Ownership and Sharing
Setting the Patent Framework For Innovation In Synthetic Biology

THE PATENT LANDSCAPE:
RECENT DECISIONS FROM THE US SUPREME COURT

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Ass'n for Molecular Pathology v. Myriad (2013)

Scalia, J., concurring:

"I join the judgment of the Court, and all of its opinion except Part I–A and some portions of the rest of the opinion going into fine details of molecular biology. I am unable to affirm those details on my own knowledge or even my own belief. It suffices for me to affirm, having studied the opinions below and the expert briefs presented here, that the portion of DNA isolated from its natural state sought to be patented is identical to that portion of the DNA in its natural state; and that complementary DNA (cDNA) is a **synthetic creation** not normally present in nature."

Recent Cases

Lab Corp. v. Metabolite, 548 U.S. 124 (2006): diagnosis of vitamin deficiency from homocysteine level in the blood

Bilski v. Kappos**,** 130 S.Ct. 3218 (2010): abstract concept of hedging purchases

Mayo v. Prometheus, 132 S.Ct. 1289 (2012): diagnosis of a dosage problem from the level of a drug's metabolite level in the blood

AMP v. Myriad (2013): patentability of isolated gDNA and cDNA sequences related to BRCA 1 and BRCA 2 genes

KSR v. Teleflex, 127 S.Ct. 1727 (2007): standard of inventiveness

Overview

1. The Case: *AMP v. Myriad*
2. The questions it raises
3. Application to synthetic biology
4. Keeping the basic building blocks accessible

Ass'n for Molecular Pathology v. Myriad

Inventions:

1. isolated DNA sequences (BRCA 1 and 2)

2. diagnostic method: drawing the conclusion from mutations that the patient is susceptible to early-onset breast cancer

3. screening methods: tests for possible therapeutics

Question: are these inventions patentable subject matter?

Diamond v. Chakrabarty, 447 U.S. 303 (1980)

"The Committee Reports accompanying the 1952 [Patent] Act inform us that Congress intended statutory subject matter to include anything under the sun that is made by man.

This is not to suggest that [the Act] has no limits or that it embraces every discovery. The laws of nature, physical phenomena, and abstract ideas have been held not patentable. … Thus, a new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter. Likewise, Einstein could not patent his celebrated law that E=mc2; nor could Newton have patented the law of gravity. Such discoveries are "manifestations of . . . nature, free to all men and reserved exclusively to none." Funk Brothers Seed Co. v. Kalo Inoculant Co., 333 U. S. 127, 130 (1948)."

Outcome in the Federal Circuit

1. Screening methods are patentable (3-0)
2. Diagnostic method is not patentable (3-0)

   "Claims "directed to 'comparing' or 'analyzing' DNA sequences are patent ineligible; such claims include no transformative steps and cover only patent-ineligible abstract, mental steps." -- J. Lourie

3. Isolated DNA sequences are patentable (2-1; 3 opinions)

U.S. Patent 5,747,282

What is claimed is:

1. An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2.

2. The isolated DNA of claim 1, wherein said DNA has the nucleotide sequence set forth in SEQ ID NO:1.

…..

5. An isolated DNA having at least 15 nucleotides of the DNA of claim 1.

6. An isolated DNA having at least 15 nucleotides of the DNA of claim 2.

……

NO:1:

