

United States Court of Appeals for the Federal Circuit

02-1109

THE BOARD OF EDUCATION
(for and on behalf of the Board of Trustees of Florida State University),
MDS RESEARCH FOUNDATION, INC., and TAXOLOG, INC.,

Plaintiffs-Appellees,

v.

AMERICAN BIOSCIENCE, INC.
(formerly known as Vivorx Pharmaceuticals, Inc.),

Defendant -Appellant,

and

CHUNLIN TAO,

Defendant.

Jeffrey T. Thomas, Gibson, Dunn & Crutcher LLP, of Irvine, California, argued for plaintiffs-appellees. With him on the brief was Mark J. Carlozzi. Of counsel on the brief was Sidney L. Matthew, Gorman & Matthew, P.A., of Tallahassee, Florida.

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Appealed from: United States District Court for the Northern District of Florida

Chief Judge Roger Vinson

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DECIDED: June 23, 2003

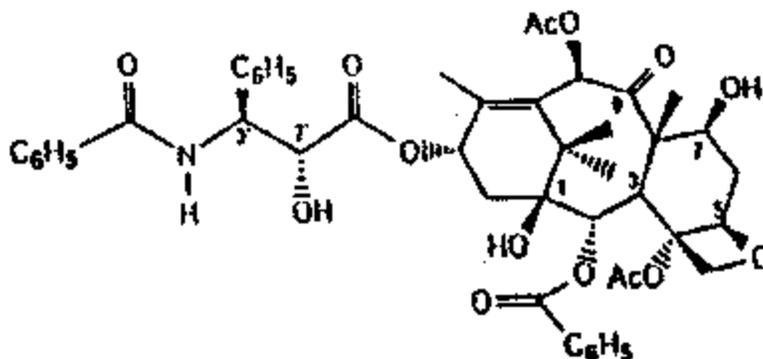
Before LOURIE, RADER, and LINN, Circuit Judges.

LOURIE, Circuit Judge.

American BioScience, Inc. (“ABI”) appeals from the decision of the United States District Court for the Northern District of Florida in an inventorship action brought by the Board of Education (for and on behalf of the Board of Trustees of Florida State University), MDS Research, Inc., and Taxolog, Inc. (collectively, “FSU”). That decision removed three inventors from U.S. Patent 5,780,653, retained one inventor, added three other inventors, and declared the patent unenforceable for inequitable conduct. Bd. of Educ. ex rel. Bd. of Trs. of Fla. State Univ. v. Am. Bioscience, Inc., No. 4:99cv131/RV, 2001 U.S. Dist. LEXIS 19480 (N.D. Fla. Oct. 31, 2001). Because the district court erred in its determination of inventorship and inequitable conduct, we affirm-in-part, reverse-in-part, and vacate-in-part.

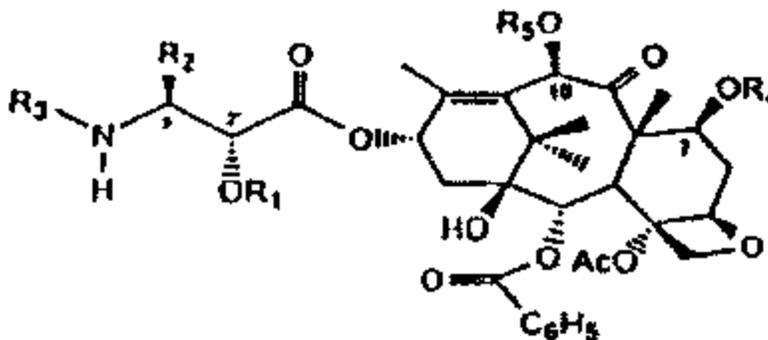
BACKGROUND

Taxol (paclitaxel)^[1] is a natural compound found in the bark of the Pacific yew tree (*Taxus brevifolia*). Over the last several decades, taxol has received considerable attention in the scientific and medical communities as an anti-cancer drug. Bd. of Educ., 2001 U.S. Dist. LEXIS 19480, at *4. In the early 1990s, scientists discovered that taxol is not only an effective chemotherapeutic agent, but that it also enhances the effectiveness of radiation therapy for killing cancer cells, especially oxygen-starved (“hypoxic”) cancer cells that are ordinarily resistant to radiation. A 1992 paper published by researchers at Columbia University disclosed the dual activities of taxol as a simultaneously cytotoxic and radiosensitizing agent. See Roy B. Tishler et al., Taxol: A Novel Radiation Sensor, 22 Int’l J. Radiation Oncology•Biology•Physics 613-17 (1992). The structural formula of taxol is shown below.



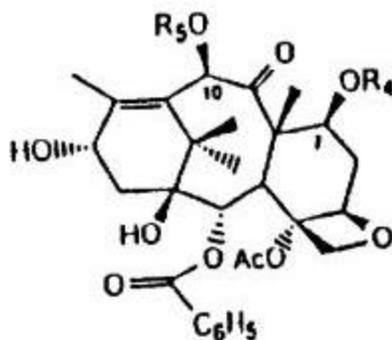
Taxol

The '653 patent, filed in the names of Chunlin Tao, Neil Desai, Patrick Soon-Shiong, and Paul Sanford, and assigned to Vivorx Pharmaceuticals, Inc., claims three compounds. Those compounds are analogs of taxotere (docetaxel).^[2] a compound that differs from taxol in two respects. First, taxotere has a 10-hydroxy (-OH) group in place of taxol's 10-acetoxy (-OCOCH₃, also abbreviated as “-OAc”) group. Second, taxotere has a tert-butoxycarbonyl (-COOC(CH₃)₃, abbreviated as “-COO-tBu”) group attached to its 3' nitrogen atom, in place of taxol's benzoyl (-COC₆H₅) group. The structural formula of taxotere is shown below.

