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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte ALEX GARVIN

Appeal 2019-001241
Application 12/008,385
Technology Center 1600

ERRATUM

The Decision on Appeal for the above-identified application mailed January 21, 2020 contains errors.

Page 3 of the Decision reads: "We REVERSE." This should read: "We AFFIRM."

Page 4 of the Decision should read:

ISSUES AND ANALYSES

> We agree with, and adopt, the Examiner's findings, reasoning, and conclusion that the claims on appeal lack written descriptive support. We do not agree with, nor do we adopt the Examiner's findings, reasoning, and conclusion that the claims are obvious over the combined cited prior art.

On page 9, the Decision reads: "We consequently reverse the Examiner's rejection of claims 40 and 45 upon this ground." Because we affirm the Examiner's rejection with respect to Section A, Issue 1, the

sentence should read: "We consequently *affirm* the Examiner's rejection of claims 40 and 45 upon this ground."

Similarly, the CONCLUSION of the Decision on page 21 of the Decision should read, in relevant part: "The Examiner's rejection of claims 40 and 45 under 35 U.S.C. § 112, first paragraph, is affirmed." Page 22 of the Decision should therefore read:

AFFIRMED

Claims Rejected	**35 U.S.C. §**	**Reference(s)/Basis**	**Affirmed**	**Reversed**
40, 45	112, first paragraph	Lack of written descriptive support	40, 45	
40, 45	103(a)	Gill, Greenspoon, Eshleman, Winkler, Bianchi, Atkinson, Nakanishi, Kwon, Latham, van Santen, Sanyal		40, 45
Overall Outcome			40, 45	

All other portions of the Decision on Appeal remain unchanged. The time period(s) established by the original Decision on Appeal mailed January 21, 2020 are reset to the mailing date of this erratum. Any confusion caused regarding this matter is regretted.

If there any questions pertaining to this Erratum, please contact the Patent Trial and Appeal Board at 571-272-9797.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte ALEX GARVIN[1]

Appeal 2019-001241
Application 12/008,385
Technology Center 1600

Before JEFFREY N. FREDMAN, JOHN G. NEW, and JAMIE T. WISZ, *Administrative Patent Judges.*

NEW, *Administrative Patent Judge.*

DECISION ON APPEAL

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[1] We use the word "Appellant" to refer to the "applicant" as defined in 37 C.F.R. § 1.142. Appellant identifies Alex M. Garvin as the real party-in-interest. App. Br. 2.

SUMMARY

Appellant files this appeal under 35 U.S.C. § 134(a) from the Examiner's Non-Final Rejection of claims 40 and 45 as unpatentable under 35 U.S.C. § 112, first paragraph, as lacking written descriptive support.

Claims 40 and 45 also stand rejected as unpatentable under 35 U.S.C. § 103(a) as being obvious over the combination of P. Gill et al., *Forensic Application of DNA "Fingerprints,"* 318 NATURE 577–79 (1985) ("Gill"), J. Eshleman et al., *Use of DNase to Eliminate Contamination in Ancient DNA Analysis*, 22 ELECTROPHORESIS 4316–19 (2001) ("Eshleman"), A. Winkler et al., *Gene Expression and Activity of Specific Opioid-Degrading Enzymes in Different Brain Regions of the AA and ANA Lines of Rats*, 1406 BIOCHEM. BIOPHYS. ACTA, 219–27 (1998) ("Winkler"); P.G. Bianchi et al., *Effect of Deoxyribonucleic Acid Protamination on Fluorochrome Staining and In Situ Nick-Translation of Murine and Human Mature Spermatozoa*, 49 BIOL. REPRO. 1083–88 (1993) ("Bianchi"), P.W. Atkinson et al., *Association of Exogenous DNA with Cattle and Insect Spermatozoa in Vitro*, 29 MOL. REPRO. DEV. 1–5 (1991) ("Atkinson"), S.A. Greenspoon et al., *Application of the BioMek® 2000 Laboratory Automation Workstation and the DNA IQ™ System to the Extraction of Forensic Casework Samples*, 49(1) J. FORENSIC SCI. 1–11 (2004) ("Greenspoon"), A. Nakanishi et al., *Gene Transfer in the Chicken by Sperm-Mediated Methods*, 36 MOL. REPRO. DEV. 258–61 (1993) ("Nakanishi"), Kwon (US 2004/0038213 A1, February 26, 2004) ("Kwon"), Latham et al. (WO 2004/090114 A2, October 21, 2004) ("Latham"), V.L. van Santen, *Characterization of the Bovine Herpesvirus 4 Major Immediate-Early Transcript*, 65(10) VIROL. 5211 (1991) ("van Santen"), and A. Sanyal et al., *An Effective Method of Completely Removing Contaminating Genomic*