AGCTCGCTGAGACTTCCTGGACCCCGCACCAGGCTGTGGGGTTTCTCAGATAACTGGGCC60CC
TGCGCTCAGGAGGCCTTCACCCTCTGCTCTGGGTAAAGTTCATTGGAACAGAAAGAA119ATGGA
TTTATCTGCTCTTCGCGTTGAAGAAGTACAAAATGTCATTAAT167MetAspLeuSerAlaLeuArgValGlu
GluValGlnAsnValIleAsn151015GCTATGCAGAAAATCTTAGAGTGTCCCATCTGTCTGGAGTTGATC
AAG215AlaMetGlnLysIleLeuGluCysProIleCysLeuGluLeuIleLys202530GAACCTGTCTCCACAAAGTG
TGACCACATATTTTGCAAATTTTGCATG263GluProValSerThrLysCysAspHisIlePheCysLysPheCysM
et354045CTGAAACTTCTCAACCAGAAGAAAGGGCCTTCACAGTGTCCTTTATGT311LeuLysLeuLe
uAsnGlnLysLysGlyProSerGlnCysProLeuCys505560AAGAATGATATAACCAAAAGGAGCCTACAAGA
AAGTACGAGATTTAGT359LysAsnAspIleThrLysArgSerLeuGlnGluSerThrArgPheSer65707580CAAC
TTGTTGAAGAGCTATTGAAAATCATTTGTGCTTTTCAGCTTGAC407GlnLeuValGluGluLeuLeuLysIle
IleCysAlaPheGlnLeuAsp859095ACAGGTTTGGAGTATGCAAACAGCTATAATTTTGCAAAAAAGGAA
AAT455ThrGlyLeuGluTyrAlaAsnSerTyrAsnPheAlaLysLysGluAsn100105110AACTCTCCTGAACATCT
AAAAGATGAAGTTTCTATCATCCAAAGTATG503AsnSerProGluHisLeuLysAspGluValSerIleIleGlnSer
Met115120125GGCTACAGAAACCGTGCCAAAAGACTTCTACAGAGTGAACCCGAAAAT551GlyTyr
ArgAsnArgAlaLysArgLeuLeuGlnSerGluProGluAsn130135140CCTTCCTTGCAGGAAACCAGTCTCAG
TGTCCAACTCTCTAACCTTGGA599ProSerLeuGlnGluThrSerLeuSerValGlnLeuSerAsnLeuGly145150
155160ACTGTGAGAACTCTGAGGACAAAGCAGCGGATACAACCTCAAAAGACG647ThrValArgThrL
euArgThrLysGlnArgIleGlnProGlnLysThr165170175TCTGTCTACATTGAATTGGGATCTGATTCTTCT
GAAGATACCGTTAAT695SerValTyrIleGluLeuGlySerAspSerSerGluAspThrValAsn180185190AAGGC
AACTTATTGCAGTGTGGGAGATCAAGAATTGTTACAAATCACC743LysAlaThrTyrCysSerValGlyAsp
GlnGluLeuLeuGlnIleThr195200205CCTCAAGGAACCAGGGATGAAATCAGTTTGGATTCTGCAAAAA
AGGCT791ProGlnGlyThrArgAspGluIleSerLeuAspSerAlaLysLysAla210215220GCTTGTGAATTTTCT
GAGACGGATGTAACAAATACTGAACATCATCAA839AlaCysGluPheSerGluThrAspValThrAsnThrGlu
HisHisGln225230235240CCCAGTAATAATGATTTGAACACCACTGAGAAGCGTGCAGCTGAGAGG8
87ProSerAsnAsnAspLeuAsnThrThrGluLysArgAlaAlaGluArg245250255CATCCAGAAAAGTATCAGG
GTAGTTCTGTTTCAAACTTGCATGTGGAG935HisProGluLysTyrGlnGlySerSerValSerAsnLeuHisValG
lu260265270CCATGTGGCACAAATACTCATGCCAGCTCATTACAGCATGAGAACAGC983ProCysGl
yThrAsnThrHisAlaSerSerLeuGlnHisGluAsnSer275280285AGTTTATTACTCACTAAAGACAGAATGAA
TGTAGAAAAGGCTGAATTC1031SerLeuLeuLeuThrLysAspArgMetAsnValGluLysAlaGluPhe2902953
00TGTAATAAAAGCAAACAGCCTGGCTTAGCAAGGAGCCAACATAACAGA1079CysAsnLysSerLys

NO 2:

MetAspLeuSerAlaLeuArgValGluGluValGlnAsnValIleAsn151015AlaMetGlnLysIleLeuGluCysProIleCysL
euGluLeuIleLys202530GluProValSerThrLysCysAspHisIlePheCysLysPheCysMet354045LeuLysLeuLe
uAsnGlnLysLysGlyProSerGlnCysProLeuCys505560LysAsnAspIleThrLysArgSerLeuGlnGluSerThrArg
PheSer65707580GlnLeuValGluGluLeuLeuLysIleIleCysAlaPheGlnLeuAsp859095ThrGlyLeuGluTyrAla
AsnSerTyrAsnPheAlaLysLysGluAsn100105110AsnSerProGluHisLeuLysAspGluValSerIleIleGlnSerMet
115120125GlyTyrArgAsnArgAlaLysArgLeuLeuGlnSerGluProGluAsn130135140ProSerLeuGlnGluThrS
erLeuSerValGlnLeuSerAsnLeuGly145150155160ThrValArgThrLeuArgThrLysGlnArgIleGlnProGlnLysT
hr165170175SerValTyrIleGluLeuGlySerAspSerSerGluAspThrValAsn180185190LysAlaThrTyrCysSerV
alGlyAspGlnGluLeuLeuGlnIleThr195200205ProGlnGlyThrArgAspGluIleSerLeuAspSerAlaLysLysAla21
0215220AlaCysGluPheSerGluThrAspValThrAsnThrGluHisHisGln225230235240ProSerAsnAsnAspLe
uAsnThrThrGluLysArgAlaAlaGluArg245250255HisProGluLysTyrGlnGlySerSerValSerAsnLeuHisValGl
u260265270ProCysGlyThrAsnThrHisAlaSerSerLeuGlnHisGluAsnSer275280285SerLeuLeuLeuThrLys
AspArgMetAsnValGluLysAlaGluPhe290295300CysAsnLysSerLysGlnProGlyLeuAlaArgSerGlnHisAsn
Arg305310315320TrpAlaGlySerLysGluThrCysAsnAspArgArgThrProSerThr325330335GluLysLysValA
spLeuAsnAlaAspProLeuCysGluArgLysGlu340345350TrpAsnLysGlnLysLeuProCysSerGluAsnProArgA
spThrGlu355360365AspValProTrpIleThrLeuAsnSerSerIleGlnLysValAsnGlu370375380TrpPheSerArgS
erAspGluLeuLeuGlySerAspAspSerHisAsp385390395400GlyGluSerGluSerAsnAlaLysValAlaAspValLe
uAspValLeu405410415AsnGluValAspGluTyrSerGlySerSerGluLysIleAspLeuLeu420425430AlaSerAsp
ProHisGluAlaLeuIleCysLysSerGluArgValHis435440445SerLysSerValGluSerAsnIleGluAspLysIlePheGl
yLysThr450455460TyrArgLysLysAlaSerLeuProAsnLeuSerHisValThrGluAsn465470475480LeuIleIleGl
yAlaPheValThrGluProGlnIleIleGlnGluArg485490495ProLeuThrAsnLysLeuLysArgLysArgArgProThrSer
GlyLeu500505510HisProGluAspPheIleLysLysAlaAspLeuAlaValGlnLysThr515520525ProGluMetIleAsn
GlnGlyThrAsnGlnThrGluGlnAsnGlyGln530535540ValMetAsnIleThrAsnSerGlyHisGluAsnLysThrLysGly
Asp545550555560SerIleGlnAsnGluLysAsnProAsnProIleGluSerLeuGluLys565570575GluSerAlaPheLy
sThrLysAlaGluProIleSerSerSerIleSer580585590AsnMetGluLeuGluLeuAsnIleHisAsnSerLysAlaProLys
Lys595600605AsnArgLeuArgArgLysSerSerThrArgHisIleHisAlaLeuGlu610615620LeuValValSerArgAs
nLeuSerProProAsnCysThrGluLeuGln625630635640IleAspSerCysSerSerSerGluGluIleLysLysLysLysT
yrAsn645650655GlnMetProValArgHisSerArgAsnLeuGlnLeuMetGluGlyLys660665670GluProAlaThrGly
AlaLysLysSerAsnLysProAsnGluGlnThr675680685SerLysArgHisAspSerAspThrPheProGluLeuLysLeuT
hrAsn690695700AlaProGlySerPheThrLysCysSerAsnThrSerGluLeuLysGlu705710715720PheValAsnP

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2. The isolated DNA of claim 1, wherein said DNA has the nucleotide sequence set forth in SEQ ID NO:1.

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5. An isolated DNA having at least 15 nucleotides of the DNA of claim 1.

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What is claimed is:

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2. The isolated DNA of claim 1, wherein said DNA has the nucleotide sequence set forth in SEQ ID NO:1.

