An iGEM-Specific Guide to U.S. Intellectual Property and Patent Law

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Table of Contents

Foreword

Intellectual property law. Hate it or love it, navigating through the storm of patents will be critical for the new generation of bioengineers. Indeed, synthetic biology is a new field with enormous promise, including the potential to create "an artificially programmable genome from standard parts" (8). However, with every wave of revolutionary technology, there is a struggle to tame and assimilate the advances into intellectual property law. Researchers and companies have already started to patent the various standard parts required for the lofty goal of a programmable genome (8). Some of synthetic biology, as evidenced by iGEM, is open-source, but nevertheless, patents will continue to be a part of the emerging field as companies seek to protect their lucrative technologies. My job here is to answer a few simple questions about intellectual property—specifically dealing with how it relates to synthetic biology—in order to provide you all with a compass of valuable information to make it safely through the storm.

I am the son of two intellectual property attorneys. Throughout my childhood, I have listened to my parents debate technological advances, curse examiners, and rejoice because of a successful patent application or amendment at the dinner table. I AM NOT, HOWEVER, AN EXPERT IN THIS TOPIC. Take everything in this guide with a grain of salt. Our team, Stanford-Brown iGEM, ran into a few snags with our Biomining project and patented genes. We came across a gene called silicase, which comes from a sea sponge and digests silica. This gene would have been very useful for the project as a BioBrick. However, silicase appeared in US Patent Application 2007/0218044. The inventors essentially wanted to patent the use of the isolated silicase gene, and any gene within 25% similarity in the amino acid sequence, for degradation of silica (9). Most of the members of our team had no idea whether this meant we could use the gene in creating a BioBrick or not. In effect, no one really knew how to approach the matter. It came up in a meeting that my parents were I.P. attorneys, and the idea to create an iGEM-based guide to patent law was born.

I will try to keep the reading light-hearted and humorous, yet also enlightening. Patent law is intricate, and while you will not be able to become an IP attorney simply after reading this guide, you should be able to answer these questions:

DISCLAIMER: I am not providing legal advice in this doccument. If you have pressing/more specific legal questions, seek consultation with a credited intellectual property attorney.

1. What is a patent?

In the U.S., a patent is a property right granted to an inventor by the United States Patent and Trademark office (USPTO). This property right gives an inventor the ability to 'exclude others from making, using, offering for sale, or selling' his or her invention in the United States and from 'importing' the invention into the United States" (3). In other words, a patent does not give the patentee the right to specifically use, sell, or import their invention; it simply denies competitors that opportunity (3).

The rights conferred by a patent persist for 20 years after the first U.S. filing date of the patent application, as long as the application was filed after June 8, 1995. On the other hand, for patents on file on or before that date, the patent rights extend for the duration of the longer of the following: 20 years from the date of filing, or 17 years from the date of issuance (see question 4 if you are wondering how to find that information) (13). The USPTO can extend the term of a patent under certain circumstances, such as delays caused by the USPTO itself during patent prosecution (7).

2. What makes an invention patentable?

In order to be granted a patent by the USPTO, an invention must fall into the category of patentable subject matter (as defined by the law), in addition to being both "novel" and "non-obvious." These three requirements are covered by U.S. Federal Statutes 35 U.S.C. § 101, § 102, and § 103, respectively.

PATENTABLE SUBJECT MATTER:

As per 35 U.S.C. § 101, "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title" (4).

You definitely had to read that more than once, right? Even still, you are probably wondering what qualifies an invention or improvement as "useful?" Let's see if we can examine the statute in plain English.

Basically, a patent is granted for the invention OR improvement of a process, machine, manufacture, or composition of matter. That's right: simply developing a better method of carrying out a process—even if that process is already established—can be patentable. So you might be a creative type and think that there should be many more patented inventions. After all, you practically come up with a new idea for an invention or improvement every day. Truthfully, it is not as easy as it sounds to obtain a patent, even if you invent or improve something. Notice the disclaimer at the end that states that the invention is "subject to the conditions and requirements of this title?" Well, there are definitely a lot of conditions and requirements in patent law.

