United States Court of Appeals for the Federal Circuit

RAPID LITIGATION MANAGEMENT LTD., FORMERLY CELSIS HOLDINGS, INC., IN VITRO, INC.,
Plaintiffs-Appellants

v.

CELLZDIRECT, INC., A DELAWARE CORPORATION AND WHOLLY-OWNED SUBSIDIARY, INVITROGEN CORPORATION, A DELAWARE CORPORATION,
Defendants-Appellees

2015-1570

Appeal from the United States District Court for the Northern District of Illinois in No. 1:10-cv-04053, Senior Judge Milton I. Shadur.

Decided: July 5, 2016

ANDREW JOHN PINCUS, Mayer Brown LLP, Washington, DC, argued for plaintiffs-appellants. Also represented by PAUL WHITFIELD HUGHES; ADAM GLENN KELLY, JOHN A. COTIGUALA, Loeb & Loeb LLP, Chicago, IL; LAURA ANN WYTSMA, Los Angeles, CA.

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ALICE O. MARTIN, Barnes & Thornburg LLP, Chicago, IL, for amicus curiae Biotechnology Industry Organization. Also represented by BRADLEY JOHN OLSON, Washington, DC; HANSJORG SAUER, Biotechnology Industry Organization, Washington, DC.

Before PROST, *Chief Judge*, MOORE and STOLL, *Circuit Judges*.

PROST, *Chief Judge*.

Appellants seek review of the district court's summary judgment determination that U.S. Patent No. 7,604,929 ("'929 patent") is invalid under 35 U.S.C. § 101. The district court concluded that the '929 patent is directed to a patent-ineligible law of nature—that hepatocytes are capable of surviving multiple freeze-thaw cycles—and that the patented process lacks the requisite inventive concept. *Celsis In Vitro, Inc. v. CellzDirect, Inc.*, 83 F. Supp. 3d 774 (N.D. Ill. 2015), *supplemented*, 94 F. Supp. 3d 940 (N.D. Ill.). Because the '929 patent claims are not directed to a patent-ineligible concept, we vacate and remand.

I

Hepatocytes are a type of liver cell that have a number of attributes useful for testing, diagnostic, and treatment purposes. For example, hepatocytes can be used to investigate how drugs under development may be metabo-

lized by the liver or can be used to measure a drug's toxicity or other effects on liver biology. Certain factors, however, limit their use: fresh hepatocytes can only be obtained from liver resections or non-transplantable livers of organ donors, and their lifespan is short. '929 patent col. 2 ll. 25-35. Supply is thus erratic, making availability limited and unpredictable. *Id.* at col. 2 ll. 22-35.

Prior to the invention of the '929 patent, scientists developed "cryopreservation" techniques to preserve hepatocytes for later use. *Id.* at col. 2 ll. 36-40. These methods generally comprised freezing hepatocytes at frigid temperatures; then, when needed, thawing them and recovering the viable cells using density gradient fractionation. *Id.* at col. 2 l. 36-col. 3 l. 4, col. 10 ll. 30-60.

The prior art cryopreservation method had its problems, however. It was understood that the process could damage the hepatocytes, leading to poor recovery numbers of viable cells. *Id.* at col. 3 ll. 5-32. Furthermore, these prior methods were unsuitable for preparing multi-donor hepatocyte pools. *Id.* at col. 3 ll. 33-60. Because hepatocytes from different donors generally have different metabolic properties, researchers desired to pool hepatocytes from various source livers to create a hepatocyte preparation approximating average liver cells. *Id.* at col. 11 ll. 5-27. Such pools are useful research tools to study a drug's impact on a representative population. But because of the limited availability of donor livers and hepatocytes' short lifespan, pooled samples from multiple donors could only be created by first accumulating and freezing enough hepatocytes from single donors, then thawing and combining them for immediate use. *Id.* at col. 3 ll. 49-60. Given the understanding that cryopreservation could damage cells, prevailing wisdom was that hepatocytes could be frozen only once and then had to be either used or discarded. *Celsis*, 83 F. Supp. 3d at 777-78. This severely limited the creation of pooled hepatocyte products. *Id.*

The inventors of the '929 patent discovered that some fraction of hepatocytes are capable of surviving multiple freeze-thaw cycles. As inventor Dr. Hardy testified, "initially we just proved that you could twice freeze the cells and still have viable cells. . . . [T]he unexpected outcome was that cells twice frozen behaved like cells that were once frozen." *Id.* at 778-79 (quoting J.A. 148-49).