3. The isolated DNA of claim 1 which contains BRCA1 regulatory sequences.

4. The isolated DNA of claim 2 which contains BRCA1 regulatory sequences.

5. An isolated DNA having at least 15 nucleotides of the DNA of claim 1.

6. An isolated DNA having at least 15 nucleotides of the DNA of claim 2.

……

Ass'n for Molecular Pathology v. Myriad (S.Ct.)

1. "It is undisputed that Myriad did not create or alter any of the genetic information encoded in the BRCA1 and BRCA2 genes."

2. Since the gDNA claims "focus on the genetic information encoded in the BRCA1 and BRCA2 genes," they are squarely within the prohibition against patenting a product of nature.

3. "The lab technician unquestionably creates something new when cDNA is made. cDNA retains the naturally occurring exons of DNA, but it is distinct from the DNA from which it was derived. As a result, cDNA is not a "product of nature" and is patent eligible …"

Questions

1. What is the difference between two things that are valuable for the same reason – they provide information on the sequence of the relevant codons?

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Ass'n for Molecular Pathology v. Myriad

"The practical effect of claim 5 is to assert a patent on any series of 15 nucleotides that exist in the typical BRCA1 gene. Because the BRCA1 gene is thousands of nucleotides long, even BRCA1 genes with substantial mutations are likely to contain at least one segment of 15 nucleotides that correspond to the typical BRCA1 gene."

Questions

1. What is the difference between two things that are valuable for the same reason – they provide information on the sequence of the relevant codons?

2. When does a sequence that mirrors something in nature destroy patentability?

- is it about the identity of the materials?
- is it about the breadth of the claims (only for short strands)?
- is it about both issues?

Myriad, fn. 8

“Some viruses rely on an enzyme called reverse transcriptase to reproduce by copying RNA into cDNA. In rare instances, a side effect of a viral infection of a cell can be the random incorporation of fragments of the resulting cDNA, known as a pseudogene, into the genome. Such pseudogenes serve no purpose; they are not expressed in protein creation because they lack genetic sequences to direct protein expression. See J. Watson et al., Molecular Biology of the Gene 142, 144, fig. 7-5 (6th ed. 2008). Perhaps not surprisingly, given pseudogenes' apparently random origins, petitioners "have failed to demonstrate that the pseudogene consists of the same sequence as the BRCA1 cDNA." *Association for Molecular Pathology* v. *United States Patent and Trademark Office*, 689 F. 3d 1303, 1356, n. 5 (CA Fed. 2012). The possibility that an unusual and rare phenomenon *might* randomly create a molecule similar to one created synthetically through human ingenuity does not render a composition of matter nonpatentable.”

Questions

1. What is the difference between two things that are valuable for the same reason – they provide information on the sequence of the relevant codons?

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- is it about the breadth of the claims (only for short strands)?
- is it about both issues?

3. When can facets of nature be ignored for deciding on patentability?

- random?
- no purpose?
- rare?

Lab Corp. v. Metabolite, 548 U.S. 124 (2006)

Breyer, J., dissenting from denial of certiorari

> “Sometimes patent protection can impede rather than promote the progress of science and useful arts.”

Questions

4. Is the distinction between “natural” and “synthetic” sufficient to safeguard competitive development of broad scientific prospects?

Mayo Collaborative Services v. Prometheus Laboratories, Inc.
132 S.Ct. 1289 (2012)

"The steps in the claimed processes (apart from the natural laws themselves) involve well-understood, routine, conventional activity previously engaged in by researchers in the field … upholding the patents would risk disproportionately tying up the use of the underlying natural laws, inhibiting their use in the making of further discoveries."

Questions

4. Is the distinction between “natural” and “synthetic” sufficient to protect competitive development of broad scientific prospects?

5. Isn’t creating cDNA a well-understood, routine, conventional way to work with sequences?

à does *Myriad* overrule *Mayo*?

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à does *Myriad* overrule *Mayo*?

6. Might there be synthetic compositions that disproportionately tie up scientific advance?

Myriad, fn 9

“We express no opinion whether cDNA satisfies the other statutory requirements of patentability. See, e.g., 35 U. S. C. §§102, 103, and 112…”

Questions

4. Is the distinction between “natural” and “synthetic” sufficient to protect competitive development of broad scientific prospects?

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6. Might there be synthetic compositions that disproportionately tie up scientific advance?