DEFINING "USEFUL":

The issue of utility was addressed in the Supreme Court case *Brenner v. Manson* of 1966. In the end, the Supreme Court ruled that "utility could not be established until a 'specific benefit exists in current available forms'" (13). In other words, the invention must present an immediate use to the respective field and cannot be in a research phase. In addition to the requirements of this ruling, the invention must have credible and either well-established or asserted utility. Credible utility simply means that a claim for an invention's utility does not violate hard-written laws of nature (13). For example, you would not be able to obtain a patent on a perpetual motion machine, which violates the second law of thermodynamics. The utility of an invention is well-established if a person of ordinary skill in the field would immediately describe the invention as useful, based on its characteristics (13). On the other hand, an inventor can assert the utility of their invention for a specific purpose in the patent application, but the assertion must be approved by the examiner (13).

An invention that satisfies utility requirements does not have to be useful in any commercial sense. In the case of the biotech arena, for example, one could patent a new cancer therapy drug even if the compound has not been approved by the FDA through clinical trials (13).

NOVELTY

35 U.S.C. § 102—which details the novelty requirements for obtaining a patent—is rather long, so here is an abridged version.

An invention is considered novel if the following conditions are met:

1. **The invention was not publicly known or used in the U.S. before the date of invention or more than one year before the filing date of the patent application.**
2. **The invention was not patented or described in a printed publication in a foreign country before the date of invention or more than one year before the filing date of the patent application. (13)**

Novelty involves examination of prior art, or previous inventions in the field. The requirements above should be pretty self-explanatory, but some significant changes will be occurring starting March 18, 2013. Congress recently passed the America Invents Act, which will effectively convert the U.S. from

SOME EXAMPLES OF SYNTHETIC BIOLOGY PATENTS GRANTED IN THE U.S.

"Artemisinic epoxide and methods for producing same." Dietrich et al.

What is patented: production of artemisinic epoxide using either Saccharomyces cerivisae or Escherichia coli cells that have been engineered to carry out the 1-deoxy-D-xylulose 5-diphosphate (DXP) pathway (1).

"Methods for cell based combinatorial logic." Sayler et al.

What is patented: A method of providing a chemical or electrical stimulus to a genetic sequence comprising a promoter and a gene in a genetically engineered cell, wherein the stimulus is applied through nanofibers, and the promoter-gene construct produces a gene product that can be detected by the presence of an output signal (12).

"Iterative optimization in the design of binding proteins." Eisenberg et al.

What is patented: A method of optimizing the binding specificity of a certain type of DNA-binding protein--a zinc finger protein--for its target sequence by obtaining the DNA-binding protein, determining its specificity, identifying an area of the target sequence that the protein does not have specific binding to, then altering the protein amino acid residues until specific binding to the new target sequence is achieved (8).

"Method and system for polynucleotide synthesis." Mulligan et al.

What is patented: A method of using an Automated Polynucleotide Synthesis Design System, and the system itself. The software decomposes a target polynucleotide into fragments, makes sure the fragments satisfy certain optimal synthesis criteria, and then outputs an order in which the fragments should be combined (8,10).

a “first to invent” country to a “first to file” country. Under the current system, if inventors A and B came up with the same patentable invention, but inventor B came with the idea first, he would be granted the patent, even if inventor A attempts to file an application earlier than inventor B. If the same situation were to occur under the new system, as long as inventor A filed an application before inventor B, he would be granted the patent (7).

NON-OBVIOUSNESS

The requirement of non-obviousness is defined in 35 U.S.C. § 103 Overall, the decision making process for non-obviousness involves looking at prior art as well, but unlike novelty, patent examiners must determine what the next obvious step would be from previous inventions (13).

“Unlike novelty, patent examiners must determine what the next obvious step would be from previous inventions”

Specifically, an invention violates this requirement if “the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains” (5).

Interestingly enough, 35 U.S.C. § 103 has specific clauses for biotechnological inventions, including processes “of genetically altering or otherwise inducing a single- or multi-celled organisms to express an exogenous nucleotide sequence, inhibit, eliminate, augment, or alter expression of an endogenous nucleotide sequence, or express a specific physiological characteristic not naturally associated with said organism” (5).