DNA from an RNA Sample to be Used for PCR, 8 MOL. BIOTECH. 135–37 (1997) ("Sanyal").[2]

We have jurisdiction under 35 U.S.C. § 6(b).

We REVERSE.

NATURE OF THE CLAIMED INVENTION

Appellant's claimed invention is directed to a method for the isolation of sperm DNA from swabs taken from rape victims without having to perform a change in buffers. Spec. Abstr.

REPRESENTATIVE CLAIM

Independent claim 40 is the only independent claim on appeal and representative. Claim 40 recites:

> 40. A method of separating human sperm DNA from human non-sperm DNA in sexual assault samples comprising:
>
> contacting a sample containing human sperm cells and human non-sperm cells with proteinase-K in an extraction buffer solution comprising t-octylphenoxypolyethoxyethanol,

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[2] Appellant also appeals the Examiner's conclusion that Appellant has not complied with one or more conditions for receiving the benefit of an earlier filing date for the patent application under 35 U.S.C. § 119(e). App. Br. 10 (citing Non-Final Act. 2–5). However, the Examiner's finding in this respect is not itself a ground for rejection of the claims, nor does it form the basis of another rejection from which Appellant appeals, nor does Appellant rely on the earlier filing date to antedate a reference. Consequently, we do not reach this issue. *See* 37 C.F.R. § 41.31(a)(1) ("Every applicant, any of whose claims has been twice rejected, may appeal from the decision of the examiner to the Board").

wherein the extraction buffer solution does not contain sodium dodecyl sulfate;

digesting the human non-sperm cells with the proteinase-K;

adding a DNAse I to the same extraction buffer solution in which the non-sperm cells were digested without a centrifugation step or a filtration step with respect to the addition of the DNAse I;

selectively degrading non-sperm DNA from the non-sperm cells with the DNAse I;

inactivating the DNAse I and lysing the sperm by adding ethylenediaminetetraacetic (EDTA) and dithiothreitol (DTT) for at least 5 minutes at 56°C; and

separating sperm DNA from the human sperm for further analysis of the sperm DNA

App. Br. 45.

ISSUES AND ANALYSES

We do not agree with, nor do we adopt, the Examiner's findings, reasoning, and conclusion that the claims on appeal lack written description or are obvious over the combined cited prior art. We address the arguments raised by Appellant below.

A. Rejection of the claims under 25 U.S.C. §112, first paragraph

Issue 1

Appellant argues that the Examiner erred in concluding that the limitation of claim 40 reciting "inactivating the DNAse I and lysing the

sperm by adding ethylenediaminetetraacetic (EDTA) and dithiothreitol (DTT) for at least 5 minutes at 56°C" lacks written descriptive support in the Specification. App. Br. 13.

Analysis

The Examiner acknowledges that Appellant's Specification discloses that: "The next step is to inactivate the nuclease, and to lyse the sperm. This is done by adding: 25 mM EDTA (ethylenediaminetetraac[etic] acid), and 50 mM DTT(dithiothreitol). Incubation is for 5 minutes at 56 degrees." Non-Final Act. 6 (quoting Spec. 7). However, the Examiner finds, the recitation of 5 minutes does not provide written descriptive support for incubation times of more than 5 minutes, which is within the scope of the amended claim. *Id.* The Examiner therefore concludes that incubation times of greater than 5 minutes is new matter that is not supported by the Specification. *Id.*

Appellant argues that the Specification's disclosure of an incubation time of 5 minutes at 56°C provides support for the incubation to be for a duration of "at least 5 minutes," as recited in the claim. App. Br. 13. According to Appellant, the disclosure of a 5 minute incubation time is a statement of the best mode of practicing the invention. *Id.* Appellant contends that a disclosure of the best mode does not limit the general disclosure that the solution is to be incubated. *Id.* Appellant asserts that a skilled artisan who understands that the best mode incubation time is 5 minutes will know that an acceptable incubation time may be more than 5 minutes, but that the incubation time must be at least 5 minutes, without requiring undue experimentation. *Id.* at 13–14. Appellant argues that the

claimed method is not limited to the specific example that is set forth in the disclosure of the best mode. *Id.* at 14.