7. What about the other criteria for getting a patent?

- novelty (new)
- nonobviousness (inventive step)
- utility (“capable of industrial application”)
- adequate description (metes and bounds, enablement)

KSR v. Teleflex
127 S.Ct. 1727 (2007)

"When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill."

A person of ordinary skill is also a person of ordinary creativity, not an automaton.

Questions

8. What does this all mean for synthetic biology?

Burk , et al. Pat. No. 7,858,350 (December 28, 2010)
Systems and methods for designing and ordering polynucleotides

Computer systems, computer program products and methods for designing oligonucleotides are provided

What is claimed is:

1. A host microbial organism transformed with nucleic acids encoding enzymes of a 1,4-butanediol (BDO) pathway, said microbial organism comprising exogenous nucleic acids encoding BDO pathway enzymes expressed in a sufficient amount to produce BDO, said BDO pathway enzymes comprising: a) 3-hydroxybutyryl-CoA dehydrogenase, said enzyme classified as EC 1.1.1.a and converting acetoacetyl-coenzyme A (CoA) to 3-hydroxybutyryl-CoA; b) 3-hydroxybutyryl-CoA dehydratase, said enzyme classified as EC 4.2.1.a and converting 3-hydroxybutyryl-CoA to crotonoyl-CoA; c) vinylacetyl-CoA A-isomerase, said enzyme classified as EC 5.3.3.3 and converting crotonoyl-CoA to vinylacetyl-CoA; d) 4-hydroxybutyryl-CoA dehydratase, said enzyme classified as EC 4.2.1.a and converting vinylacetyl-CoA to 4-hydroxybutyryl-CoA; and e) 4-hydroxybutyryl-CoA reductase (alcohol forming), said enzyme classified as EC 1.1.1.c and converting 4-hydroxybutyryl-CoA to 1,4-butanediol; or 4-hydroxybutyryl-CoA reductase, said enzyme classified as EC 1.2.1.b and converting 4-hydroxybutyryl-CoA to 4-hydroxybutanal, and 1,4-butanediol dehydrogenase, said enzyme classified as EC 1.1.1.a and converting 4-hydroxybutanal to 1,4-butanediol.

2. The host microbial organism of claim 1, wherein said BDO pathway comprises 4-hydroxybutyryl-CoA reductase (alcohol forming).

3. The host microbial organism of claim 1, wherein said BDO pathway comprises 4-hydroxybutyryl-CoA reductase and 1,4-butanediol dehydrogenase.

4. The host microbial organism of claim 1, wherein said BDO pathway comprises 4-hydroxybutyryl-CoA reductase (alcohol forming), 4-hydroxybutyryl-CoA reductase, and 1,4-butanediol dehydrogenase.

5. The host microbial organism of claim 1, wherein at least one exogenous nucleic acid is a heterologous nucleic acid.

6. The host microbial organism of claim 1, wherein said host microbial organism is in a substantially anaerobic culture medium.

Pat. No. 7,858,350 (cont'd)

7. A method for producing BDO, comprising culturing the host microbial organism of claim 1 under conditions and for a sufficient period of time to produce BDO.

8. The method of claim 7, wherein said BDO pathway comprises 4-hydroxybutyryl-CoA reductase (alcohol forming).

9. The method of claim 7, wherein said BDO pathway comprises 4-hydroxybutyryl-CoA reductase and 1,4-butanediol dehydrogenase.

10. The method of claim 7, wherein said BDO pathway comprises 4-hydroxybutyryl-CoA reductase (alcohol forming), 4-hydroxybutyryl-CoA reductase, and 1,4-butanediol dehydrogenase.

11. The method of claim 7, wherein said non naturally occurring host microbial organism is in a substantially anaerobic culture medium.

12. The method of claim 7, wherein at least one exogenous nucleic acid is a heterologous nucleic acid.

Devroe, Patent No. 7,785,861 (August 31, 2010)
Hyperphotosynthetic organisms

The present disclosure identifies pathways and mechanisms to confer improved industrial fitness on engineered organisms. It also discloses engineered organisms having improved industrial fitness.