Taxotere: R₁ = -H, R₂ = -C₆H₅, R₃ = -COO-tBu, R₄ = -H, R₅ = -H

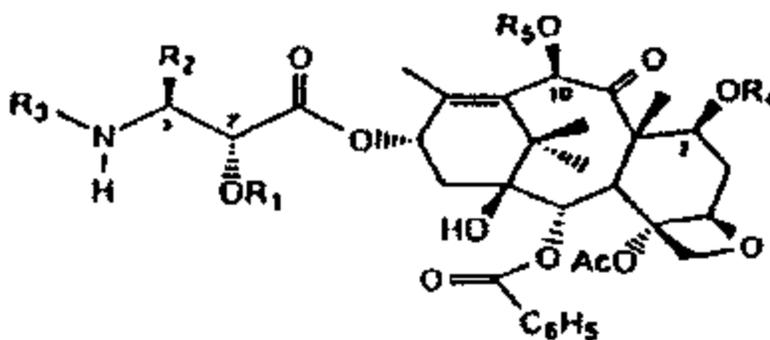
The following history sets forth the events that led to the filing of the '653 patent application.

At the time these events began to unfold, Professor Robert Holton had been conducting a research group at FSU working with taxols. Chunlin Tao, a chemist, joined that group as a post-doctoral research assistant in July 1992. Bd. of Educ., 2001 U.S. Dist. LEXIS 19480, at *7. Dr. Tao worked on two projects in the Holton group. First, he was part of a team of researchers who in December 1993 completed the total synthesis of taxol. Id. He was also part of a team that made taxol analogs using a “semi-synthetic” process beginning with baccatin III, a natural product found in the needles of a European yew variety (*Taxus baccata*). As shown below, baccatin III has a hydroxy group in place of taxol's side chain, but is otherwise identical to taxol.

Baccatin III: $R_4 = -H$, $R_5 = -Ac$

The semi-synthetic process requires relatively few steps, and it appears that that process was at that time the standard method for making taxol and its analogs.^[3]

While he was at FSU, Tao apparently also developed a close relationship with a visiting faculty member, Dr. Li-Xi Yang. *Id.* at *18-19. Dr. Yang is a radiation biologist who arrived at FSU in March 1993 as a “courtesy professor.” *Id.* at *12. Yang had in the past developed several compounds having increased radiosensitivity for anti-cancer applications, and his research focused on increasing the radiosensitivity of hypoxic cells. *Id.* at *13. Several months after arriving at FSU, Yang visited Holton and proposed a collaborative project to develop “chemotherapeutic radiosensitizing taxanes” (“CRTs”). *Id.* Holton agreed, and he assigned one of his post-doctoral research assistants, Dr. Hossein Nadizadeh, the responsibility of synthesizing taxol analogs that Holton and Yang believed would prove to be effective CRTs. Holton and Yang focused particularly on the attachment of “nitro electron affinic groups,” which were known to be radiosensitizing, in an attempt to increase taxol’s radiosensitivity. *Id.* at *14-15. Even before Yang’s arrival, however, members of the Holton group had already synthesized a number of nitro-taxols, and some of those were also given to Yang for testing. The structural formula of one such pre-synthesized compound, referred to as “PNIP,” is shown below.

PNIP: $R_1 = -H$, $R_2 = -p-C_6H_4-NO_2$, $R_3 = -COOC(CH_3)_3$, $R_4 = -H$, $R_5 = -Ac$

One should note that PNIP has the 10-acetoxy group of the taxols. PNIP showed potential in Yang’s earliest tests in January 1994, and Yang testified that he had told Tao at around that time that PNIP was the most effective radiosensitizer among the compounds that he tested. *Id.* at *19.

There is no evidence that Tao ever synthesized PNIP himself. However, the method for making PNIP was apparently the subject of numerous discussions within the Holton group during Tao’s tenure at FSU because, prior to Tao’s joining the Holton group in 1992, Dr. Nadizadeh had developed a “secret” method for making a beta-lactam compound used to attach a side chain to baccatin III to make PNIP. *Id.* at *10-11. Nadizadeh’s method differed from a published prior art method of making beta-lactams in two respects: in the ordering of its four steps, and in the use of acid hydrolysis rather than base hydrolysis in one of those steps. *Id.* at *11.^[4]

In 1992, Dr. Patrick Soon-Shiong, a transplant surgeon, was the CEO of VivoRx Pharmaceuticals, Inc., as ABI was

then known, and of VivoRx, Inc. (“VivoRx”), a related company focused on diabetes research. Id. at *21-22. In 1994, Dr. Soon-Shiong became the CEO of ABI. Id. at *22 n.13. Dr. Neil Desai is an organic chemist, and was VivoRx’s Senior Research Scientist in 1992. That year, Drs. Soon-Shiong and Desai filed a patent application directed to a method of encapsulating taxol analogs for direct delivery to tumors. They subsequently attended the “Second NCI Workshop on Taxol and Taxus,” a conference at which they heard presentations regarding the effectiveness of taxol analogs, the use of taxol as a radiosensitizer, the use of nitro groups to enhance radiosensitization, and the use of the taxol side chain’s 3’-position as a point for attachment of functional groups to the taxol structure. Among the speakers at the conference was Holton, who spoke about the synthesis of taxol. Soon-Shiong has said that he “was probably present” during Holton’s presentation. Id. at *23 n.14. After the conference, apparently based on what they had learned there and from the existing scientific literature regarding taxol and radiosensitization, Soon-Shiong and Desai discussed the possibility of creating radiosensitizers that they believed would be more potent than taxol by using taxotere instead of taxol as a core structure. Id. at *23.