Inventions in this category—even if they are considered novel and non-obvious as defined above—have additional requirements to be deemed fully non-obvious. Basically, the composition of matter and process used in these inventions must both be clearly defined in the claims and either contained within the same patent application or another application owned by the same person (5). This prevents someone from patenting, for example, a modified enzymatic pathway, when another group has a patent on the method to obtain that pathway.

With relation to synthetic biology, patents have fallen into two categories in the U.S.:

1. **“Biological tools, methods, and products” (11).**
2. **Computer programs, involved both in the design of biological parts and the modeling of activity within cells (11).**

3. What does a patent look like?

Many of you have probably heard of engineer-extraordinaire Jay D. Keasling. In 2006, Keasling successfully synthesized the anti-malarial wonder drug artemisinin using S. cerivisiae and E. coli. Artemisinin is 90 percent effective against the malarial parasite, but it costs about 20 times more than other anti-malarial drugs because of the difficulty of extracting the compound from its native wormwood plant (14). Keasling managed to recreate the entire synthetic pathway using native genes of the host cell and genes from the wormwood plant (14). We're now going to move step by step through U.S. Patent No. 8,101,399 entitled "Artemisinic epoxide and methods for producing same" (1).

US008101399B2

(12) **United States Patent**
Dietrich et al.

(10) **Patent No.: US 8,101,399 B2**
(45) **Date of Patent: Jan. 24, 2012**

(54) **ARTEMISINIC EPOXIDE AND METHODS FOR PRODUCING SAME**

(75) Inventors: **Jeffrey Allen Dietrich**, Berkeley, CA (US); **Yasuo Yoshikuni**, Berkeley, CA (US); **Jay D. Keasling**, Berkeley, CA (US); **Michelle Chia-Yu Chang**, Berkeley, CA (US)

(73) Assignee: **The Regents of the University of California**, Oakland, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 955 days.

(21) Appl. No.: **11/955,154**

(22) Filed: **Dec. 12, 2007**

(65) **Prior Publication Data**

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Related U.S. Application Data

(60) Provisional application No. 60/874,600, filed on Dec. 12, 2006.

(51) **Int. Cl.**

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C12N 1/21	(2006.01)
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(52) **U.S. Cl.** **435/255.1**; 435/252.1; 435/252.3; 435/254.2

(58) **Field of Classification Search** ..... None
See application file for complete search history.

(56) **References Cited**

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2005/0059128	A1	3/2005	Arnold et al.
2006/0063226	A1	3/2006	Matuschek et al.

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Ro et al., "Production of the antimalarial drug precursor artemisinic acid in engineered yeast," Nature, 2006, 440 (7086):940-943.

Primary Examiner — Michele K Joike
(74) *Attorney, Agent, or Firm* — Paula A. Borden; Bozicevic Field & Francis LLP