We claim:

1. An engineered cyanobacterial cell for fuel production, wherein said cell comprises a recombinant nucleic acid encoding Vitamin B.sub.12 independent methionine synthase, wherein said Vitamin B.sub.12 independent methionine synthase is at least 95% identical to Escherichia coli K12 MetE of SEQ ID NO: 20, and wherein said cyanobacterial cell lacks an endogenous Vitamin B.sub.12 independent methionine synthase.

2. The engineered cyanobacterial cell of claim 1, wherein said Vitamin B.sub.12 independent methionine synthase is Escherichia coli K12 MetE of SEQ ID NO: 20.

3. The engineered cyanobacterial cell of claim 1, wherein said cyanobacterial cell is a Synechococcus species.

4. The engineered cyanobacterial cell of claim 2, wherein said cyanobacterial cell is a Synechococcus species.

5. The engineered cyanobacterial cell of claim 3 or 4, wherein said Synechococcus species is Synechococcus sp. PCC 7002.

6. A method for conferring Vitamin B.sub.12 independence to a cyanobacterial cell, comprising transforming said cyanobacterial cell with a nucleic acid encoding a Vitamin B.sub.12 independent methionine synthase at least 95% identical to Escherichia coli K12 MetE of SEQ ID NO: 20, wherein said cyanobacterial cell requires exogenous Vitamin B.sub.12 for growth prior to said transformation.

7. The method of claim 6, wherein said Vitamin B.sub.12 independent methionine synthase is Escherichia coli K12 MetE of SEQ ID NO: 20.

No. 7,785, 861 (cont'd)

8. The method of claim 7, wherein said cyanobacterial cell is a Synechococcus species.

9. The method of claim 6, wherein said cyanobacterial cell is a Synechococcus species.

10. The method of claim 6 or 7, further comprising culturing said transformed cells in media lacking Vitamin B.sub.12, wherein said media selects for the growth of said transformed cells.

11. The method of claim 8 or 9, wherein said Synechococcus species is Synechococcus sp. PCC 7002.

12. A method to produce a carbon-based product of interest, comprising culturing an engineered cyanobacterial cell in the presence of CO.sub.2 and light under conditions suitable to produce a carbon-based product of interest, wherein said engineered cyanobacterial cell is Vitamin B.sub.12 independent, and wherein said engineered cyanobacterial cell comprises a recombinant nucleic acid encoding a Vitamin B.sub.12 independent methionine synthase, wherein said Vitamin B.sub.12 independent methionine synthase is at least 95% identical to Escherichia coli K12 MetE of SEQ ID NO: 20, and wherein said cyanobacterial cell lacks an endogenous Vitamin B.sub.12 independent methionine synthase.

13. The method of claim 12, wherein Vitamin B.sub.12 independent methionine synthase is Escherichia coli K12 MetE of SEQ ID NO: 20.

14. The method of claim 12, wherein said cyanobacterial cell is a Synechococcus species.

15. The method of claim 13, wherein said cyanobacterial cell is a Synechococcus species.

16. The method of claim 14 or 15, wherein said Synechococcus species is Synechococcus sp. PCC 7002.

Lee, Patent No. 7,973,214 (July 5, 2011)
Designer organisms for photosynthetic production of ethanol from carbon dioxide and water

The present invention provides a revolutionary photosynthetic ethanol production technology based on designer transgenic plants, algae, or plant cells

What is claimed is:

1. A method for photosynthetic production of ethanol comprising growing a transgenic designer plant or plant cells in a liquid medium, wherein the plant or plant cells are genetically engineered to express a set of enzymes in the chloroplast that act on an intermediate product of the Calvin cycle and convert the intermediate product into ethanol by utilizing NADPH and ATP generated from photosynthesis in said plant or plant cells; and recovering ethanol from said liquid medium.

2. The method according to claim 1, wherein said plant is an aquatic or non-aquatic plant.

3. The method of claim 2, wherein said plant is an alga.

4. The method of claim 1, wherein said set of enzymes consists of phosphoglycerate mutase, enolase, pyruvate kinase, pyruvate decarboxylase, and alcohol dehydrogenase.

5. The method of claim 1, wherein said set of enzymes consists of glyceraldehyde-3-phosphate dehydrogenase, phosphoglycerate kinase, phosphoglycerate mutase, enolase, pyruvate kinase, pyruvate decarboxylase, and alcohol dehydrogenase.

