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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte JAMES DOUGLAS WATSON, CLARE ELTON, and DAVID REX MUSGRAVE[1]

Appeal 2016-000791
Application 13/930,852
Technology Center 1600

Before DEMETRA J. MILLS, ERIC B. GRIMES, and ULRIKE W. JENKS, *Administrative Patent Judges*.

GRIMES, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to methods of detecting the presence or monitoring progression of a disorder, which have been rejected for lack of adequate written description, being directed to patent-ineligible subject matter, anticipation, and obviousness. We have jurisdiction under 35 U.S.C. § 6(b).

We affirm.

STATEMENT OF THE CASE

The Specification states that "[t]he present disclosure relates to methods and compositions for diagnosing and defining the staging or

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[1] Appellants identify the Real Party in Interest as Caldera Health Ltd. (Br. 3.)

progress of disorders such as prostate cancer." (Spec. 1:10–11.) "Unlike many cancer types, specific patterns of gene expression have not been consistently identified in prostate cancer progression. . . . However, a few genes have emerged . . . which have been shown experimentally to have probable roles in prostate carcinogenesis." (*Id.* at 5:8–28.)

The Specification states that "[t]he methods disclosed herein allow the determination of the frequency of multiple RNA biomarkers simultaneously using a process known as multiplexing." (*Id.* at 8:35–36.) "More specifically, the disclosed methods employ oligonucleotides specific for RNA biomarkers known to be associated with the presence and/or progression of a disorder, such as prostate cancer." (*Id.* at 9:12–14.)

> Massive parallel sequencing made possible by next generation sequencing (NGS) technologies is another way to approach the enumeration of RNA transcripts in a tissue sample and RNA-seq is a method that utilizes this. It is currently the most powerful analytical tool used for transcriptome analyses, including gene expression level difference between different physiological conditions, or changes that occur during development or over the course of disease progression.

(*Id.* at 7:15–20.)

Claims 1, 3–20, 23, and 24 are on appeal. Claims 1 and 12 are the independent claims and read as follows:

> Claim 1: A method for detecting the presence of a disorder in a subject, comprising:
>
> (a) determining the relative frequency of expression of a plurality of ribonucleic acid (RNA) biomarkers simultaneously in a biological sample obtained from the subject, wherein the relative frequency of expression is determined using next generation sequencing of an amplicon deoxyribonucleic acid (DNA) library prepared using a plurality of oligonucleotide primers specific for the plurality of RNA biomarkers; and

(b) comparing the relative frequency of expression of the plurality of RNA biomarkers in the biological sample with a predetermined threshold value, wherein increased or decreased relative frequency of expression of the plurality of RNA biomarkers in the biological sample relative to the predetermined threshold value indicates the presence of the disorder in the subject.

Claim 12: A method for monitoring progression of a disorder in a subject, comprising:

(a) determining the relative frequency of expression of a plurality of RNA biomarkers simultaneously in a biological sample obtained from the subject at a first time point, and determining the relative frequency of expression of the plurality of RNA biomarkers simultaneously in a biological sample obtained from the subject at a second, subsequent, time point, wherein the relative frequency of expression is determined using next generation sequencing of an amplicon DNA library prepared using a plurality of oligonucleotide primers specific for the plurality of RNA biomarkers; and

(b) comparing the relative frequency of expression of the plurality of RNA biomarkers in the biological sample with a predetermined threshold value, wherein an increase or decrease in the relative frequency of expression of the plurality of RNA biomarkers in the biological sample at the second time point compared to the relative frequency of expression of the plurality of RNA biomarkers at the first time point indicates the progression of the disorder in the subject.

The claims stand rejected as follows:

Claims 1, 3–20, 23, and 24 under 35 U.S.C. § 101 as being directed to patent-ineligible subject matter (Ans. 6);

Claims 1, 3–20, 23, and 24 under 35 U.S.C. § 112, first paragraph, for lack of adequate written description in the Specification (Ans. 3);

Claims 1, 3, 11–13, 20, 23, and 24 under 35 U.S.C. § 102(a) as anticipated by Joyce,[2] as evidenced by Applied Biosystems,[3] Illumina,[4] and Illumina Sequencing[5] (Ans. 9); and

Claims 1, 3–20, 23, and 24 under 35 U.S.C. § 103(a) as obvious based on Hood,[6] Twine,[7] and Prensner,[8] as evidenced by Illumina, Illumina Sequencing, Chasin,[9] and Joyce (Ans. 11).