We are not persuaded by Appellant's argument. The standard for satisfying the written description requirement is whether the disclosure "allow[s] one skilled in the art to visualize or recognize the identity of the subject matter purportedly described." *Alcon Research Ltd. v. Barr Labs., Inc.*, 745 F.3d 1180, 1190 (Fed. Cir. 2014) (quoting *Enzo Biochem, Inc. v. Gen–Probe Inc.*, 323 F.3d 956, 968 (Fed. Cir. 2002). "[T]he critical inquiry is whether the patentee has provided a description that 'in a definite way identifies the claimed invention' in sufficient detail that a person of ordinary skill would understand that the inventor was in possession of it at the time of filing." *Alcon*, 745 F.3d 1190–91 (quoting *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1352 (Fed. Cir. 2010)). However, "a description that merely renders the invention obvious does not satisfy the requirement." *Ariad*, 598 F.3d at 1352.

Appellant's Specification expressly discloses that: "Incubation is for 5 minutes at 56 degrees." Spec. 7. However, the claim 40 recites "at least 5 minutes," thus including within its scope intervals much longer than the claimed interval.

Our reviewing court has held that: "[T]he PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims." *In re Wertheim*, 541 F.2d 257, 263-264 (C.C.P.A. 1976). "By pointing to the fact that claim 1 reads on embodiments outside the scope of the description, the PTO has satisfied its burden." *Id.* The burden therefore falls upon Appellant to show that a person of ordinary skill in the art would

be able to recognize that the identity of the subject matter described includes intervals longer than, indeed potentially much longer than, the 5 minutes disclosed by the Specification. *Id.*; *Alcon*, 745 F.3d at 1190. Appellant has failed to meet this burden by offering objective evidence of record, and we consequently are not persuaded by Appellant's arguments in this regard.

Issue 2

Appellant argues that the Examiner erred in finding that Appellant's Specification fails to provide written descriptive support for the limitation of claim 40 reciting: "adding a DNAse I to the same extraction buffer solution in which the non-sperm cells were digested without a centrifugation step or a filtration step with respect to the addition of the DNAse I." App. Br. 14.

Analysis

The Examiner acknowledges that Appellant's Specification discloses general support for excluding centrifuging and filtration. Non-Final Act. 6. However, the Examiner finds, the Specification does not reveal support for excluding centrifuging and filtration from the step adding DNAse I. *Id.* at 6–7. The Examiner reasons that this step is a new embodiment which is not specifically described by the original Specification and therefore introduces new matter. *Id.* at 7.

Appellant argues that, because the Specification generally excludes centrifugation and filtration, that general exclusion applies to any and all specific instances of excluding centrifugation and filtration in the claimed method. App. Br. 15. According to Appellant, excluding centrifugation and filtration from the step of adding DNAse I to the same extraction buffer solution in which the non-sperm cells were digested is not a new

embodiment and is therefore not new matter. *Id.* Appellant contends that the Specification, as originally filed, discloses that the DNase I is added to the solution without centrifugation or filtration at any step of the claimed method, and that the limitation is therefore fully supported by the disclosures of the Specification. *Id.*

We agree with Appellant. Appellant's Specification does not disclose the use of centrifugation or filtration in any step of the claimed method, either in its general description or in the Examples provided. Because the claims recite "without a centrifugation step or a filtration step," this negative limitation requires that the Specification disclose a reason why such steps are excluded. *See Santarus, Inc. v. Par Pharm. Inc.*, 694 F.3d 1344, 1351 (Fed Cir. 2012) (holding that "[n]egative claim limitations are adequately supported when the specification describes a reason to exclude the relevant limitation"). Nevertheless, the Specification discloses that "Unfortunately, the processes of centrifugation and careful removal of supernatant are difficult to automate, labor intensive, and result in the loss of some sperm." Spec. 4. Furthermore, the Specification discloses that, with respect to filtration, the prior art discloses filtration methods, but:

> Unfortunately the pores of these filters will expand under pressure requiring that only gravity be used as the driving force to minimize the unwanted passage of epithelial cells. In the absence of a strong driving force, capillary action on the filter surface competes with gravity flow through the filter and results in a large retention volume and difficulties with sample handling (present applicant's observation). Furthermore, DNA from epithelial cells lysed by the harsh detergent required for efficient cell re-suspension will pass through the filter with intact sperm.

Spec. 5. The Specification also discloses that, with respect to the teachings of the prior art: "Although this [filtration-based] method avoids centrifugation, it still requires a separation step, and the sperm DNA must be eluted from the filter, a process that can result in sperm DNA loss." *Id.* at 7.

When considered in view of the Specification's disclosure that its: "preferred method is fast, suitable for automation, and provides reliable results even when the amount of sperm present in a test sample is much smaller than the amount of non-sperm cells" (Spec. 6), we conclude that the Specification has disclosed sufficient reason to exclude centrifugation and filtration generally from the claimed method. Furthermore, the exclusion of centrifugation and filtration generally from the method also supports the exclusion of centrifugation and filtration from all of the steps of the claimed method, including the recited step.

We consequently reverse the Examiner's rejection of claims 40 and 45 upon this ground.

B. Rejection of the claims under 35 U.S.C. 103(a)

Issue

Appellant argues that the Examiner erred because: (1) the combined cited prior art does not meet all the claim limitations; and (2) the Examiner has not provided proper analysis supporting rationale why a person skilled in the art would have combined the applied art to arrive at the claimed invention. App. Br. 16.

Analysis

The Examiner finds that Gill teaches that "sperm nuclei can be separated from vaginal cellular debris, obtained from semen contaminated vaginal swabs, enabling positive identification of the male donor/suspect. It is envisaged that DNA fingerprinting will revolutionize forensic biology particularly with regard to the identification of rape suspects." Non-Final Act. 8 (quoting Gill 577). The Examiner finds that Gill further teaches that:

> Because preliminary experiments showed that semen-contaminated vaginal swabs contained large amounts of DNA from the female, tending to obscure many of the bands from the sperm, female cells were preferentially lysed by preliminary incubation in an SDS/proteinase K mixture. Sperm nuclei are impervious to this treatment because they are ramified with cross-linked thiol-rich proteins14 and can therefore be separated from the female component by centrifugation.

Id. (quoting Gill 578).

The Examiner also finds that Gill teaches lysis of sperm nucleic with SDS/proteinase K and DTT mixture. Non-Final Act. 8 (citing Gill 578). Therefore, the Examiner finds, Gill recognizes the issues of contaminating DNA from the female (non-sperm DNA), and demonstrates that methods of isolating sperm DNA contaminated with vaginal epithelial cells and vaginal epithelial cells by using a protease and a detergent were known in the prior art. *Id.* However, the Examiner acknowledges, Gill neither teaches nor suggests the use of a nuclease to remove contaminating epithelial cell DNA without centrifugation or filtration. *Id.* at 9.

The Examiner finds that Greenspoon teaches the use of the DNA IQ system (Promega Corp.) for isolation of DNA for analysis of forensic samples including sexual assault samples. Non-Final Act. 9. The Examiner finds that Greenspoon teaches that an advantage of this system is that it does

not use centrifugation or filtration, allowing for hands-off automation. *Id.* (citing Greenspoon 1).

The Examiner finds that Eshleman teaches the use of DNAse I to eliminate contaminating DNA. Non-Final Act. 9 (citing Eshleman 4316).

The Examiner finds that Winkler teaches the use of DNase I to degrade contaminating DNA in samples prior to PCR analysis. Non-Final Act. 9 (citing Winkler 221).

The Examiner finds that Bianchi teaches that mature sperm cells are resistant to DNase 1. Non-Final Act. 9 (citing Bianchi 1087).

The Examiner finds that Atkinson teaches a study in which extracellular DNA is degraded from sperm samples of *Bos taurus*, *Lucilia cuprina* and *Apis melifera*, but chromosomal DNA was left intact. Non-Final Act. 9 (citing Atkinson 4).