In 1994, Soon-Shiong directed Desai to begin creating analogs of taxotere. Shortly thereafter, Desai attended a conference in India, where he learned of a source of 10-deacetylbaaccatin (“10-DAB”), a compound similar to baaccatin III, but having the 10-hydroxy group of taxotere rather than the 10-acetoxy group of baaccatin III and taxol. Id. at *26 n.18.

At around the same time, Tao was finishing his post-doctoral research at FSU, and Soon-Shiong and Desai interviewed him for a job at VivoRx. During his interview, Tao presented details of his taxol analog research. Id. at *25. Looking to expand their work in cancer research, and apparently realizing that Tao could help them to finally pursue the ideas that they had discussed after the 1992 conference, Soon-Shiong and Desai hired Tao to work on the taxotere project. Id.

Upon Tao’s arrival at VivoRx in December 1994, Desai discussed the published literature on radiosensitizers with Tao, and assigned to him the task of creating chemotherapeutic radiosensitizing taxotere analogs with modified side chains, using the 10-DAB supplied by his Indian contact. Id. at *27. Desai was responsible for making the final decisions as to which compounds to pursue. Id. After Tao had made several compounds, Desai and Soon-Shiong forwarded information concerning those compounds to ABI’s patent attorney, Dr. Stephen Reiter. Id. at *31-32.

Reiter then filed a patent application naming Tao, Desai, Soon-Shiong, and Dr. Paul Sandford as inventors. He initially filed thirteen claims, including six to a method of making a compound, six to compounds, and one to a method of using the compounds as both cytotoxic agents and radiosensitizers. Id. at *31. Following a restriction requirement, Reiter cancelled the method of use claim. The PTO then rejected the remaining claims over the prior art. Reiter accordingly cancelled all of the pending claims, replacing them with narrower compound claims. Id. at *34. After the PTO rejected the new claims as obvious over two Holton/FSU patents, Reiter successfully traversed the rejection on the ground that those patents did not disclose or suggest analogs lacking taxol’s 10-acetoxy group, and the ’653 patent accordingly issued in July 1998 with four claims. Id. at *34-35.

Claim 1, the sole independent claim of the ’653 patent, reads as follows:

1. A dual functional compound having both cytotoxic properties and radiosensitizing properties, wherein said compound is selected from the group consisting of:

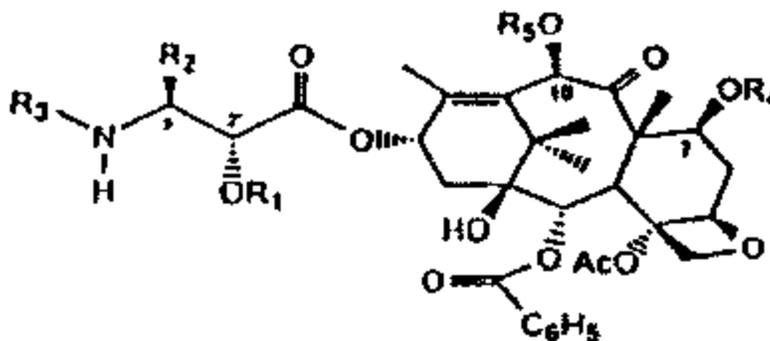
3’-Desphenyl-3’-(4-nitrophenyl)-N-debenzoyl-N-(t-butoxy-carbonyl)-10-deacetylaxol;

3’-Desphenyl-3’-(4-nitrophenyl)-N-debenzoyl-N-(isopropoxycarbonyl)-10-deacetylaxol;

3’-Desphenyl-3’-(4-nitrophenyl)-N-debenzoyl-N-(isobutoxycarbonyl)-10-deacetylaxol.

Dependent claims 2-4 separately claim the three compounds set forth in claim 1’s Markush group, shown below as

Compounds 1, 2, and 3, respectively:



Compound 1: $R_1 = -H$, $R_2 = -p-C_6H_4-NO_2$, $R_3 = -COOC(CH_3)_3$, $R_4 = -H$, $R_5 = -H$

Compound 2: $R_1 = -H$, $R_2 = -p-C_6H_4-NO_2$, $R_3 = -COOCH(CH_3)_2$, $R_4 = -H$, $R_5 = -H$

Compound 3: $R_1 = -H$, $R_2 = -p-C_6H_4-NO_2$, $R_3 = -COOCH_2CH(CH_3)_2$, $R_4 = -H$, $R_5 = -H$

The three claimed compounds all have the 10-hydroxy group of taxotere, as well as a 3'-(4-nitrophenyl) group. The first compound additionally has the N-(tert-butoxycarbonyl) group of taxotere. The second and third compounds have isopropoxycarbonyl ($-COOCH(CH_3)_2$, abbreviated as “-COO-iPr”) and isobutoxycarbonyl ($-COOCH_2CH(CH_3)_2$, abbreviated as “-COO-iBu”) groups, respectively, in place of the tert-butoxycarbonyl group of the first compound.