I

The Examiner has rejected all of the claims on appeal under 35 U.S.C. § 101, on the basis that "the claimed invention is directed to a judicial exception (i.e., a law of nature, a natural phenomenon, or an abstract idea) without significantly more." (Ans. 6.) Specifically,

> the claims are directed to a natural phenomenon and an abstract idea, which are the natural presence of naturally occurring RNA in a subject that may be differentially expressed in a subject with a disorder and the mathematical analysis and/or correlation of the

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[2] Cailin E. Joyce et al., *Deep sequencing of small RNAs from human skin reveals major alterations in the psoriasis miRNAome*, 20 HUM. MOL. GEN. 4025–40 (2011).
[3] Product Bulletin, *TaqMan® MicroRNA Assays, Quantitate microRNAs with the specificity and sensitivity of TaqMan® assay chemistry*, APPLIED BIOSYSTEMS 1–4 (2006).
[4] Data Sheet: Illumina® Sequencing, *TruSeq™ RNA and DNA Sample Preparation Kits v2*, Illumina® 1–4 (2011).
[5] Illumina®, *Multiplexed Sequencing with the Illumina Genome Analyzer System*, ILLUMINA® SEQUENCING 1–4 (2008).
[6] Hood et al., WO 2008/021290 A2; publ. Feb. 21, 2008.
[7] Twine et al., US 7,611,839 B2; iss. Nov. 3, 2009.
[8] John R. Prensner et al., *Transcriptome sequencing across a prostate cancer cohort identifies PCAT-1, an unannotated lincRNA implicated in disease progression*, 29 NAT. BIOTECHNOL. 742–50 (2011).
[9] Chasin et al., US 2013/0217585 A1; publ. Aug. 22, 2013.

> relative frequency of expression of biological markers with a disorder.

(*Id*. at 7.)

"Appellant acknowledges that independent claims 1 and 12 recite the judicial exception of RNA biomarkers that are differentially expressed in the presence of a disorder." (Br. 16.)

The Examiner finds that "claim(s) 1 and 12 do not recite something significantly different than a judicial exception" because "the detection and quantification of RNA biomarkers, the use of oligonucleotide primers specific for a plurality of RNA biomarkers and comparing the frequency of expression of a subject with that of a reference value[] are well-known, purely conventional or routine in the art." (Ans. 7–8.) The Examiner cites Marguerat,[10] Ren,[11] and Prensner as evidence that "the determination of the relative frequency of expression of RNA biomarkers using next generation sequencing (NGS) and oligonucleotide primer pairs specific for a biomarker is well-known, conventional and routine." (*Id*. at 8.)

Appellants argue "both claims 1 and 12 recite additional elements that ensure that the claims amount to significantly more than the judicial exception." (Br. 16.) Appellants submit that,

> [i]n response to the Examiner's assertion that the claimed methods are well-known, routine and conventional in the art as evidenced by the US 2008/0274458 to Latham et al. and WO 2010/120803A2 to Kazakov et al., . . . neither of these references

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[10] Samuel Marguerat & Jürg Bähler, *RNA-seq: from technology to biology*, 67 CELL. MOL. LIFE SCI. 569–79 (2010).

[11] Shancheng Ren et al., *RNA-seq analysis of prostate cancer in the Chinese population identifies recurrent gene fusions, cancer-associated long noncoding RNAs and aberrant alternative splicings*, 22 CELL RES. 806–21 (2012).

> teaches or suggests the use of NGS to determine the relative frequency of expression of a plurality of RNA biomarkers in a biological sample and thereby either detect the presence of a disorder (as recited in claim 1) or monitor the progression of a disorder (as recited in claim 12).

(*Id.*)

We conclude that the rejection under § 101 is supported by a preponderance of the evidence of record. Marguerat states that "[n]ext-generation sequencing technologies are now being exploited not only to analyse static genomes, but also dynamic transcriptomes in an approach termed RNA-seq." (Marguerat 569, Abstract.) Marguerat reviews "[a]pplying RNA-seq to probe the breadth and depth of genome transcription" and "[a]pplying RNA-seq to interrogate post-transcriptional gene regulation." (*Id.* at 571, 573.)