The Examiner finds that Nakanishi teaches that: "some of the DNA associated with the sperm was DNase I resistant, suggesting internalization of exogenous DNA." Non-Final Act. 9 (citing Nakanishi 259).

The Examiner therefore concludes that it would have been *prima facie* obvious to one of ordinary skill in the art to improve the method of Gill to include the use of DNase I. Non-Final Act. 9. The Examiner reasons that a skilled artisan would have been motivated to degrade contaminating DNA and protein are degraded such that they do not interfere with the assay of DNA from sperm. *Id.* at 9–10. The Examiner further reasons that a skilled artisan would have been motivated to exclude centrifugation and exclude filtration from the DNAse I addition step, because it would have allowed for hands-free automation. *Id.* at 10.

The Examiner finds that Gill, Eshleman, Bianchi, Atkinson, Nakanishi, and Greenspoon do not teach or suggest the use of DNase I in a buffer that has not been changed. Non-Final Act. 10. The Examiner finds that Kwon teaches a method of genotyping animals *via* lysing samples with proteinase K in a solution comprising a buffer agent, triton X-100, and other salts. *Id.* (citing Kwon ¶ 106).

The Examiner finds that Latham teaches DNase I digestion of DNA using DNase I with triton-X-100 and a salt solution with an ionic strength of greater than 25 mM. Non-Final Act. 10 (citing Latham ¶ 21). The Examiner finds that Latham teaches triton X-100 enhances DNase I activity, and that that EDTA quenches DNAse I activity. *Id.* (citing Latham Exs. 19, 14, ¶ 116).

The Examiner finds that Van Santen teaches that "[t]o inactivate DNase and liberate viral DNA, sodium dodecyl sulfate (SDS) was added." Non-Final Act. 11. The Examiner therefore finds that the prior art teaches that the presence of SDS inhibits DNAse I. *Id.*

Finally, the Examiner finds that Sanyal teaches that:

> We have found that heating alone [(at 65°C)] is not enough to inactivate DNase I. Inclusion of ethylenediamine tetraacetic acid (EDTA) before heat inactivation of the enzyme is virtually obligatory to completely destroy the DNase I. If DNase I is not completely inactivated, then the cDNA will not be stable and will be refractory to PCR. Here we present a method using DNase I for the preparation of cDNA devoid of contaminating genomic DNA.

Non-Final Act. 12 (quoting Sanyal 135). The Examiner finds that Sanyal teaches inactivation of DNAse I using 25 mM EDTA for 10 minutes. *Id.*

The Examiner therefore concludes that it would have been *prima facie* obvious to one of ordinary skill in the art to exclude the use of SDS from the protease digestion and that DNase I can be used with triton-X100. Non-Final Act. 11. The Examiner reasons that a skilled artisan would have been motivated to eliminate the need to change buffers to minimize SDS and inactivation of DNAse I. *Id.*

Appellant argues that the cited references neither teach nor suggest all of the limitations of the claims on appeal. App. Br. 18. Appellant also disputes the Examiner's citation to eleven separate references which, Appellant alleges, have only been put together using Appellant's Specification as a blueprint. *Id.* at 16–17. Appellant points to, *inter alia*, the Board's prior decision in *Ex parte Haymond*, 41 USPQ2d 1217 (B.P.A.I. 1996), which stated that "we note that it is impermissible to use the claimed invention as an instruction manual or 'template' to piece together isolated disclosures and teachings of the prior art so that the claimed invention may be rendered obvious." *Id.* at 17 (quoting *Haymond*, 41 USPQ2d at 1220).

Appellant argues all of the prior art methods use a buffer change, filtration, or centrifugation, and the present invention does not. App. Br. 18. Appellant contends that a desire to eliminate the "time and handling required for centrifugation or filtering," as cited by the Examiner is irrelevant and inoperative if the prior art method requires a buffer change, centrifugation, or filtration. *Id.* According to Appellant, the concept of adding a nuclease to the same extraction buffer in which the non-sperm cells were digested comes from the disclosures of Appellant's Specification, and not from the prior art. *Id.* Similarly, Appellant argues, the concept of adding a nuclease to the same extraction buffer in which the non-sperm cells were digested,

without a centrifugation or filtration step, with respect to the addition of the nuclease also comes from the disclosures of the Specification, and not from the prior art. *Id.* at 18–19.