In September 1998, FSU sued Tao in the United States District Court for the Northern District of Florida, alleging that he had misappropriated trade secrets and used them to apply for a patent in his own name. Arguing that Florida was an improper forum, ABI and Tao then sued FSU in the Central District of California, alleging infringement of the '653 patent, seeking monetary damages and injunctive relief, and seeking a declaration of inventorship. FSU voluntarily dismissed its claims and successfully moved to transfer the California action to the Northern District of Florida. FSU filed an answer and counterclaims for breach of contract, malicious interference with an advantageous business relationship, statutory theft of trade secrets, unjust enrichment, constructive fraud, and misappropriation of trade secrets in violation of the Florida Uniform Trade Secrets Act, as well as a count entitled “Cause of Action for Declaratory Judgment of the Invalidity of the Vivorx Pharmaceuticals' Patent,” which alleged that the '653 patent is invalid under 35 U.S.C. §§ 102, 103, and 112. ABI and Tao dismissed all of their claims, apparently on the basis of representations from FSU that it was not making, using, or selling the claimed compounds. Because only FSU's counterclaims then remained, the district court realigned the parties, designating FSU as plaintiff and ABI and Tao as defendants. Later, all but the last of FSU's counterclaims involving invalidity were dismissed or settled. Additionally, during a pretrial conference, FSU withdrew its claim that the '653 patent is invalid, seeking instead to add Holton, Yang, and Nadizadeh to the patent as inventors and to remove Soon-Shiong, Desai, and Sandford. FSU also sought a declaratory judgment that the patent was unenforceable due to inequitable conduct.

Following a bench trial, the district court found, *inter alia*, that: (1) Soon-Shiong and Desai had not seen any literature that discussed the use of a taxol analog as a chemotherapeutic radiosensitizing agent prior to November 1994 when Tao interviewed at ABI, and no one at VivoRx had ever attempted to synthesize a taxane with such dual functional properties, *id.* at *22-24; (2) Tao had used confidential information that he learned at FSU, namely Nadizadeh's “secret” beta-lactam method, in synthesizing the three specific compounds that are claimed in the '653 patent, *id.* at *28; (3) Tao had used his knowledge and experience from FSU in selecting the isopropoxycarbonyl and isobutoxycarbonyl functional groups, also on the basis of FSU's proprietary information, *id.*; (4) the '653 patent specification disclosed the general concept, developed by Yang, of attaching electron “affinic” substituents to a taxane to impart radiosensitizing properties, *id.* at *31; and (5) “[b]ecause 10-DAB and Baccatin III are essentially interchangeable starting materials, Dr. Nadizadeh and Dr. Holton obviously knew that 10-DAB could be used to create FSU's PNIP and they knew how to reduce that knowledge to practice,” *id.* at *45.

The court then concluded that “Dr. Soon-Shiong, Dr. Desai, and Dr. Sandford did not contribute to the inventions claimed in the '653 patent,” *id.* at *44; and that, because Holton had “determined which taxol analogs were likely to possess

the dual properties of a CRT,” and because Tao had learned “the concept and the specifics of a CRT from Dr. Yang” and had used Nadizadeh’s method to synthesize the patented compounds, “clear and convincing evidence demonstrates that Dr. Holton, Dr. Yang, and Dr. Nadizadeh contributed to the invention of the patented compounds made by Dr. Tao,” *id.* at *40-41, and hence were coinventors. The court also found that Soon-Shiong and Desai could be charged with knowledge of Holton’s, Yang’s, and Nadizadeh’s contributions to the invention, and that they had accordingly engaged in inequitable conduct by not telling Reiter of Tao’s former employment at FSU. *Id.* at *52. It concluded that the ’653 patent was therefore unenforceable. *Id.* at *56.

ABI now appeals. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

DISCUSSION

A. Inventorship

The patent statute, 35 U.S.C. § 256, provides for district court jurisdiction over inventorship disputes. That statute provides that:

The error of omitting inventors or naming persons who are not inventors shall not invalidate the patent in which such error occurred if it can be corrected as provided in this section. The court before which such matter is called in question may order correction of the patent on notice and hearing of all parties concerned and the Director shall issue a certificate accordingly.

35 U.S.C. § 256 (2000). This appeal involves such an inventorship dispute.

Inventorship is a question of law that we review *de novo*. Ethicon, Inc. v. U.S. Surgical Corp., 135 F.3d 1456, 1460, 45 USPQ2d 1545, 1547 (Fed. Cir. 1998). We review the district court’s underlying findings of fact for clear error. *Id.* Because the issuance of a patent creates a presumption that the named inventors are the true and only inventors, *id.*, the burden of showing misjoinder or nonjoinder of inventors is a heavy one and must be proved by clear and convincing evidence, Hess v. Advanced Cardiovascular Sys., Inc., 106 F.3d 976, 980, 41 USPQ2d 1782, 1785 (Fed. Cir. 1997) (citing Garrett Corp. v. United States, 422 F.2d 874, 880, 164 USPQ 521, 526 (Ct. Cl. 1970)).

Conception is “the touchstone of inventorship,” and each joint inventor must generally contribute to the conception of the invention. Ethicon, 135 F.3d at 1460, 45 USPQ2d at 1548 (quoting Burroughs Wellcome Co. v. Barr Labs., Inc., 40 F.3d 1223, 1227-28, 32 USPQ2d 1915, 1919 (Fed. Cir. 1994)). “Conception” is the “formation in the mind of the inventor, of a definite and permanent idea of the complete and operative invention, as it is hereafter to be applied in practice.” Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1376, 231 USPQ 81, 87 (Fed. Cir. 1986) (quoting 1 Robinson on Patents 532 (1890)). “An idea is sufficiently ‘definite and permanent’ when ‘only ordinary skill would be necessary to reduce the invention to practice, without extensive research or experimentation.’” Ethicon, 135 F.3d at 1460, 45 USPQ2d at 1548 (quoting Burroughs Wellcome, 40 F.3d at 1228, 32 USPQ2d at 1919). One does not qualify as a joint inventor merely by assisting the actual inventor. *See id.* (“One who simply provides the inventor with well-known principles or explains the state of the art without ever having ‘a firm and definite idea’ of the claimed combination as a whole does not qualify as a joint inventor.”).