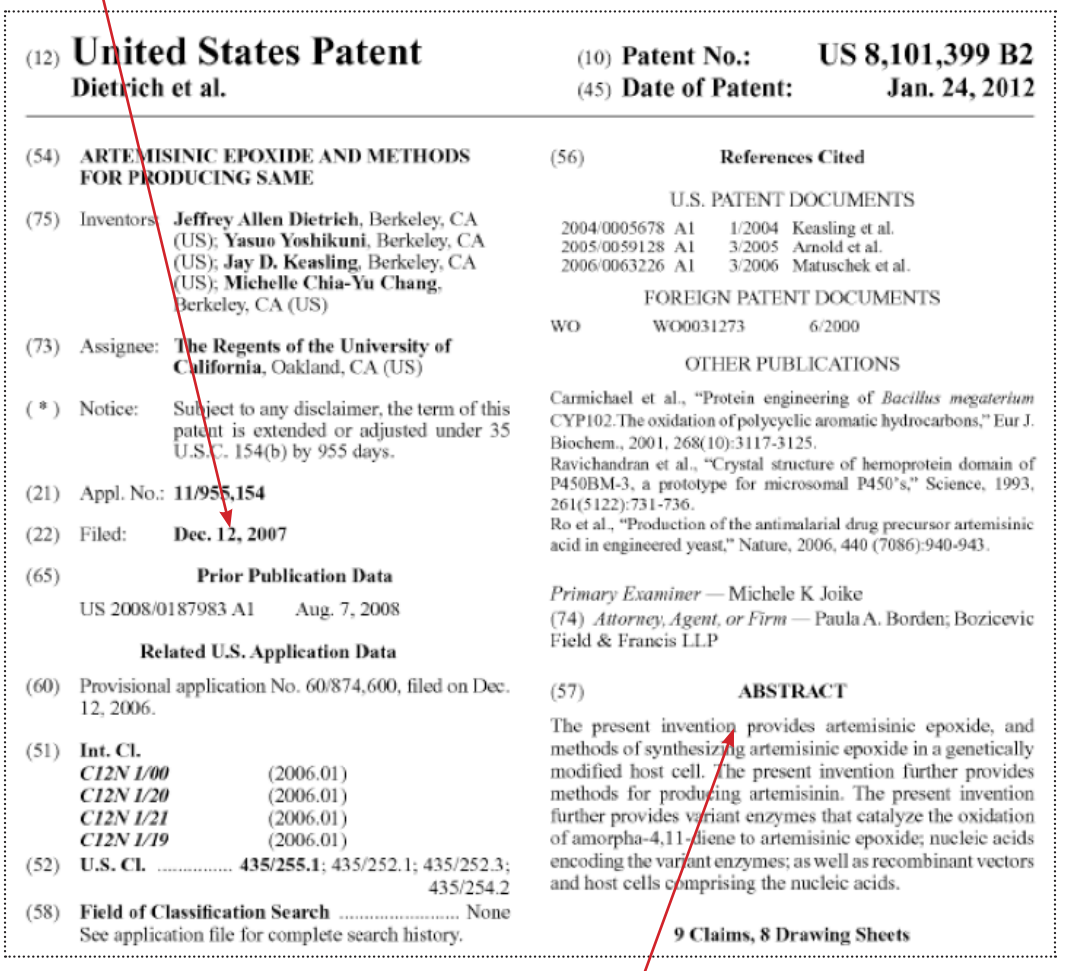
(57) **ABSTRACT**

The present invention provides artemisinic epoxide, and methods of synthesizing artemisinic epoxide in a genetically modified host cell. The present invention further provides methods for producing artemisinin. The present invention further provides variant enzymes that catalyze the oxidation of amorpha-4,11-diene to artemisinic epoxide; nucleic acids encoding the variant enzymes; as well as recombinant vectors and host cells comprising the nucleic acids.

9 Claims, 8 Drawing Sheets

1. The first page of a patent contains information concerning the invenators, the assignee, the filing date, the examiner, the attorney, and the abstract.

This patent was **filed on Dec. 12, 2007**, meaning it expires on Dec. 12, 2027.



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(54) **ARTEMISINIC EPOXIDE AND METHODS FOR PRODUCING SAME**

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C12N 1/19 (2006.01)

(52) **U.S. Cl.** **435/255.1**; 435/252.1; 435/252.3; 435/254.2

(58) **Field of Classification Search** ..... None
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2006/0063226	A1	3/2006	Matuschek et al.

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Ravichandran et al., "Crystal structure of hemoprotein domain of P450BM-3, a prototype for microsomal P450's," Science, 1993, 261(5122):731-736.
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9 Claims, 8 Drawing Sheets

The abstract is similar to that of a scientific paper. In about a paragraph, the abstract describes the invention in a non-binding sense (the exact invention is not defined here) (2). As you can see, the abstract for this patent explains that the invention involves synthesis of artemisinic epoxide inside a genetically modified host cell, and a method to take that artemisinic epoxide to artemisinin using specific pathways encoded by recombinant vectors. **Thus, the abstract gives a useful background, but you must read the claims in order to figure out exactly what is patented.**

In addition, the patent examiner often chooses one figure they found most representative of the subject matter in the patent to put on the first page (7), but this patent lacks that.