With respect to the Gill reference, Appellant argues that Gill teaches that, when subjected to treatment with a mixture of SDS and Proteinase K, "female cells [i.e., non-sperm cells] were preferentially lysed by preliminary incubation in an SDS/proteinase K mixture." App. Br. 19 (quoting Gill 578). Appellant contends that Gill teaches that "Sperm nuclei are impervious to this treatment because they are ramified with cross-linked thiol-rich proteins and can therefore be separated from the female component by centrifugation. Sperm nuclei were subsequently lysed by treatment with an SDS/proteinase K/DTT mixture." *Id.* at 20. However, argues Appellant, Gill teaches lysing the non-sperm cells with a mixture of SDS and proteinase K, whereas Appellant's claimed method does not use SDS.

Appellant further asserts that Gill also teaches using SDS in the mixture that lyses the sperm nuclei after the sperm nuclei have been separated by centrifugation. App. Br. 20. Appellant notes that, whereas Gill teaches the required use of centrifugation to separate the sperm nuclei from "the female component," Appellant's claimed method does not separate the sperm pellet from the buffer in which the non-sperm cells are digested with the protease. *Id.*

Turning to the Greenspoon reference, Appellant contends that Greenspoon teaches a robotic system (the DNA IQ™ System) that is used to automate the extraction of evidentiary DNA from forensic casework samples. App. Br. 21. According to Appellant, the Greenspoon system

"employs a silica coated paramagnetic resin that binds DNA with high affinity in the presence of chaotropic agents such as guanidinium. Because no centrifugation or filtration steps are needed with this system, it readily lends itself to the application of 'hands off' automated extraction." *Id.* (quoting Greenspoon 1). Appellant also notes that Greenspoon teaches that "Moreover, the DNA remains tightly coupled to the silica coated paramagnetic resin for the entire process until the elution step." *Id.* (quoting Greenspoon, Abstr.).

Appellant asserts that Greenspoon's system operates on a principle that is totally different when compared to the principle of operation of Appellant's claimed invention. App. Br. 22. Appellant contends that Greenspoon requires, *inter alia*, the use of a paramagnetic resin and a magnet, and further teaches that: "The most notable features added by the Promega scientists are a magnetic plate on the deck (MagnaBot), a shaking platform attached as a right side module (DPC, Los Angeles, CA) and a thermal exchange unit which sits atop the shaking platform, attached to a water bath by tubing." *Id.* (quoting Greenspoon 1).

Appellant asserts that Greenspoon's teaching that "no centrifugation or filtration steps are needed with this system" applies only to that portion of the Greenspoon system during which the DNA remains tightly coupled to the silica coated paramagnetic resin." App. Br. 22. Specifically, Appellant argues that the differential extraction procedure of Greenspoon "relies on previously published techniques (10), until the point at which a sperm pellet was generated and washed three times." App. Br. 23 (quoting Greenspoon 3). Appellant points out that footnote (10) of Greenspoon, referred to in the quoted passage, refers to the Gill reference, and that Greenspoon thus

teaches the use of the centrifugation technique of Gill to generate a sperm pellet. *Id.*

Appellant also argues that Greenspoon teaches that: "Initial experience with mixed stains, consisting of sperm and non-sperm cells, demonstrated that the BioMek® 2000/DNA IQ™ System could complete the DNA extraction once the sperm cells were separated from the non-sperm cells (data not shown)." App. Br. 24. Appellant therefore argues that Greenspoon teaches that an intact sperm pellet must be separated from the non-sperm cells before the robot extraction can complete the DNA extraction using the Greenspoon system. *Id.*

Appellant argues that, even if it were, *arguendo*, proper to combine the teachings of Greenspoon with the teachings of Gill and with the teachings of the other cited references, the combined Greenspoon-Gill method would still require (1) the use of SDS and (2) the use of centrifugation for separating the sperm nuclei. App. Br. 27. Appellant argues that the Examiner's proposed combination of Greenspoon with Gill, Eshleman, Winkler, Bianchi, Atkinson, Nakanishi, Kwon, Latham, van Santen, and Sanyal would still not disclose or suggest the method of the present invention. *Id.*