On appeal, ABI argues that the district court erred in changing the names of the inventors on the ’653 patent and concluding that the patent is unenforceable as a result of inequitable conduct. According to ABI, the only pertinent question concerning inventorship is whether FSU personnel contributed to the invention of the three specific compounds claimed in the ’653 patent, and they did not. In ABI’s view, the court did not limit its inventorship analysis to the granted claims and the

evidence is wholly lacking in support of the court's decision. ABI argues that it would be "nonsensical" to list as inventors persons who contributed only to non-issued, abandoned claims, and that that is nonetheless what the district court did in this case. According to ABI, the district court failed to recognize that the '653 patent as issued does not claim methods of making any compounds, and improperly based its decision on evidence regarding the beta-lactam method for making the compounds. ABI contends that there are other viable methods for making the claimed compounds. ABI also accuses FSU of engaging in discovery abuses, springing evidence regarding the beta-lactams on ABI at the last minute, preventing ABI from rebutting that evidence, and refusing to produce critical notebook pages relating to that evidence on the ground that they included trade secrets.

According to ABI, the court also incorrectly dismissed the distinction between taxotere/10-DAB and taxol/baccatin III as insignificant. ABI points out that the PTO specifically determined that ABI's use of 10-DAB rather than baccatin III was non-obvious and justified patentability, but the district court concluded that Drs. Holton, Yang, and Nadizadeh should have been listed as inventors simply because they made seemingly similar compounds. ABI points out that it is undisputed in the record that all of FSU's taxol analogs had a 10-acetoxy group, whereas the claimed compounds have a 10-hydroxy group; that Tao never made an analog having a 10-hydroxy group while he was at FSU; that no one at FSU ever made or even suggested making any of the 10-hydroxy compounds claimed in the '653 patent; and that the patentable idea to make 10-DAB-derived nitro compounds came from Soon-Shiong and Desai.

FSU counters that the district court's factual findings were correct and based on clear and convincing evidence that supports the district court's holding. According to FSU, the sum total of Tao's knowledge and experience with taxol and taxanes was gained at FSU in Holton's laboratory, and Tao's work at ABI was simply a continuation of scientific investigations begun by the Holton group at FSU. FSU asserts that the one difference between FSU's PNIP and the first claimed compound in the '653 patent is only that Tao used 10-DAB, a starting material that he learned of at FSU, to make the claimed compound at ABI. FSU further contends that the use of that starting material cannot differentiate ABI's claimed compounds from FSU's compounds, because FSU itself used 10-DAB and baccatin III interchangeably, depending on which was commercially available at a given time. FSU argues that ABI's decision to use 10-DAB was, likewise, simply based on the availability of that compound in 1994.

It should not matter, according to FSU, that no one at FSU made the compounds claimed in ABI's patent, because there is no requirement in the patent law that a coinventor of a chemical compound prove actual reduction to practice. According to FSU, a contribution qualifying a person as an inventor may be based on either a contribution to conception or a contribution to the reduction to practice of the invention, and an inventive contribution to the method of making a claimed compound is also a contribution to the conception of the compound. FSU alleges that, before ABI hired Tao, no one at ABI knew how to synthesize taxane analogs or how to increase radiosensitization. According to FSU, ABI actively recruited Tao because of his association with FSU's "groundbreaking research team." FSU further asserts that Soon-Shiong hired Tao and encouraged him to continue the very work he had performed at FSU, even if that meant using confidential information he learned at FSU, including Nadizadeh's beta-lactam method and Yang's discovery of PNIP's radiosensitizing activity. Although the claims are directed to compounds, according to FSU, their preambles require radiosensitizing and cytotoxic activities, and Tao learned about radiotherapy, radiation biology, and radiosensitization from Yang at FSU. Thus, FSU asserts, although ABI succeeded in obtaining a patent, it was the knowledge that was imparted to Tao while he was at FSU that led to the selection of the compounds claimed in that patent, and the district court properly held that Nadizadeh and Yang are coinventors of the compounds claimed in the '653 patent, whereas Soon-Shiong and Desai are not.

We agree with ABI, first, that the district court erred in concluding that Soon-Shiong and Desai are not coinventors of the three compounds claimed in the '653 patent. The burden was on FSU to demonstrate by clear and convincing evidence that Soon-Shiong and Desai were misjoined as inventors. Contrary to the district court's conclusions and FSU's assertions, the record indicates that it was the VivoRx scientists who had the idea of making compounds having both a 10-hydroxy group and a nitro group. Because there is no evidence of record that the idea of making taxol analogs having both a 10-hydroxy group (*i.e.*, taxoteres) and a nitro functional group came from anyone other than Soon-Shiong and Desai, we conclude that FSU did not meet its burden.

Tao also contributed to the conception of the claimed invention. The record reflects that Tao introduced the idea of

incorporating tert-butoxycarbonyl, isobutoxycarbonyl, and isopropoxycarbonyl groups, and chose the attachment point for the nitro group. The district court correctly retained Tao as a coinventor and that issue is not before us.