Armed with this discovery, the inventors developed an improved process of preserving hepatocytes, claimed in the '929 patent. In general, the improved process comprises: (A) subjecting previously frozen and thawed cells to density gradient fractionation to separate viable cells from non-viable ones; (B) recovering the viable cells; and (C) refreezing the viable cells. '929 patent col. 19 l. 56-col. 20 l. 20. The claims specify that the resulting hepatocyte preparation can be thawed and used immediately, exhibiting 70% viability after the second thaw. *Id.*

The '929 patented process has a number of advantages over the prior art. By separating out and refreezing only the viable cells, the preserved hepatocyte preparations can be thawed and used later without unacceptable loss of viability. *Id.* at col. 3 ll. 64-67. Pooled hepatocyte preparations are also much more easily made: hepatocyte samples from single donors can be pooled together to create a composite preparation that can be refrozen for later use. *Id.* at col. 3 l. 67-col. 4 l. 6, col. 11 l. 2-col. 12 l. 27. This was not possible with the prior art cryopreservation techniques. Appellant employs the improved process in its LiverPool™ product, which comprises multi-cryopreserved, pooled hepatocyte preparations useful for a wide variety of research purposes.

Claim 1 is representative of the '929 patent. It recites:

> 1. A method of producing a desired preparation of multi-cryopreserved hepatocytes, said hepatocytes being capable of being frozen and thawed

> at least two times, and in which greater than 70% of the hepatocytes of said preparation are viable after the final thaw, said method comprising:
>
> (A) subjecting hepatocytes that have been frozen and thawed to density gradient fractionation to separate viable hepatocytes from non-viable hepatocytes,
>
> (B) recovering the separated viable hepatocytes, and
>
> (C) cryopreserving the recovered viable hepatocytes to thereby form said desired preparation of hepatocytes without requiring a density gradient step after thawing the hepatocytes for the second time, wherein the hepatocytes are not plated between the first and second cryopreservations, and wherein greater than 70% of the hepatocytes of said preparation are viable after the final thaw.

Additional dependent claims are directed to the type of density gradient fractionation, the type of hepatocytes, viability, and pooling. For example, with respect to pooling, claim 5 recites:

> 5. The method of claim 1, wherein said preparation comprises a pooled preparation of hepatocytes of multiple sources.

IVT sued LTC for infringing the '929 patent.[1] In response, LTC filed a motion for summary judgment of

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[1] The original suit was brought by Celsis In Vitro, Inc. against CellzDirect, Inc. and Invitrogen Corporation. After various corporate transactions, the named parties are now Plaintiffs-Appellants, Rapid Litigation Management Ltd. and In Vitro, Inc. (collectively, "IVT"), and

invalidity under 35 U.S.C. §§ 101 and 112. The district court granted the motion, finding the '929 patent invalid under § 101 and dismissing the action with prejudice (without reaching the § 112 issues). *Celsis*, 83 F. Supp. 3d at 785-86. In finding the patent invalid under § 101, the court applied the Supreme Court's two-step framework for determining patent eligibility. *See Alice Corp. v. CLS Bank Int'l*, 134 S. Ct. 2347, 2355 (2014) (citing *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1294, 1296-98 (2012)). At step one, the court concluded that the '929 patent "is directed to an ineligible law of nature: the discovery that hepatocytes are capable of surviving multiple freeze-thaw cycles." *Celsis*, 83 F. Supp. 3d at 783. At step two, the court determined that "the patented process lacks the requisite inventive concept," observing that, upon discovering the cells' capability of surviving multiple freeze-thaw cycles, the inventors simply "reapplied a well-understood freezing process." *Id.* at 783-84.

IVT appeals the court's decision. We have jurisdiction under 28 U.S.C. § 1295(a)(1). We review the court's grant of summary judgment under the law of the regional circuit; here, the Seventh Circuit's de novo standard. *Memorylink Corp. v. Motorola Sols., Inc.*, 773 F.3d 1266, 1270 (Fed. Cir. 2014) (citing *Chaklos v. Stevens*, 560 F.3d 705, 710 (7th Cir. 2009)). The issue of patent-eligibility under § 101 is a question of law that we review without deference. *CyberSource Corp. v. Retail Decisions, Inc.*, 654 F.3d 1366, 1369 (Fed. Cir. 2011).

