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Federal Circuit Friday

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Occasionally Federal Circuit Friday becomes "District Court Friday" when a district court issues a decision involving an interesting or useful point.

On December 24, the U.S. District Court for the Northern District of California granted summary judgement in *Illumina v. Ariosa Diagnostics et al*. that all asserted claims of two Illumina Non-Invasive Prenatal Test ("NIPT") patents were invalid for lack of patent eligibility.[1] The claims of both patents related to selectively removing *maternal* cell-free DNA from a mother's blood sample to thereby enrich for *fetal* cell-free DNA in the sample. The technological basis for these claimed inventions was what Illumina called a "surprising finding" that fetal cell-free DNA tended to be 500 base pairs or less, allowing for size-discrimination to selectively remove maternal cell-free DNA.

***Alice* Step 1: Is the claim directed to a patent ineligible concept?**

The district court found that the claims were directed to naturally-occurring fetal DNA, *i.e.,* the natural phenomenon of fetal DNA that had been in the maternal blood sample all along and that was not structurally altered in any way by the claimed method. The district court explained that "[b]oth patents claim results from a test of naturally occurring fetal DNA and do not transform the naturally occurring product into something new."[2] The court further explained that the inclusion in the claim of "analyzing" the naturally occurring fetal DNA "is insufficient to overcome the 'directed to' inquiry."[3]

Illumina argued that the claimed methods yielded a structural change in the overall set of cell-free DNA fragments in the maternal blood sample in that the ratio of fetal to maternal cell-free DNA was increased (*i.e.,* relatively less maternal and more fetal). The district court dismissed that argument because "[c]hanging the ratio of two natural products in a mixture and analyzing one of those products does not impact whether an invention is directed towards a natural phenomenon."[4]

***Alice* Step 2: Is there an inventive concept to ensure the patent in practice amounts to significantly more than a patent on the ineligible concept itself?**

The district court found that the claims did not include an inventive concept separate from the natural phenomenon – "the claims extend only to isolation and analysis of a naturally-occurring phenomenon and employ routine, well-known laboratory techniques."[5]

In concluding that the claims were not patent-eligible, the district court explained that "[t]he 'novelty' of an idea is not enough in itself to confer patentability, where the novelty does not exceed the 'inventive concept' limitations."[6]

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1 Order Granting Defendants' Motion for Summary Judgment, Case 3:18-cv-02487, December 24, 2018 (J. Susan Illston) (hereinafter "Order").

2 Order at 9-10.

3 *Id.* at 10.

4 *Id.* at 9.

5 *Id.* at 13. The court explained further: "The claims of each patent are not inventive. The independent claims require three phases: extraction, size production, and selective removal. Each of the steps is described as well-known and conventional." *Id.*

6 *Id.*

Distinguishing *CellzDirect*:

An interesting and useful part of this decision was how the district court distinguished *Rapid Litigation Management. v. CellzDirect*[7] (herein "*CellzDirect*"), a case in which claims relating to cryogenically freezing hepatocytes were held patent-eligible.

At *Alice Step 1*, the district court explained that in *CellzDirect* the claims were not directed to the ability of hepatocytes to survive multiple freeze-thaw cycles, a natural phenomenon, but were instead directed to a "new and useful laboratory technique for preserving hepatocytes" that exploited that natural phenomenon. The district court noted in particular that in *CellzDirect* "the end result was cryogenically frozen useful liver cells that did not occur in nature" while in the instant case the end result was naturally-occurring, "a testable quantity of genetic information found in nature."[8] In essence, then, at *Alice Step 1* the *CellzDirect* claims were directed a non-naturally occurring thing (cryogenically frozen and useful liver cells) while the Illumina claims were directed to an enriched sample of a naturally-occurring thing (fetal cell-free DNA in maternal blood).

At *Alice Step 2*, the district court explained that the *CellzDirect* claims "went beyond applying a known laboratory technique to a newly discovered natural phenomenon, and instead created an entirely new laboratory technique that 'is not simply an observation or detection' based on the natural phenomenon" whereas the Illumina claims "extend only to isolation and analysis of a naturally occurring phenomenon and employ routine, well-known laboratory techniques."[9]

The graphic on the following page compares an exemplary Illumina claim with an exemplary claim from *CellzDirect* to show how the claims differed in ways relevant to patent eligibility.