Sandford was the fourth inventor named on the patent. According to the district court, Sandford testified that he “did not contribute to the inventions claimed in the 653 patent, even though he was named as a co-inventor.” Bd. of Educ., 2001 U.S. Dist. LEXIS 19480, at *31 n.24. The district court therefore dropped him as an inventor and ABI does not appeal that conclusion.

Having concluded that the district court erred in determining that Soon-Shiong and Desai were not inventors, the remaining question is whether the district court erred in determining that the FSU scientists were true inventors of the claimed compounds. Invention requires conception, and “conception does not occur unless one has a mental picture of the structure of the chemical . . . or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property” Amgen Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991). Moreover, general knowledge regarding the anticipated biological properties of groups of complex chemical compounds is insufficient to confer inventorship status with respect to specifically claimed compounds. Id. ABI has argued that neither Yang nor anyone in the Holton group ever actually made any of the compounds claimed in the '653 patent. While we agree with FSU that the law does not usually require actual reduction to practice to establish conception of a chemical compound, cf. id. (holding that “when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the gene has been isolated”), invention does require conception, and there is no evidence that FSU’s inventors conceived any of the claimed compounds. Having in mind specific portions of a claimed compound is not the same as conceiving the compound with all of its components. One must have a conception of the specific compounds being claimed, with all of their component substituents, and the record does not support a finding that Holton or any of his co-workers conceived the three claimed compounds, all of which lack taxol’s 10-acetoxy group.

The grant of the '653 patent itself supports the conclusion that the claimed taxotere compounds, all of which have a 10-hydroxy group, a side chain having a 3'-(4-nitrophenyl) group, and either an N-tert-butoxycarbonyl group, an N-isobutoxycarbonyl group, or an N-isopropoxycarbonyl group, were novel and nonobvious over the prior art, and hence not the invention of the FSU scientists. Although PNIP made at FSU also contained the N-tert-butoxycarbonyl and 3'-(4-nitrophenyl) groups, it did not include the 10-hydroxy group of the claimed compounds.

The district court found that baccatin III and 10-DAB were used interchangeably as starting materials in Holton’s group at FSU, depending on availability. Regardless which starting material was used, however, the record reflects that all of FSU’s product analogs had a 10-acetoxy group. There is no evidence that any analogs that were made having a 10-hydroxy

group were contemplated as ends in themselves, rather than simply as intermediates in the semi-synthetic preparation of 10-acetoxy analogs starting with 10-DAB. The fact that all of FSU's analogs include a 10-acetoxy group shows that, to the extent that FSU used 10-DAB as a starting material at all, Holton and his co-workers acetylated the 10-hydroxy group to make a 10-acetoxy group in an intermediate step during the synthesis of those analogs.^[5] Thus, the fact that 10-DAB may have been used at FSU is not probative of inventorship of the compounds claimed in the '653 patent.

Much of FSU's appeal brief is devoted to extolling Holton's scientific accomplishments, the implication being that he must be an inventor of the three claimed compounds. FSU's strongest arguments for Holton's being a coinventor of the three claimed compounds are that (1) "[t]he sum total of Tao's knowledge and experience with taxol and taxanes was gained in the laboratories of FSU as a member of the Holton research team"; (2) "Tao's . . . work at ABI was simply a continuation of scientific investigations begun by the Holton group at FSU"; and (3) the first compound listed in claim 1 of the '653 patent "includes the exact same side chain from the PNIP compound created by Drs. Holton and Nadizadeh at FSU." The district court additionally found that "Holton would identify the analogs or compounds that he wanted his research assistants to attempt to synthesize," Bd. of Educ., 2001 U.S. Dist. LEXIS 19480, at *9, and that, "[w]hile at FSU and in collaboration with Dr. Holton, Dr. Tao created taxol analogs with isopropoxycarbonyl and isobutoxycarbonyl attached at the N position of the side chain," id. at *42.

FSU's arguments and the district court's findings together fall short of meeting the clear and convincing evidence standard required for finding that Holton was a coinventor of the three specific compounds claimed in the '653 patent. While Holton may have invented many of the compounds synthesized in his laboratory, including PNIP, there is nonetheless no evidence of conception by Holton or anyone else at FSU of analogs having the combination of a 10-hydroxy group, a nitrophenyl group, and an N-alkoxy-carbonyl (*i.e.*, tert-butoxycarbonyl, isopropoxycarbonyl, or isobutoxycarbonyl) substituent. The taxol analogs having isopropoxycarbonyl and isobutoxycarbonyl groups referred to by the district court did not include either a nitro group or a 10-hydroxy group. Thus, even assuming that Holton himself conceived all of the compounds synthesized within his laboratory, about which we express no opinion, there is no evidence of Holton's conception of the three compounds covered by the '653 patent. Moreover, the tert-butyl, isopropyl, and isobutyl side chains of those compounds did not originate in FSU's laboratories, but are common branched alkyl groups. Indeed, taxotere itself also includes the N-tert-butoxycarbonyl group, and there is no serious dispute that the nitrophenyl substituent was also in the prior art. It is a longstanding principle of patent law that "[o]ne who simply provides the inventor with well-known principles or explains the state of the art without ever having 'a firm and definite idea' of the claimed combination as a whole does not qualify as a joint inventor." Ethicon, 135 F.3d at 1460, 45 USPQ2d at 1548 (quoting O'Reilly v. Morse, 56 U.S. (15 How.) 62, 111 (1853)).