Ren describes a study of transcriptome profiles in prostate cancers and normal counterparts in the Chinese population using RNA-seq. (Ren 806, abstract.) Ren states that the study showed diversity among prostate cancers with respect to gene fusions, long noncoding RNAs, alternative splicing and somatic mutations. (*Id.*) Prensner describes an RNA-Seq analysis of long intergenic noncoding RNAs (lincRNAs) in prostate cancer tissue samples and cell lines. (Prensner 742, left col.) Prensner

> characterized one ncRNA, *PCAT-1*, as a prostate-specific regulator of cell proliferation and show[ed] that it is a target of the Polycomb Repressive Complex 2 (PRC2). We further found that patterns of *PCAT-1* and PRC2 expression stratified patient tissues into molecular subtypes distinguished by expression signatures of *PCAT-1*–repressed target genes.

(*Id.* at 742, abstract.)

The Examiner concludes that these disclosures demonstrate that "the determination of the relative frequency of expression of RNA biomarkers using next generation sequencing (NGS) and oligonucleotide primer pairs specific for a biomarker is well-known, conventional and routine." (Ans. 8.) Appellants dispute that conclusion, but only on the basis that Latham (US 2008/0274458 A1) and Kazakov (WO 2010/120803 A2), do not "teach[] or suggest[] the use of NGS to determine the relative frequency of expression of a plurality of RNA biomarkers in a biological sample and thereby either detect the presence of a disorder (as recited in claim 1) or monitor the progression of a disorder (as recited in claim 12)." (Br. 16.)

The Examiner, however, does not rely on Latham or Kazakov to provide evidence in support of the rejection; the Examiner relies on Marguerat, Ren, and Prensner. Granted, the Examiner relied on Latham and Kazakov for the same purpose in the Final Office Action (mailed March 6, 2015), but Appellants did not petition to have the rejection in the Answer designated a new ground of rejection, nor did Appellants file a Reply Brief responding to the Examiner's citation of Marguerat, Ren, and Prensner. Thus, Appellants have not disputed, on this record, that Marguerat, Ren, and Prensner support the proposition for which the Examiner has cited them. We therefore conclude that the rejection is supported by a preponderance of the evidence in the record.

Appellants also argue that "claims l and 12 do not prevent anyone from using RNA biomarkers in other methods (such as RT-PCR) to diagnose the presence and/or monitor the progression of a disorder and therefore do not tie-up any law of nature or pre-empt others from using a law of nature." (Br. 16–17.)

This argument is unpersuasive. "While preemption may signal patent ineligible subject matter, the absence of complete preemption does not demonstrate patent eligibility. . . . Where a patent's claims are deemed only to disclose patent ineligible subject matter under the *Mayo* framework, as they are in this case, preemption concerns are fully addressed and made moot." *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F3d 1371, 1379 (Fed. Cir. 2015).

For the reasons discussed above, we affirm the rejection of claims 1 and 12 under 35 U.S.C. § 101. Claims 3–11, 13–20, 23, and 24 have not been argued separately and therefore fall with claims 1 and 12. 37 C.F.R. § 41.37(c)(1)(iv).

II

The Examiner has rejected all of the claims on appeal on the basis that they lack adequate written description in the Specification. The Examiner finds that

> the instant claims broadly embrace all RNA biomarkers for any disorder detected using any oligonucleotide primer specific for the plurality of RNA biomarkers in any subject. While the specification provides guidance for the use of a specific set of probes for next generation sequencing for diagnosing the presence of, and/or monitoring the progression of, prostate cancer, . . . it does not provide guidance for the use of any and/or all oligonucleotide probes specific for any/all biomarkers for detecting the presence of any other disease, disorder or other cancer type in any subject.

(Ans. 5.)

The Examiner also finds that the Specification's

> disclosure is not deemed to be descriptive of the wide-range of genetic variation for determining RNA biomarkers among

> different races or different species, particularly, in conjunction with all possible disorders and all possible oligonucleotide primers, as one of skill in the art cannot envision all the modified forms based on the teachings in the specification.
>
> This limited information is not deemed sufficient to reasonably convey to one skilled in the art that Applicant is in possession of the claimed genus of RNA biomarkers and oligonucleotide primers specific a plurality of RNA biomarker[s] to detect all disorders in all subject/species at the time the invention was made.

(*Id.* at 6.)