II

Section 101 permits the patenting of "any new and

Defendants-Appellees, Cellzdirect, Inc. and Invitrogen Corporation (which merged with another corporation to form Life Technologies Corporation) (collectively, "LTC").

useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof," subject to other requirements of the title. 35 U.S.C. § 101. The Supreme Court has "interpreted § 101 and its predecessors . . . for more than 150 years" to "contain[] an important implicit exception: Laws of nature, natural phenomena, and abstract ideas are not patentable." *Alice*, 134 S. Ct. at 2354 (quoting *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107, 2116 (2013)). The concern underlying these judicial exclusions is that "patent law not inhibit further discovery by improperly tying up the future use of these building blocks of human ingenuity." *Id.* (internal quotation marks omitted) (quoting *Mayo*, 132 S. Ct. at 1301).

The Supreme Court has recently articulated a two-part test for distinguishing patents that claim one of the patent-ineligible exceptions from those that claim patent-eligible applications of those concepts. *Id.* (citing *Mayo*, 132 S. Ct. at 1294, 1296-97). Step one asks whether the claim is "directed to one of [the] patent-ineligible concepts." *Id.* If the answer is no, the inquiry is over: the claim falls within the ambit of § 101. If the answer is yes, the inquiry moves to step two, which asks whether, considered both individually and as an ordered combination, "the additional elements 'transform the nature of the claim' into a patent-eligible application." *Id.* (quoting *Mayo*, 132 S. Ct. at 1297). Step two is described "as a search for an 'inventive concept.'" *Id.* (quoting *Mayo*, 132 S. Ct. at 1294). At step two, more is required than "well-understood, routine, conventional activity already engaged in by the scientific community," which fails to transform the claim into "significantly more than a patent upon the" ineligible concept itself. *Mayo*, 132 S. Ct. at 1298, 1294.

A

We begin with step one: whether the claims here are

"directed to" a patent-ineligible concept. The district court concluded that they were: that "the patent is directed to an ineligible law of nature: the discovery that hepatocytes are capable of surviving multiple freeze-thaw cycles." *Celsis*, 83 F. Supp. 3d at 783. We disagree.

Claim 1 recites a "method of producing a desired preparation of multi-cryopreserved hepatocytes." '929 patent col. 19 l. 56-col. 20 l. 20. The method requires an artisan to carry out a number of concrete steps to achieve the desired preparation: step (A) requires performing density gradient fractionation on a set of previously frozen and thawed cells to separate out the viable ones; step (B) requires recovering the separated viable cells; and step (C) requires cryopreserving the recovered cells. The end result is a preparation of multi-cryopreserved cells that can be thawed for immediate use, retaining 70% viability. Claim 5 adds to the method, reciting "a pooled preparation of hepatocytes of multiple sources." *Id.* at col. 20 ll. 31-33. The resulting preparation, and the process for creating it, achieved a notable advance over prior art techniques for preserving hepatocytes. J.A. 2513-14.

The district court identified in these claims what it called a "natural law"—the cells' capability of surviving multiple freeze-thaw cycles. We need not decide in this case whether the court's labeling is correct. It is enough in this case to recognize that the claims are simply not directed to the ability of hepatocytes to survive multiple freeze-thaw cycles. Rather, the claims of the '929 patent are directed to a new and useful laboratory technique for preserving hepatocytes. This type of constructive process, carried out by an artisan to achieve "a new and useful end," is precisely the type of claim that is eligible for patenting. *Alice*, 134 S. Ct. at 2354 (quoting *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972)). The inventors certainly discovered the cells' ability to survive multiple freeze-thaw cycles, but that is not where they stopped, nor is it what they patented. Rather, "as the first party with

knowledge of" the cells' ability, they were "in an excellent position to claim applications of that knowledge." *Myriad*, 133 S. Ct. at 2120 (quoting *Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office*, 689 F.3d 1303, 1349 (Fed. Cir. 2012) (Bryson, J., concurring in part and dissenting in part)). That is precisely what they did. They employed their natural discovery to create a new and improved way of preserving hepatocyte cells for later use.