Regarding Nadizadeh's status as a putative inventor, the district court found that Tao had apparently learned

Nadizadeh's "secret" beta-lactam method while he was at FSU and used that method to make the compounds claimed in the '653 patent. On the basis of those findings, the court concluded that Nadizadeh was therefore a coinventor. That was error. As we have indicated, the '653 patent claims just three compounds; it does not claim any method of making those compounds. There is no indication that Nadizadeh directly contributed to the conception of any of the claimed compounds, and we see no other basis for regarding him as a coinventor.

FSU points out that this court held in Burroughs Wellcome that "[c]onception of a chemical substance includes knowledge of both the specific chemical structure of the compound and an operative method of making it." 40 F.3d at 1229, 32 USPQ2d at 1921. That is true, but, despite the fact that Nadizadeh may have developed a method of making PNIP and other taxol derivatives, the record in the present case indicates that he did not conceive the claimed compounds; only ABI's inventors were in possession of both the structure of the claimed compounds and an operative method of making those compounds. The fact that similar compounds had been made at FSU in the past by using essentially the same method is of no consequence, because neither that method nor those similar compounds themselves are claimed in the '653 patent.

If Tao, Soon-Shiong, and Desai had conceived the structures of the claimed compounds, but were then unable to make them without Nadizadeh's help, Nadizadeh might have been a coinventor. That is not this case, however. Here, there is no evidence in the record that Nadizadeh knew that Tao, Soon-Shiong, and Desai were attempting to make any of the claimed compounds, or even that Tao, Soon-Shiong, or Desai had any contact at all with Nadizadeh after the claimed compounds were conceived. Nadizadeh neither made the claimed compounds nor attempted to make them, and he did not have "a firm and definite idea" of the claimed combination as a whole." Although Tao may have learned the beta-lactam method from Nadizadeh, teaching skills or general methods that somehow facilitate a later invention, without more, does not render one a coinventor.^[6]

Finally, to the extent that Nadizadeh's beta-lactam method was proprietary, a question of misappropriation of FSU's trade secrets may have existed. That question was not decided by the district court and is not before us, and indeed appears to have been the subject of a prior settlement agreement between the parties. In any event, the fact that FSU may have kept Nadizadeh's method secret does not implicate Nadizadeh as a coinventor of the three compounds claimed by ABI. Accordingly, we conclude that Nadizadeh is not a coinventor of the claimed compounds.

The district court held that Yang was a coinventor of the compounds claimed in the '653 patent on the basis of Tao's having had knowledge of Yang's discovery that PNIP was the best dual functional radiosensitizer among the taxol analogs that Holton provided to him to test. However, the '653 patent does not claim PNIP or the compounds Holton provided to Yang. Moreover, the court also found that PNIP was made by Nadizadeh prior to Yang's arrival at FSU. Thus, Yang could not have contributed to the conception of the structure of even that compound. Although Tao's choice of side chains may have been informed by his earlier conversations with Yang regarding the efficacy of PNIP, that alone does not make Yang a coinventor of the claimed compounds.

For the preceding reasons, we conclude that Soon-Shiong and Desai are coinventors with Tao of the compounds

claimed in the '653 patent, but that Holton, Nadizadeh, and Yang are not.^[7]

B. Inequitable Conduct

Inequitable conduct includes affirmative misrepresentation of a material fact, failure to disclose material information, or submission of false material information, coupled with an intent to deceive. Molins PLC v. Textron, Inc., 48 F.3d 1172, 1178, 33 USPQ2d 1823, 1826 (Fed. Cir. 1995).^[8] Determination of inequitable conduct requires a two-step analysis. PerSeptive Biosystems v. Pharmacia Biotech, 225 F.3d 1315, 1318, 56 USPQ2d 1001, 1005 (Fed. Cir. 2000). First, the trial court must determine whether the conduct meets a threshold level of materiality. The trial court must then also determine whether the evidence shows a threshold level of intent to mislead the PTO. Id. at 1318-19, 56 USPQ2d at 1003 (citing Baxter Int'l, Inc. v. McGaw, Inc., 149 F.3d 1321, 1327, 47 USPQ2d 1225, 1228-29 (Fed. Cir. 1998)). These threshold determinations are reviewed by this court for clear error. Id.; Kingsdown Med. Consultants, Ltd. v. Hollister, Inc., 863 F.2d 867, 872, 9 USPQ2d 1384, 1389 (Fed. Cir. 1988). Once the threshold levels of materiality and intent have been established, the trial court is required to weigh them. PerSeptive, 225 F.3d at 1319, 56 USPQ2d at 1003; Molins, 48 F.3d at 1178, 33 USPQ2d at 1826-27. In light of all the circumstances, the court must then determine whether the applicant's conduct is so culpable that the patent should be held unenforceable. PerSeptive, 225 F.3d at 1319, 56 USPQ2d at 1003; LaBounty Mfg., Inc. v. U.S. Int'l Trade Comm'n, 958 F.2d 1066, 1070, 22 USPQ2d 1025, 1028 (Fed. Cir. 1992). We review the district court's ultimate determination of inequitable conduct under an abuse of discretion standard. PerSeptive, 225 F.3d at 1319, 56 USPQ2d at 1003; Kolmes v. World Fibers Corp., 107 F.3d 1534, 1541, 41 USPQ2d 1829, 1834 (Fed. Cir. 1997).

ABI argues that, because the evidence does not support the district court's judgment regarding inventorship, "[a] fortiori, the inequitable conduct finding is also error." FSU responds that ABI has not pointed to any error in the court's findings on materiality or intent, leaving it undisputed that the PTO was deprived of material information concerning inventorship by ABI's inequitable conduct in failing to disclose to its patent attorney Tao's connection to FSU.