We agree with the Examiner that the Specification does not demonstrate that Appellants were in possession of the methods of claims 1 and 12 at the time the instant application was filed. "[T]he test for sufficiency [of written description] is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc).

> [A] sufficient description of a genus . . . requires the disclosure of either a representative number of species falling within the scope of the genus or structural features common to the members of the genus so that one of skill in the art can "visualize or recognize" the members of the genus.

Id. at 1350.

Here, claims 1 and 12 recite a genus of RNA biomarkers; specifically, RNA biomarkers that indicate the presence (claim 1) or progression (claim 12) of a disorder when their expression is increased or decreased relative to a threshold value. Claims 1 and 12 are generic to any such biomarkers that are diagnostic for any disorder. Thus, an adequate written description of the

genus requires description of either a set of species that are representative of the genus, or structural features that are common to the genus.

The Specification identifies no structural characteristics of RNA biomarkers that are diagnostic of a disorder when over- or underexpressed. The Specification does disclose a number of species of RNA biomarkers that are either overexpressed (Table 1) or underexpressed (Table 2) in subjects with prostate cancer. (Spec. 23:24–27.) However, the Specification discloses no such RNA biomarkers for any disorder other than prostate cancer. We therefore conclude that the Specification does not provide a written description of the methods of claims 1 and 12 that demonstrates that Appellants were in possession of the claimed genus. *See AbbVie Deutschland GmbH & Co. v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1299–1300 (Fed. Cir. 2014):

> One factor in considering the question is how large a genus is involved and what species of the genus are described in the patent. . . . [A]nalogizing the genus to a plot of land, if the disclosed species only abide in a corner of the genus, one has not described the genus sufficiently to show that the inventor invented, or had possession of, the genus. He only described a portion of it.

Appellants argue that

> claims 1 and 12 . . . are drawn to specific methods employing NGS in which RNA biomarkers that have been previously identified as being specific for a particular disorder are employed in the diagnosis of, and/or monitoring the progression of, that disorder in much the same way that pre-determined biomarkers can be employed in other methodologies.

(Br. 11–12.)

This argument is unpersuasive, because claims 1 and 12 are not limited to using any particular RNA biomarkers, such as those that had been

previously identified as diagnostic of the presence or progression of a particular disorder as of the filing date of the instant application. Rather, as the Examiner has pointed out (Ans. 5), they read on using *any* RNA biomarkers that are over- or underexpressed in any disorder in order to detect the presence or progression of the disorder.

Appellants argue that the methods of claims 1 and 12 "are described at page 20, line 34 – page 23, line 19, of the present specification." (Br. 12.) Appellants also argue that the Specification describes "over 120 RNA biomarkers showing either elevated or reduced expression levels in prostate cancer compared to normal, or healthy, tissues, together with primers for these RNA biomarkers." (*Id.*)

These arguments are also unpersuasive. Regarding the specific biomarkers that are disclosed in the Specification, as discussed above, they are all limited to those that are diagnostic of prostate cancer; no biomarkers that are diagnostic for any other disorder are described. The specific biomarkers therefore do not show possession of the genus of RNA biomarkers that is recited in claims 1 and 12.

In addition, the Specification describes (at pages 20–23), four methods for determining "[t]he relative frequency of expression of specific RNA biomarkers." (Spec. 20:35.) This portion of the Specification, however, does not provide a description of the genus of RNA biomarkers, or any species within that genus, that is recited in claims 1 and 12.

With regard to claims 4, 6, 8, 14, and 17, Appellants argue that these claims are limited to prostate cancer and to oligonucleotide primer pairs that are specifically described in the Specification as being over- or

underexpressed in prostate cancer tissue. (Br. 12–13.) Appellants make a similar argument with respect to claims 10 and 19. (*Id.* at 13.)

We agree with Appellants that claims 4, 6, 8, 10, 14, 17, and 19 find adequate written descriptive support in the Specification. These claims are limited to methods of detecting the presence or progression of prostate cancer using specific, structurally defined primers (claims 4, 6, 8, 14, and 17) or genes (claims 10 and 19) that are disclosed in the Specification as being either overexpressed or underexpressed in prostate cancer tissue.