The claims in this case are immediately distinguishable from those we have found patent ineligible in cases since *Mayo* and *Alice*. In recent cases, we found claims "directed to" a patent-ineligible concept when they amounted to nothing more than observing or identifying the ineligible concept itself. For example, in *Genetic Technologies*, the claim recited methods for detecting a coding region of DNA based on its relationship to non-coding regions. *Genetic Techs., Ltd. v. Merial L.L.C.*, 818 F.3d at 1369, 1373-74 (Fed. Cir. 2016). Because the relationship between coding and non-coding sequences was a law of nature, the claim amounted to nothing other than identifying "information about a patient's natural genetic makeup." *Id.* at 1375. Likewise in *Ariosa*, the claims recited methods for detecting paternally inherited cffDNA in the blood or serum of a pregnant female. *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1373-74 (Fed. Cir. 2015), *cert. denied*, No. 15-1102, 2016 WL 1117246 (June 27, 2016). The existence and location of cffDNA is a natural phenomenon; identifying its presence was merely claiming the natural phenomena itself. *Id.* at 1376. And in *In re BRCA*, the claims recited methods for screening human germline for an altered BRCA1 gene by comparing the target DNA sequence with wild-type sequence. *In re BRCA1- & BRCA2-Based Hereditary Cancer Test Patent Litig.*, 774 F.3d 755, 761-62 (Fed. Cir. 2014). But comparing two sequences to detect alterations is a patent-ineligible "abstract mental process." *Id.* at 763. Although the claims in each of these cases employed

method steps, the end result of the process, the essence of the whole, was a patent-ineligible concept.

The same is not true here. The end result of the '929 patent claims is not simply an observation or detection of the ability of hepatocytes to survive multiple freeze-thaw cycles. Rather, the claims are directed to a new and useful method of preserving hepatocyte cells. Indeed, the claims recite a "*method of producing* a desired preparation of multi-cryopreserved hepatocytes." '929 patent col. 19 l. 56-col. 20 l. 20 (emphasis added). Through the recited steps, the patented invention achieves a better way of preserving hepatocytes. The '929 patent claims are like thousands of others that recite processes to achieve a desired outcome, e.g., methods of producing things, or methods of treating disease. That one way of describing the process is to describe the natural ability of the subject matter to *undergo* the process does not make the claim "directed to" that natural ability. If that were so, we would find patent-ineligible methods of, say, producing a new compound (as directed to the individual components' ability to combine to form the new compound), treating cancer with chemotherapy (as directed to cancer cells' inability to survive chemotherapy), or treating headaches with aspirin (as directed to the human body's natural response to aspirin).

Our conclusion applies even more so to claim 5, which requires the additional step of pooling hepatocytes from multiple donors. Conventional preparation methods were unable to create a frozen hepatocyte preparation that could be stored for a long duration and then, upon thawing, result in a pool of hepatocytes from multiple donors with viability upwards of 70%. Because the claimed process involves both multiple freeze-thaw cycles and pooling cells from various donors, it results in a preparation that is both new and vastly more useful for research than hepatocyte preparations made by conventional methods.

LTC asserts that claim 5, including the additional requirement of pooling of hepatocyte cells, is indistinguishable from the claims held patent ineligible in *Funk Bros. Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948). There the Supreme Court held that a mixture of different bacterial species was not patent eligible because "[n]o species acquires a different use," "[e]ach species has the same effect it always had," and "[t]he bacteria perform in their natural way." *Id.* at 131. But *Funk Bros.* involved product claims, and the court explicitly noted that it was not "presented [with] the question whether the methods of selecting and testing the non-inhibitive strains are patentable." *Id.* at 130. Here, regardless of whether the individual hepatocytes in the pool of multi-cryopreserved hepatocytes have the same effect they always had or perform in their natural way, the claims are directed to a new and useful process of creating that pool, not to the pool itself.

Nor is LTC correct in arguing that the claims of the '929 patent are just like the isolated DNA found unpatentable in *Myriad*, 133 S. Ct. 2107, or the methods of detecting cffDNA found unpatentable in *Ariosa*, 788 F.3d 1371. In *Myriad*, while holding the composition claims to isolated DNA patent ineligible, the Supreme Court stated: "It is important to note what is *not* implicated by this decision. First, there are no method claims before this Court. Had Myriad created an innovative method of manipulating genes while searching for the BRCA1 and BRCA2 genes, it could have possibly sought a method patent. But the processes used by Myriad to isolate DNA were well understood . . . and are not at issue in this case." 133 S. Ct. at 2119-20. Here, the inventors developed an innovative method of manipulating hepatocytes, a particular kind of liver cell which, prior to this invention, had been very difficult to preserve for future use. *See id.* The claims are thus distinguishable from those held unpatentable in *Myriad*. They are also distinguisha-

ble from those held unpatentable in *Ariosa*, 788 F.3d 1371. Although the claims in *Ariosa* were also written as process claims, the court concluded that they were "directed to" the patent-ineligible cffDNA itself. *Id.* at 1376. The claims of the '929 patent, as explained above, are not similarly infirm.