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Patent eligibility is confusing and the case results oftentimes seem arbitrary. But there is principle and logic underlying (most of) the cases. For example, using the metaphor of tree and leaf, Illumina claimed a method for plucking a leaf from a tree for subsequent analysis of the leaf while the patentee in *CellzDirect* claimed a novel method for preserving a plucked leaf for later study.

Other related cases can also helpfully be viewed using variations on the "tree-leaf" metaphor:

- *Genetic Techs. v. Merial:*[10] Claims not patent-eligible because they merely identified the presence of a naturally-occurring allele by looking at the sequence of a genetically-linked non-coding region – akin to inferring that a tree is a maple from the shape of its leaves.
- *Ariosa Diagnostics v. Sequenom:*[11] Claims not patent-eligible because they merely amplified and detected naturally-occurring paternally-inherited fetal cell-free DNA in a maternal blood sample – akin to using binoculars to see a leaf on a distant tree.
- *In re BRCA1- & BRCA2-Based Hereditary Cancer Test Patent Litigation:*[12] Claims not patent-eligible because they merely identified the presence of a naturally-occurring mutation by comparing a sample's sequence to wild-type sequences – akin to identifying a tree by comparing one of its leaves to pictures in the AUDUBON SOCIETY FIELD GUIDE TO TREES.

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7 827 F.3d 1042 (Fed. Cir. 2016).

8 Order at 11.

9 *Id.* at 12-13.

10 818 F.3d at 1369, 1373-74 (Fed. Cir. 2016).

11 788 F.3d 1371, 1373-74 (Fed. Cir. 2015), *cert. denied,* No. 15-1102, 2016 WL 1117246 (June 27, 2016).

12 774 F.3d 755, 761-62 (Fed. Cir. 2014).

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Federal Circuit Friday: Patent Eligibility & *Illumina v. Ariosa Diagnostics*

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Overall focus = enriching for naturally-occurring cell-free fetal DNA

Claim expressly focuses on cell-free ***fetal*** DNA ("analyzing a genetic locus involved in a fetal chromosomal aberration").

Extraction step = routine, conventional.

Size discrimination & selective removal steps = routine, conventional.

End result = the ***same fetal DNA*** (a natural phenomenon) that was present in original sample, merely separated or purified from part of its prior environment.

Analyzing step adds nothing specific and appears to be routine, conventional.

Illumina	CellzDirect
1. A method for preparing a deoxyribonucleic acid (DNA) fraction from a pregnant human female useful for analyzing a genetic locus involved in a fetal chromosomal aberration, comprising:	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) extracting DNA from a substantially cell-free sample of blood plasma or blood serum of a pregnant human female to obtain extracellular circulatory fetal and maternal DNA fragments;	(A) subjecting hepatocytes that have been frozen and thawed to density gradient fractionation to separate viable hepatocytes from nonviable hepatocytes, (B) recovering the separated viable hepatocytes, and
(b) producing a fraction of the DNA extracted in (a) by:	(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,
(i) size discrimination of extracellular circulatory DNA fragments, and	
(ii) selectively removing the DNA fragments greater than approximately 500 base pairs,	
wherein the DNA fraction after (b) comprises a plurality of genetic loci of the extracellular circulatory fetal and maternal DNA; and	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.
(c) analyzing a genetic locus in the fraction of DNA produced in (b).	-

Overall focus = "a new and improved way of preserving hepatocyte cells for later use"

Claim expressly focuses on "***multi***-cryopreserved hepatocytes" having "greater than 70%" viability.

Employing a ***second cryogenic freezing*** = a novel additional method step (prior art taught away, too).

End result = ***frozen viable hepatocytes*** (non-naturally occurring) not merely a subset of hepatocytes that were present in the original sample of hepatocytes.

End result = frozen hepatocytes having useful property not found in all of original hepatocytes.