For the reasons discussed above, we affirm the rejection of claims 1 and 12 under 35 U.S.C. § 112, first paragraph, for lack of adequate written description. Claims 3, 5, 7, 9, 11, 13, 15, 16, 18, 20, 23, and 24 have not been argued separately and therefore fall with claims 1 and 12. 37 C.F.R. § 41.37(c)(1)(iv). We reverse the rejection under 35 U.S.C. § 112, first paragraph, for lack of adequate written description with respect to claims 4, 6, 8, 10, 14, 17, and 19.

III

The Examiner has rejected claims 1, 3, 11–13, 20, 23, and 24 as anticipated by Joyce, as evidenced by Applied Biosystems, Illumina, and Illumina Sequencing. The Examiner finds that Joyce teaches analyzing miRNA (microRNA) expression profiles in psoriasis "where **small RNA** reads representing known and putative novel miRNAs were generated and analyzed by **next generation sequencing** (Abstract, lines 1-5). Joyce et al. teach that **relative frequency of expression was calculated**." (Ans. 9.) The Examiner also finds that Joyce teaches that "qRT-PCR of mature miRNAs was performed with TaqMan miRNA assays according to manufacturer's instructions, which includes **target-specific** stem loop

primers as evidenced by Applied Biosystems (corresponding to primers specific for RNA biomarkers)." (*Id.* at 10.)

Appellants argue that Joyce "describe[s] the use of NGS to sequence the **entire** miRNAome from normal and psoriatic skin." (Br. 22.) Appellants argue that Joyce does not "teach or suggest methods for the diagnosis of, and/or for monitoring the progression of, a disorder wherein NGS is performed on amplicon DNA libraries prepared using a plurality of oligonucleotide primers specific for a set of predetermined biomarkers, as recited in independent claims 1 and 12." (*Id.* at 22–23.).

We agree with Appellants that Joyce does not disclose a method meeting all of the limitations of claims 1 and 12, which both require determining relative frequency of expression "using next generation sequencing of an amplicon deoxyribonucleic acid (DNA) library prepared using a plurality of oligonucleotide primers specific for [a] plurality of RNA biomarkers."

Joyce "describe[s] a comprehensive analysis of the normal and psoriatic skin miRNAome with next-generation sequencing." (Joyce 4025, abstract.) Joyce "generated 6.7 x 10^8 small RNA reads representing 717 known and 284 putative novel microRNAs (miRNAs)." (*Id.*) Joyce "identified 80 known and 18 novel miRNAs that were differentially expressed." (*Id.* at 4026, left col.)

More specifically, Joyce "extracted total RNA using a method that preserved small RNAs and constructed small RNA libraries. . . . [Joyce] independently sequenced each of the 67 libraries on the Illumina GAIIx platform, generating 1.1 billion raw and 670 million qualified reads." (*Id.* at 4026, right col.) Illumina, which the Examiner has cited as an evidentiary

reference, describes its RNA sample preparation method as follows: "Starting with total RNA, the messenger RNA is first purified using polyA selection . . . , then chemically fragmented and converted into single-stranded cDNA using random hexamer priming." (Illumina 2.)

We agree with Appellants that Joyce does not describe "using next generation sequencing of an amplicon deoxyribonucleic acid (DNA) library prepared using a plurality of oligonucleotide primers specific for the plurality of RNA biomarkers," as required by claims 1 and 12. Rather, Joyce describes using next generation sequencing to generate hundreds of millions of reads from the total RNA of psoriatic and healthy tissue. Joyce's method does not use oligonucleotide primers specific for particular RNA biomarkers; it uses random hexamer primers that, collectively, would amplify the entire RNA transcriptome.

The Examiner points to Joyce's disclosure that "qRT-PCR of mature miRNAs was performed with TaqMan miRNA assays . . . , which includes target-specific stem loop **primers** as evidenced by Applied Biosystems (corresponding to primers specific for RNA biomarkers)." (Ans. 10.) Reverse transcription/quantitative PCR (qRT-PCR or RT-qPCR), however, is a different technique than next-generation sequencing. *See* Spec. 7:5–17 ("A common technology used for measuring RNA abundance is RT-qPCR where reverse transcription (RT) is followed by real-time quantitative PCR (qPCR). . . . Massive parallel sequencing made possible by *next generation sequencing (NGS) technologies is another way* to approach the enumeration of RNA transcripts in a tissue sample and RNA-seq is a method that utilizes this." (emphasis added)).