We are also not persuaded by LTC's conjecture that, if the claimed multi-cryopreservation process is sufficient to imbue the '929 patent claims with patent-eligibility, "then any frozen or preserved cell, bacteria, or other product of nature would be patent eligible." Appellees' Br. 24. Not so. It is the *process* of preservation that is patent eligible here, not necessarily the end product. In any event, LTC's argument proves too much: if LTC were correct, no one could ever get a patent on cryopreservation, or on any other innovative method that acts on something that is naturally occurring, simply because of the nature of the underlying subject matter. Section 101 is not so narrow.

LTC argues that our approach improperly shoehorns the step two analysis into step one: that focusing on the claims' *application* of the cells' ability to survive multiple freeze-thaw cycles in a new preservation process properly falls under step two's inquiry into "whether the additional elements 'transform the nature of the claim' into a patent-eligible application." *See Alice*, 134 S. Ct. at 2355 (quoting *Mayo*, 132 S. Ct. at 1297). But it is LTC's approach, not ours, that collapses the inquiry into a single step. Under the Supreme Court's test, some claims will be "directed to" a patent-ineligible concept and some, necessarily, will not. This is true even if "all inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas." *Mayo*, 132 S. Ct. at 1293. As the Supreme Court has made clear, "an invention is not rendered ineligible for patent simply because it involves" one of the patent-ineligible concepts. *Alice*, 134 S. Ct. at 2354. Indeed, to preclude the patenting of an invention simply because it touches on some-

thing natural would "eviscerate patent law." *Mayo*, 132 S. Ct. at 1293.

At step one, therefore, it is not enough to merely identify a patent-ineligible concept underlying the claim; we must determine whether that patent-ineligible concept is what the claim is "directed to." Here, the plain claim language shows that it is not. The '929 patent does not simply claim hepatocytes' ability to survive multiple freeze-thaw cycles. The '929 patent instead claims a "method of producing a desired preparation of multi-cryopreserved hepatocytes." '929 patent col. 19 l. 56-col. 20 l. 20. This new and improved technique, for producing a tangible and useful result, falls squarely outside those categories of inventions that are "directed to" patent-ineligible concepts.

B

Even if LTC were correct that the '929 patent is "directed to" hepatocytes' natural ability to survive multiple freeze-thaw cycles, and that we must proceed to step two, we would find the claims patent-eligible at that point as well. Under step two, claims that are "directed to" a patent-ineligible concept, yet also "improve[] an existing technological process," are sufficient to "transform[] the process into an inventive application" of the patent-ineligible concept. *Alice*, 134 S. Ct. at 1358 (quoting *Mayo*, 132 S. Ct. at 1299) (discussing *Diamond v. Diehr*, 450 U.S. 175 (1981). The claims of the '929 patent do precisely that: they recite an improved process for preserving hepatocytes for later use. The benefits of the improved process over the prior art methods are significant. The claimed method is used to create hepatocyte preparations that no longer exhibit unacceptable loss of viability. And it allows researchers to pool samples together in advance and preserve them for later use, rather than needing to wait until enough single samples are accumulated that can be pooled and used immediate-

ly. The claimed method is patent eligible because it applies the discovery that hepatocytes can be twice frozen to achieve a new and useful preservation process. *See Mayo*, 132 S. Ct. at 1293-94 ("[A]n *application* of a law of nature or mathematical formula to a known structure or process may well be deserving of patent protection.") (quoting *Diehr*, 450 U.S. at 187).