We agree with ABI that inequitable conduct did not occur here. The district court's conclusion of inequitable conduct was based on its finding that Soon-Shiong and Desai failed to disclose to their attorney that Tao formerly worked at FSU. Since we have concluded that the FSU scientists were not inventors, Tao's having worked at FSU was not material to any issue of patentability in this case.

In practice, patent examiners do not normally engage in determination of the respective contributions of the individual members of an inventive entity as part of making an ex parte examination;^[9] rather, it is the responsibility of the applicants and their attorneys to ensure that the inventors named in a patent application are the only true inventors. The patent examiner assigned to ABI's application concluded that the three compounds claimed in ABI's issued patent were novel and non-obvious in view of the prior art, including several of Holton's earlier patents. Neither the district court nor FSU explains how

the disclosure of Tao's former association with Holton would have affected the examiner's conclusion of patentability.

Inventorship is indeed relevant to patentability under 35 U.S.C. § 102(f), and patents have in the past been held unenforceable for failure to correctly name inventors in cases where the named inventors acted in bad faith or with deceptive intent. See, e.g., Frank's Casing Crew & Rental Tools, Inc. v. PMR Techs., Ltd., 292 F.3d 1363, 63 USPQ2d 1065 (Fed. Cir. 2002) (holding a patent unenforceable due to inequitable conduct where two named inventors deliberately concealed a true inventor's involvement in the conception of the invention and "engaged in a pattern of intentional conduct designed to deceive the attorneys and patent office as to who the true inventors were"); PerSeptive (holding a patent unenforceable where the named inventors had intended to deceive the PTO, and the falsehoods and omissions to the PTO were material to inventorship). Nonetheless, FSU cites no precedent for a patent being held unenforceable simply because an applicant did not disclose his former employers to the PTO. Who Tao formerly worked for is more relevant to ownership than to patentability. Rule 56 imposes a duty to disclose information material to patentability. There is no evidence that ABI withheld any information material to patentability. Finding no other evidence in the record to support a holding of inequitable conduct, we vacate the district court's conclusion.

We have considered FSU's other arguments, and find them unpersuasive.

CONCLUSION

The district court erred in its determination of inventorship. Tao, Soon-Shiong, and Desai are the true and rightful coinventors of the subject matter in the '653 patent, and Holton, Nadizadeh, Yang, and Sandford are not coinventors. The district court also erred in declaring the '653 patent unenforceable for inequitable conduct. The court's decision is therefore

AFFIRMED-IN-PART, REVERSED-IN-PART, and VACATED-IN-PART.

COSTS

Each party to bear its own costs.

[11] “Taxol” is Bristol-Myers Squibb’s registered trademark for paclitaxel. In this opinion, we follow the practice of the district court and the parties of referring to the compound only by that trademark.

[12] “Taxotere” is Aventis’s registered trademark for docetaxel. In this opinion, we follow the practice of the district court and the parties of referring to the compound only by that trademark.

[13] Although taxol is itself a natural product, it is present in only very low concentrations in nature. Moreover, its isolation requires stripping the bark from the yew, thereby killing the trees. Bd. of Educ., 2001 U.S. Dist. LEXIS 19480, at *4-5. Accordingly, semi-synthesis from starting materials obtained from yew needles or other renewable sources is desirable.

[14] Tao was also listed as a coinventor on Holton’s U.S. Patent 5,739,362, which issued in 1998 from a seventh generation continuation-in-part application that described the synthesis of more than 120 different taxol analogs, including, inter alia, PNIP and two compounds that Tao had synthesized himself.

[15] The Joint Appendix submitted by the parties to this appeal includes an “FSU ‘Master List’ of Compounds” listing about 250 taxol derivatives. Significantly, every one of those compounds includes the 10-acetoxy group.

[16] It is also not evident from the record that Nadizadeh’s method truly facilitated Tao’s reduction to practice of the claimed invention. It appears that Nadizadeh’s method differed from a published prior art beta-lactam method principally in its use of acid hydrolysis rather than the base hydrolysis called for by the prior art. Bd. of Educ., 2001 U.S. Dist. LEXIS 19480 at *11. The record does not suggest that the prior art methods were inoperative, but merely that Nadizadeh’s method provided a better yield of FSU’s desired PNIP.

[17] We have noted earlier in this opinion that the ’653 patent application was originally filed with broader claims than finally issued. It is conceivable, although we express no opinion on that matter, that other persons may have had an inventorship role with respect to the subject matter that was cancelled. Nonetheless, it is the granted patent with the limited claims that is before us, and any possible inventorship with respect to the cancelled claims is not at issue here.

[18] The duty to disclose information material to patentability is set forth in PTO Rule 56:

(a) . . . Each individual associated with the filing and prosecution of a patent application has a duty of candor and good faith in dealing with the [U.S. Patent and Trademark] Office, which includes a duty to disclose to the Office all information known to that individual to be material to patentability

(b) Under this section, information is material to patentability when it is not cumulative to information already of record or being made of record in the application, and (1) [i]t establishes, by itself or in combination with other information, a prima facie case of unpatentability of a claim; or (2) [i]t refutes, or is inconsistent with a position the applicant takes in: (i) [o]pposing an argument of unpatentability relied on by the Office, or (ii) [a]sserting an argument of patentability.

37 C.F.R. § 1.56 (2002). Rule 56 was amended on September 8, 2000, at 65 Fed. Reg. 54,666. However, the amendments did not affect the quoted portion of the regulation. The quoted portion has been unchanged since January 17, 1992, which is prior to the filing of the application that led to the ’653 patent.

[19] Cf., e.g., interference determinations and requests to correct inventorship.