filed; (3) the
13 invention was described in someone else's patent before the
14 patent applicant invented what is claimed; or (4) the invention
15 was made in this country by another inventor before it was
16 invented by the applicant, and the other inventor did not
17 abandon, suppress, or conceal his invention. See 35 U.S.C. §
18 102(a); (b); (e) (2); (g) (2).

19 An earlier invention will not "anticipate" a later
20 invention unless there is "no difference between the claimed
21 invention and the reference disclosure, as viewed by a person of
22 ordinary skill in the field of the invention." Scripps Clinic
23 and Research Found. v. Genentech, Inc., 927 F.2d 1565 (Fed. Cir.
24 1991). Thus, anticipation requires the presence in a single
25 prior art disclosure of each and every element of a claimed
26 invention. Electro Med. Sys., S.A. v. Cooper Life Sciences,
27 Inc., 34 F.3d 1048, 1052 (Fed. Cir. 1994). Whether an earlier
28 reference anticipates a claim or claims of a patent is a question

1 of fact. Scripps, 927 F.3d at 1575.

2 It is undisputed that the 2G8 antibody and the '439
3 patent pre-date the invention of the monoclonal antibodies
4 claimed in the '561 patent. It is also undisputed that the 2G8
5 antibody does not anticipate claims 3, 7, 11, 15, 21, and 25 of
6 the '561 patent, which are directed toward monoclonal antibodies
7 that bind to the extracellular domain of the HER2 antigen.
8 (See '561 Patent, Claims 3, 7, 11, 15, 21, 25.) Because the 2G8
9 antibody binds to phosphotyrosine moieties which exist only on
10 the intracellular domain of the HER2 protein, Genentech concedes
11 that the 2G8 antibody does not invalidate the extracellular
12 domain claims.

13 The question for the court, therefore, is whether the
14 2G8 antibody anticipates the claims of the '561 patent that do
15 not have the extracellular domain limitation. One element common
16 to all of the claims of the '561 patent is that the monoclonal
17 antibody must bind to the HER2 antigen. Thus, in order for the
18 2G8 antibody to anticipate any of the claims of the '561 patent,
19 it must bind to the HER2 antigen.

20 In an order dated April 22, 2002, the court construed
21 the term "binds" to mean "a degree of attachment that is
22 immunologically significant, i.e. a degree of attachment that is
23 (1) above background levels; (2) specific; (3) selective for
24 cancer as opposed to normal cells and/or tissues; and (4) has a
25 useful degree of affinity." (Apr. 22, 2002 Order, at 42.)

26 In that order, the court explained that antigen-
27 antibody binding is "specific" in the sense that antibodies are
28 custom-tailored to fit around or attach to a particular binding

1 site on a particular antigen. The court further noted that
2 although an antibody may sometimes randomly and weakly attach at
3 a site other than the specific one it recognizes, the term
4 "binds" as it is used in the patent does not refer to this kind
5 of background binding.

6 With the court's claim construction in mind, it is
7 clear from the undisputed evidence in the record that the 2G8
8 antibody is not specific for the HER2 antigen at all. Rather, it
9 is specific for phosphotyrosine, which appears on many proteins
10 other than HER2, and which does not appear on all HER2 antigens.
11 The fact that 2G8 binds to phosphotyrosine moieties present on
12 HER2 therefore does nothing to prove that 2G8 is custom-tailored
13 for HER2. Because 2G8 is not specific for HER2, it does not
14 "bind" to HER2 within the meaning of the patent, and therefore
15 does not anticipate the claims of the patent.²

16 Based on the court's claim construction and the
17 undisputed factual record, the court finds that neither Dr.
18 Frackelton's 2G8 antibody nor the '439 patent invalidate any of
19 the claims of the '561 patent.

20 IT IS THEREFORE ORDERED that summary judgment be, and
21 the same hereby is, GRANTED to Chiron on:

- 22 (1) Genentech's affirmative defense and counterclaim
23 that the claims of the '561 patent are invalid in view
24 of the 2G8 antibody and the Frackelton '439 patent;

25
26 ² The parties also dispute whether the 2G8 antibody binds
27 "selectively" or "with a useful degree of affinity" to HER2. The
28 court need not address these questions. The fact that the 2G8
antibody does not bind specifically to HER2 is sufficient to
resolve the question of whether it anticipates the claims of the
'561 patent.

1 (2) Genentech's affirmative defense and counterclaim
2 that the claims of the '561 patent are invalid in view
3 of the MOPC 21 antibody;

4 (3) Genentech's affirmative defense and counterclaim
5 that the claims of the '561 patent are invalid in view
6 of the Drebin 1984 article and the Drebin/Greene
7 antibodies;

8 (4) Genentech's affirmative defenses and counterclaims
9 that the claims of the '561 patent are invalid in view
10 of the publications by Hapgood, Waterfield, Yuan,
11 Colcher, Sato, Papsidero, Gooi, Richert, Schreiber,
12 Krolick, Menard, Grimm, Kwamoto, Schlom, and Loop, and
13 the patents by Mendelsohn, Waterfield, Sakamoto,
14 Bander, Fradet, Cairncross, Mattes, Albino, Cardiff,
15 Harvey, Cote, Keydar, Koprowski, and Schlom cited in
16 Appendix A to Chiron's motion.

17 DATED: June 24, 2002

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WILLIAM B. SHUBB
UNITED STATES DISTRICT JUDGE