That each of the claims' individual steps (freezing, thawing, and separating) were known independently in the art does not make the claim unpatentable. It is true that, at step two, a claim that recites only "well-understood, routine, conventional activity already engaged in by the scientific community" will not be patent eligible. *Mayo*, 132 S. Ct. at 1298. Thus, in *Mayo*, the claims failed step two because the steps of administering the drug, measuring metabolite levels, and adjusting dosage were already being performed by those in the field; adding knowledge of the natural law was insufficient to render the claims patent eligible. *Id.* Likewise in *Ariosa*, the steps of preparing, amplifying, and detecting genetic sequences were already being done; performing those same steps on a newly discovered, naturally-occurring substrate (cffDNA in maternal plasma or serum) did not rise to the level of an inventive concept. 788 F.3d at 1377-78. That is not to say, however, that all process claims that employ only independently known steps will be unpatentable. To the contrary, in examining claims under step two, we must view them as a whole, considering their elements "both individually and 'as an ordered combination.'" *Alice*, 134 S. Ct. at 2355 (quoting *Mayo*, 132 S. Ct. at 1298). Thus, "a new combination of steps in a process may be patentable even though all the constituents of the combination were well known and in common use before the combination was made." *Diehr*, 450 U.S. at 188.

Here, the claimed process involves freezing and thawing hepatocytes twice. The individual steps of freezing

and thawing were well known, but a process of preserving hepatocytes by repeating those steps was itself far from routine and conventional. As the examiner noted when allowing the patent, "[t]he prior art only discloses methods having *one* freeze-thaw cycle of hepatocytes, wherein, upon thawing, a gradient centrifugation step is required to remove the non-viable cells." J.A. 2513-14 (emphasis added). Likewise, during reexamination, the examiner explained that "[t]he prior art evidence[d] cellular damage produced by cryopreservation, and a lack of any experimentation with *multiply* cryopreserved cells." J.A. 7157 (emphasis added). We made similar observations earlier in this litigation, noting that "the prior art taught away from multiple freezings," as "[a] single round of freezing severely damages hepatocyte cells and results in lower cell viability." *Celsis In Vitro, Inc. v. CellzDirect, Inc.*, 664 F.3d 922, 928 (Fed. Cir. 2012); *see also id.* (stating that "the present invention is in an art well-known for its unpredictability" and the "art was a crowded field for many years and yet there was not one reference to *multi*-cryopreservation"). As aptly summarized by the district court: "Prevailing wisdom . . . taught that cells could be frozen only once and then had to be used or discarded." *Celsis*, 83 F. Supp. 3d at 777-78.

Repeating a step that the art taught should be performed only once can hardly be considered routine or conventional. This is true even though it was the inventor's discovery of something natural that led them to do so. Just as in *Diehr*, it is the particular "combination of steps" that is patentable here. 450 U.S. at 188. The inventors discovered that some percentage of hepatocytes can survive multiple freeze-thaw cycles and applied that discovery to improve existing methods for preserving hepatocytes. To require something more at step two would be to discount the human ingenuity that comes from applying a natural discovery in a way that achieves

a "new and useful end." *Alice*, 134 S. Ct. at 2354 (quoting *Gottschalk*, 409 U.S. at 67).

C

We end with two additional points. First, the crux of LTC's argument seems to be that, once it was discovered that hepatocytes could survive multiple freeze-thaw cycles, it would have been a simple task to repeat the known freeze-thaw process to arrive at the claimed invention. But patent-eligibility does not turn on ease of execution or obviousness of application. Those are questions that are examined under separate provisions of the Patent Act. *Mayo*, 132 S. Ct. at 1304.[2]

Second, while pre-emption is not the test for determining patent-eligibility, *Ariosa*, 788 F.3d at 1378-79, it is certainly the "concern that undergirds . . . § 101 jurisprudence," *Alice*, 134 S. Ct. at 2358. Here, while not resting our opinion on them, we note the district court's findings that the '929 patent "does not lock up the natural law in its entirety" and that "LTC has already managed to engineer around the patent." *Celsis*, 83 F. Supp. 3d at 785. These findings accord with our conclusion that the

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[2] Indeed, the obviousness of the '929 patent claims under 35 U.S.C. § 103 has been addressed in prior proceedings. During original examination, and then again during post-grant reexamination, the U.S. Patent and Trademark Office found the claims non-obvious given the knowledge that cryopreservation damages cells and the prior art's lack of experimentation with multi-cryopreserved cells. J.A. 2513-14; J.A. 7157. On a preliminary record, we made similar observations in affirming the district court's entry of preliminary injunction. *See Celsis*, 664 F.3d at 928 (noting that "the prior art taught away from multiple freezings").

patent is not "directed to" a patent-ineligible building block of human ingenuity.

III

Because the '929 patent claims are not directed to a patent-ineligible concept, we vacate and remand for further proceedings consistent with this opinion.

VACATED AND REMANDED

COSTS

Costs to appellants.