6. The method of claim 1, wherein said set of enzymes consists of aldolase, triose phosphate isomerase, glyceraldehyde-3-phosphate dehydrogenase, phosphoglycerate kinase, phosphoglycerate mutase, enolase, pyruvate kinase, pyruvate decarboxylase, and alcohol dehydrogenase.

7,973,214 (cont'd)

7. The method of claim 1, wherein said set of enzymes consists of phosphofructose kinase, aldolase, triose phosphate isomerase, glyceraldehyde-3-phosphate dehydrogenase, phosphoglycerate kinase, phosphoglycerate mutase, enolase, pyruvate kinase, pyruvate decarboxylase, and alcohol dehydrogenase.

8. The method of claim 1, wherein said set of enzymes consists of amylase, starch phosphorylase, hexokinase, phosphoglucomutase, glucose-phosphate isomerase, phosphofructose kinase, aldolase, triose phosphate isomerase, glyceraldehyde-3-phosphate dehydrogenase, phosphoglycerate kinase, phosphoglycerate mutase, enolase, pyruvate kinase, pyruvate decarboxylase, and alcohol dehydrogenase.

9. The method of claim 1, wherein said set of enzymes is genetically engineered to be inserted into the chloroplasts of the transgenic designer plant or plant cells, wherein said insertion is directed by a stroma signal peptide.

10. The method of claim 1, wherein the expression of a said enzyme is controlled by an inducible promoter.

11. The method of claim 10, wherein said promoter is selected from the group consisting of hydrogenase promoters and nitrate reductase promoters.

12. The method of claim 1, wherein the plant or plant cells are genetically engineered to also contain a DNA construct coding for at least one enzyme that facilitates the NADPH/NADH conversion for enhanced photobiological production of ethanol.

13. The method of claim 1, wherein the plant or plant cells are genetically engineered to also inactivate starch-synthesis activity.

14. The method of claim 1, wherein the plant or plant cells are genetically engineered to also inducibly express an additional set of designer enzymes that facilitate starch degradation and glycolysis in the stroma region of the chloroplast.

15. The method of claim 4, wherein said alcohol dehydrogenase utilizes NADPH.

16. The method according to any one of claims 5-8, wherein said glyceraldehydes-3-phosphate dehydrogenase is NAD+-dependent. …..

Application to Synthetic Biology:
1. What is protectable?

1. New molecules with specific end uses
    - substitutions within natural structures (e.g. replace C with Si)
    - based on natural structures, interactions, scaffolding
    - derived from living cells
        - modifications of existing molecules
    - "minimal genomics"
    - wholly synthetic

2. Building blocks/parts/systems

3. Research tools

4. Assembly techniques (direct assembly vs. directed evolution)

5. Design and evaluation techniques (computer simulations, models to predict effects)

[6. Databases: not protected by patents, but by sui generis European right]

Myriad

“Claim 5 of the `282 patent claims a subset of the data in claim 1. In particular, it claims ‘[a]n isolated DNA having at least 15 nucleotides of the DNA of claim 1.’ The practical effect of claim 5 is to assert a patent on any series of 15 nucleotides that exist in the typical BRCA1 gene. Because the BRCA1 gene is thousands of nucleotides long, even BRCA1 genes with substantial mutations are likely to contain at least one segment of 15 nucleotides that correspond to the typical BRCA1 gene.”

Application to Synthetic Biology:
1. What is protectable?

1. New molecules with specific end uses
    - substitutions within natural structures (e.g. replace C with Si)
    - based on natural structures, interactions, scaffolding
    - derived from living cells
        - modifications of existing molecules
    - "minimal genomics"
    - wholly synthetic

2. Building blocks/parts/systems

3. Research tools

4. Assembly techniques (direct assembly vs. directed evolution)

5. Design and evaluation techniques (computer simulations, models to predict effects)

Application to Synthetic Biology:
2. Limits on infringement (freedom to operate)

1. Exceptions to infringement liability for research, diagnostics, interoperability

2. Compulsory licenses

3. Limitations on patent scope

4. Special rules for blocking patents

5. Antitrust (Competition Law) scrutiny

Application to Synthetic Biology:
3. Self help possibilities

1. Put in public domain
    - risk downstream patents on socially-significant improvements

2. Patent, then license or pool with conditions (e.g. grantbacks) or create standard setting organizations (SSOs) requiring RAND licensing
    - expensive
    - depends on the legality of the constraints imposed
    - requires enforcement of terms