Specifically, Appellant contends that Eshleman teaches the use of DNAse to eliminate contaminating DNA in tubes and reaction mixes that are used in the Eshleman process before introducing the DNA sample to be analyzed. App. Br. 27. Appellant argues that Eshleman teaches that: "The addition of a DNAse to tubes and reaction mixes prior to the introduction of the ancient DNA template can eliminate contaminant DNA produce unless the template itself is contaminated." *Id.* (quoting Eshleman 4316).

Appellant asserts that the process taught by Eshleman is not able to eliminate contaminating DNA when the template itself contains the contaminating DNA. *Id.*

Appellant argues that Winkler teaches the use of DNAse to degrade contaminating DNA in a sample of RNA before a PCR process, in the absence of RNase. App. Br. 30 (citing Winkler 221). Appellant contends that Winkler neither teaches nor suggests combining the use of a DNAse with a protease. *Id.*

Appellant next disputes the Examiner's conclusion that, although Bianchi, Atkinson and Nakanishi teach that DNA of intact sperm is not sensitive to DNAse, that it would have been obvious for a person who is skilled in the art "to improve the method of Gill to include the use of DNase I." App. Br. 31 (quoting Non-Final Act. 9). Appellant contends that the motivation reasoned by the Examiner for combining the references with the Gill method (minimizing contamination by non-sperm DNA) does not exist because the Gill method requires the use of centrifugation to separate the sperm nuclei, prior to lysis of the sperm cells. *Id.* Appellant argues that the motivation proposed by the Examiner for combining the references is legally insufficient because there would have been no need to add DNAse to the Gill method, which has separated the sperm cells by centrifugation. *Id.*

Appellant also disputes the Examiner's finding that the combination of Kwon and Latham and van Santen teach or suggest the limitation of claim 40 requiring the use of DNase I in a buffer that has not been changed. App. Br. 34. Appellant disputes the Examiner's finding that Kwon teaches lysis of samples by proteinase K and that Latham teaches DNAse I digestion of DNA. *Id.* at 35 (citing Non-Final Act. 10). According to Appellant, the

Examiner's conclusion that motivation would have existed for a person of ordinary skill in the art to combine the references with Gill is deficient because there is no need to add DNAse to the Gill method, which separates the sperm cells by centrifugation. *Id.* Furthermore, Appellant argues, the Gill method still requires (1) the use of SDS and (2) the use of centrifugation for separating the sperm nuclei, both of which are excluded by the claimed method, and which the combination of Gill with Eshleman, Winkler, Bianchi, Atkinson, Greenspoon, Nakanishi, Kwon and Latham neither teaches nor suggests. *Id.* at 36.

Appellant argues further that van Santen teaches that, to isolate viral DNA from host DNA one must add DNase I to destroy the host DNA. App. Br. 38 (citing van Santen 5212). Appellant contends that the van Santen method employs multiple centrifugations and multiple buffers, requiring a first centrifugation (low speed) to remove cell debris and a second centrifugation (25,000 rpm) to pellet the virions. *Id.* Moreover, argues Appellant, van Santen also teaches the use of 2% SDS to deactivate DNAse, which is not present in the claims. *Id.* at 39.

Finally, Appellant argues that Sanyal teaches removing genomic DNA from an RNA sample. App. Br. 40. Appellant asserts that Sanyal is silent concerning the selective removal of a first type DNA from a DNA sample that contains two types of DNA. *Id.* Appellant also points out that Sanyal teaches a two-step method requiring: (1) adding the EDTA to the RNA sample at room temperature (approximately 22°C); and then (2) applying a heat inactivation process at 65°C for ten minutes. *Id.* Appellant argues that, in contrast, Appellant's claimed method uses: (1) both EDTA and DTT for inactivating the DNAse I; and (2) performs the inactivation step at a

temperature of 56°C (equal to 133°F) for at least five minutes. *Id.* Appellant argues that the claimed method requires only one temperature, and does not require an additional heating step at an increased temperature level. *Id.*

We are not persuaded that the Examiner has established motivation to combine the references sufficient to support a *prima facie* conclusion of obviousness. As an initial matter, we do not find persuasive many of Appellant's arguments with respect to why the references could not have been combined. We remind Appellant that:

> The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art.