"[A]nticipation requires that the four corners of a single, prior art document describe every element of the claimed invention, either expressly or inherently, such that a person of ordinary skill in the art could practice the invention without undue experimentation." *Advanced Display Sys., Inc. v. Kent State Univ.*, 212 F.3d 1272, 1282 (Fed. Cir. 2000). Because Joyce does not describe every element of claims 1 and 12, either expressly or inherently, we reverse the rejection of those claims, and dependent claims 3, 11, 13, 20, 23, and 24, as anticipated by Joyce.

IV

The Examiner has rejected all of the claims on appeal as obvious based on Hood, Twine, and Prensner, as evidenced by Illumina, Illumina Sequencing, Chasin, and Joyce. The Examiner finds that Hood teaches, among other things, "that substantially all transcripts from a **cDNA library** are identified using **sequencing by synthesis** (SBS), **massively parallel sequencing** (MPSS) or similar technology, such as that developed by Solexa (now part of Illumina, as noted in Hood et al.) (corresponding to next generation sequencing of an amplicon cDNA library)." (Ans. 12.)

Appellants argue that that Hood

> teaches the use of MPSS and SBS to identify and/or to measure the actual frequency of expression of **all** RNA sequences within a specific tissue sample. This is essentially the same as the known use of next-generation sequencing to examine expression of every transcript within an entire genome as referenced on page 7, lines 15-25, of the current specification.

(Br. 27–28.) Appellants argue that, in contrast to the claimed method, "Hood does not teach or suggest . . . the relative frequency of expression of a plurality of RNA biomarkers . . . by preparing NGS ready targeted cDNA

amplicon libraries using a plurality of oligonucleotide primers specific for the plurality of RNA biomarkers." (*Id.* at 28.)

We agree with Appellants that Hood does not teach the disputed limitation. The Examiner points to Hood's disclosure that:

> A short signature sequence of about 16-20 base pairs (Brenner, P. *et al.*, *supra*) is generated simultaneously from each of the hundreds of thousands of beads (or more) in the flow cell, each having attached thereto copies of a unique transcript from the sample. This technique is termed massively parallel signature sequencing (MPSS).
>
> The resulting sequences (*e.g.*, MPSS signature sequences), are generally about 17-20 bases in length.

(Hood 165:30 to 166:7.)

The beginning of the paragraph that ends with a discussion of MPSS reads as follows: "All or substantially all of the unique transcripts of RNA or from a cDNA library, *e.g.*, representing virtually or substantially all genes functioning in the organ of interest, can be identified and quantified using any of a variety of techniques known in the art." (*Id.* at 165:6–9.) Thus, the context of Hood's discussion of MPSS is for use in identifying and quantifying RNA transcripts representing virtually or substantially all of the genes functioning in an organ of interest. We therefore agree with Appellants that Hood does not teach or suggest the limitation of claims 1 and 12 requiring "using next generation sequencing of an amplicon deoxyribonucleic acid (DNA) library prepared using a plurality of oligonucleotide primers specific for [a] plurality of RNA biomarkers."

The Examiner has not pointed to any disclosure in the other cited references that makes up for this deficiency in Hood. *See* Ans. 13–15. We therefore reverse the rejection of claims 1 and 12, and dependent claims 3–

11, 13–20, 23, and 24, under 35 U.S.C. § 103(a) based on Hood, Twine, and Prensner, as evidenced by Illumina, Illumina Sequencing, Chasin, and Joyce.

SUMMARY

We affirm the rejection of claims 1, 3–20, 23, and 24 under 35 U.S.C. § 101.

We affirm the rejection of claims 1, 3, 5, 7, 9, 11–13, 15, 16, 18, 20, 23, and 24 under 35 U.S.C. § 112, first paragraph, for lack of adequate written description.

We reverse the rejection of claims 4, 6, 8, 10, 14, 17, and 19 under 35 U.S.C. § 112, first paragraph, for lack of adequate written description.

We reverse the rejection of claims 1, 3, 11–13, 20, 23, and 24 under 35 U.S.C. § 102(a) as anticipated by Joyce, as evidenced by Applied Biosystems, Illumina, and Illumina Sequencing.

We reverse the rejection of claims 1, 3–20, 23, and 24 under 35 U.S.C. § 103(a) based on Hood, Twine, and Prensner, as evidenced by Illumina, Illumina Sequencing, Chasin, and Joyce.

TIME PERIOD FOR RESPONSE

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

AFFIRMED