3. Place in database (information commons) and license with restrictions
    - outside EU, may require secrecy to enforce
    - risk downstream patents on socially-significant improvement

4. Monitor the landscape and make good use of opposition procedures

Myriad v. Ambry (July 9, 2013)
Myriad v. Gene by Gene (July 10, 2013)

“Defendant is infringing, contributing to the infringement of, and/or inducing others to infringe [each of the nine asserted patents] by making, manufacturing, promoting, marketing, advertising, distributing, offering for sale and selling and/or causing to be offered or sold BRCA1 and BRCA2 products that infringe at least the following claim of [each of the patents in suit] literally and/or under the doctrine of equivalents [].”

U.S. Patent 5,747,282

6. An isolated DNA having at least 15 nucleotides of the DNA of claim 2.

US Patent No. 5,74, 282

16. A pair of single-stranded DNA primers for determination of a nucleotide sequence of a BRCA1 gene by a polymerase chain reaction, the sequence of said primers being derived from human chromosome 17q, wherein the use of said primers in a polymerase chain reaction results in the synthesis of DNA having all or part of the sequence of the BRCA1 gene.

U.S. Patent No. 5,709,999

[1. A method for detecting a germline alteration in a BRCA1 gene, said alteration selected from the group consisting of the alterations set forth in Tables 12A, 14, 18 or 19 in a human which comprises analyzing a sequence of a BRCA1 gene or BRCA1 RNA from a human sample or analyzing a sequence of BRCA1 cDNA made from mRNA from said human sample with the proviso that said germline alteration is not a deletion of 4 nucleotides corresponding to base numbers 4184-4187 of SEQ ID NO:1.]

6. The method of claim 1 wherein a germline alteration is detected by amplifying all or part of a BRCA1 gene in said sample using a set of primers specific for a wild-type BRCA1 gene to produce amplified BRCA1 nucleic acids and sequencing the amplified BRCA1 nucleic acids.

U.S. Patent No. 6,033,857

4. A method for diagnosing a predisposition for breast cancer in a human subject which comprises comparing the germline sequence of the BRCA2 gene or the sequence of its mRNA in a tissue sample from said subject with the germline sequence of the wild-type BRCA2 gene or the sequence of its mRNA, wherein an alteration in the germline sequence of the BRCA2 gene or the sequence of its mRNA of the subject indicates a predisposition to said cancer, wherein the detection in the alteration in the germline sequence is determined by an assay selected from the group consisting of:

(a) observing shifts in electrophoretic mobility of single-stranded DNA on non-denaturing polyacrylamide gels,

(b) hybridizing a BRCA2 gene probe to genomic DNA isolated from said tissue sample,

(c) hybridizing an allele-specific probe to genomic DNA of the tissue sample,

(d) amplifying all or part of the BRCA2 gene from said tissue sample to produce an amplified sequence and sequencing the amplified sequence,

(e) amplifying all or part of the BRCA2 gene from said tissue sample using primers for a specific BRCA2 mutant allele,

(f) molecularly cloning all or part of the BRCA2 gene from said tissue sample to produce a cloned sequence and sequencing the cloned sequence,

(g) identifying a mismatch between (1) a BRCA2 gene or a BRCA2 mRNA isolated from said tissue sample, and (2) a nucleic acid probe complementary to the human wild-type BRCA2 gene sequence, when molecules (1) and (2) are hybridized to each other to form a duplex,

(h) amplification of BRCA2 gene sequences in said tissue sample and hybridization of the amplified sequences to nucleic acid probes which comprise wild-type BRCA2 gene sequences,

(i) amplification of BRCA2 gene sequences in said tissue sample and hybridization of the amplified sequences to nucleic acid probes which comprise mutant BRCA2 gene sequences,

(j) screening for a deletion mutation in said tissue sample,

(k) screening for a point mutation in said tissue sample,

(l) screening for an insertion mutation in said tissue sample,

(m) in situ hybridization of the BRCA2 gene of said tissue sample with nucleic acid probes which comprise the BRCA2 gene.