In re Keller, 642 F.2d 413, 425 (C.C.P.A. 1981). Furthermore, all elements of each prior art reference need not read on the claimed invention, rather, the proper test for obviousness is what the combined teachings would have suggested to a person of ordinary skill in the art. *In re Kotzab*, 217 F.3d 1365, 1370 (Fed. Cir. 2000). Appellant's arguments that, e.g., many of the cited references could not be used to modify Gill, because Gill requires certain other steps, is not persuasive when those steps could be obviated by the substitution of steps taught in the other references. Rather, the essence of obviousness is what the *combined* teachings of the references would have suggested to a person of ordinary skill in the art. *Keller*, 642 F.2d at 425.

Nevertheless, a *prima facie* conclusion of obviousness requires "a reason that would have prompted a person of ordinary skill in the relevant

field to combine the elements in the way the claimed new invention does." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007). In the appeal before us, the references, from significantly disparate fields of endeavor, cited against the relatively simple, independent claim on appeal militates against a *prima facie* conclusion of obviousness, and strongly suggests, as Appellant argues, the employment of hindsight analysis.

In analyzing whether hindsight was employed in assembling the rejection, the proper analysis in this context is whether "an artisan of ordinary skill in the art at the time of the invention, confronted by the same problems as the inventor and with no knowledge of the claimed invention, … [would] have selected the various elements from the prior art and combined them in the manner claimed." *Princeton Biochemicals, Inc. v. Beckman Coulter, Inc.*, 411 F.3d 1332, 1337 (Fed. Cir. 2005).

In the Examiner's rejection, the author cites references directed to, *inter alia*: (1) the use of a silica coated paramagnetic resin to bind sample DNA in an automated system (Greenspoon); (2) use of DNase to eliminate contamination in ancient DNA analysis (Eshleman); (3) investigating the activity and gene expression of neutral endopeptidase and angiotensin converting enzyme in different brain regions of alcohol-preferring and alcohol-avoiding lines of rats *via* HPLC analysis (Winkler); (4) examining the efficacy of gene transfer by sperm-mediated methods (Nakanishi, Atkinson); (5) maturation of human and murine spermatozoa (Bianchi); compositions and methods for making and using a synthetic bovine DNase I (Latham); (6) characterizing the bovine herpesvirus 4 major immediate-early transcript (van Santen); (7) genotyping by *in situ* PCR amplification of a polynucleotide in a tissue biopsy; and (8) a method for

removing contaminating genomic DNA from an RNA sample to be used for PCR (Sanyal). The Examiner's findings and conclusions provide no clues as to why a person of ordinary skill in this particular art would have had reason to combine these references differing in subject matter, and which are largely irrelevant to the claimed subject matter.

Furthermore, the Examiner's reasoning that it would have been obvious to combine the references to arrive at the claims, because the references teach various steps recited in the claims, borders dangerously on the tautological. The Examiner concludes that a skilled artisan would have looked to the cited references as teaching the various steps recited in the claims, because the references teach elements of the individual limitations, without explaining why a person of ordinary skill would have looked to combine those particular references.

In our review of this appeal, the initial burden falls upon the Examiner to establish a *prima facie* case of obviousness. Because we conclude that the Examiner has failed to "articulate[ ] reasoning with some rational underpinning to support the legal conclusion of obviousness" and, specifically, "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does," we reverse the Examiner's rejection of claims 40 and 45 upon this ground. *See KSR*, 550 U.S. at 418.

CONCLUSION

The Examiner's rejection of claims 40 and 45 under 35 U.S.C. § 112, first paragraph, is reversed.

The Examiner's rejection of claims 40 and 45 under 35 U.S.C.

§ 103(a) is reversed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv).

REVERSED

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
40, 45	112, first paragraph	Lack of written descriptive support		40, 45
40, 45	103(a)	Gill, Greenspoon, Eshleman, Winkler, Bianchi, Atkinson, Nakanishi, Kwon, Latham, van Santen, Sanyal		40, 45
Overall Outcome				40, 45