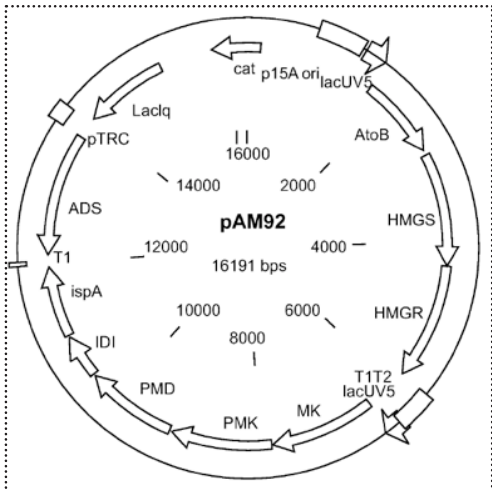


FIG. 4

2. After the first page comes the barrage of various figures that will be referenced throughout the patent.

There is no set number of figures, but each appear in a format such as the one shown below, with a label underneath the figure and no description. It might be easy to understand the figures as they stand alone, but it is not a fruitful endeavor. **Have patience: they will be explained for you throughout the patent.**

3. We have reached the body of the patent. This is where things start getting interesting. The format of this section usually goes something like this:

A. BACKGROUND:

This section, which can range anywhere from a few paragraphs to about a page or so, establishes the problem the invention is intended to solve and sets the stage for why the invention or method would be useful (7). Here, this patent explains the cause of malaria and the current problems with artemisinin synthesis, as discussed above.

BACKGROUND

Malaria is an infectious disease caused by protozoans of the genus *Plasmodium*, and is transmitted by the bite of infected *Anopheles* mosquitoes. The species *P. falciparum* accounts for the preponderance of global morbidity and mortality, and 41 percent of the world's population live in areas where malaria is endemic. Malaria is a preventable and treatable disease but it is estimated to kill one to three million people each year, primarily young children.

Artemisinin is a potent anti-malarial agent produced naturally in the plant *Artemisia annua*. Malaria has become increasingly resistant to first-line drug therapies, but combination drugs containing artemisinin derivatives show nearly 100 percent effectiveness against the malaria parasite. Production of sufficient quantities of artemisinin from natural sources to meet current global demands suffers from a combination of low yield, difficulty of isolating pure compounds, and resource-intensive cultivation.

There is a need in the art for alternative methods of producing artemisinin.

B. SUMMARY OF THE INVENTION:

In this particular patent, the summary is literally the same as the abstract, word for word, and the section is followed by another entitled "Features of the Invention." Other patents, such as Mulligan et al. (10) and Sayler et al. (12), go right from the Summary to the Brief Description of the Drawings. In a general sense, the Summary of the Invention is intended to describe what the patent's independent claims cover (more on that later...) (7).

Do not assume that this section is accurate because it is written in view of the claims as originally filed, and this section is not typically revised to reflect the scope of the final claims after prosecution has been completed (7).

From the abstract, we learned that the invention of the patent involves production of artemisinic epoxide in a genetically modified host cell which contains all necessary enzymes to transform amorpha-4,11-diene to artemisinic epoxide, in addition to a further method to synthesize artemisinin. In "Features of the Invention", we get our first real glimpse into the legal language in a patent, and how tough it can be to read. "In some embodiments," and "In other embodiments" are written so many times they feel like being beaten over the head with a hammer. It's extremely hard to sift through the barrage and figure out what exactly the invention is, and I do not recommend trying to do so. But if you're courageous, see if you can get more than what I got out of it (and do not cheat by looking at the claims!!)

C. BRIEF DESCRIPTION OF THE DRAWINGS

Exactly how it sounds, this section describes what is depicted by each of the figures shown at the beginning of the patent.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is a schematic depiction of the conversion of amorpha-4,11-diene to artemisinic acid (AA) via artemisinic-11S, 12-epoxide (AAE). (AAOH=artemisinic alcohol; AAA=artemisinic aldehyde).

FIG. **2** is a schematic representation of the mevalonate ("MEV") pathway for the production of isopentenyl pyrophosphate ("IPP").

FIG. **3** is a schematic representation of the 1-deoxy-D-xylulose 5-diphosphate ("DXP") pathway for the production of isopentenyl pyrophosphate ("IPP") and dimethylallyl pyrophosphate ("DMAPP").

FIG. **4** is a schematic depiction of expression plasmid pAM92.

FIG. **5**A depicts full scan GC-MS traces of artemisinic-11S,12-epoxide that was synthesized chemically (2), and amorpha-4,11-diene (1) and artemisinic-11S,12-epoxide (2) that was produced by an *Escherichia coli* DH1 host strain harboring expression plasmids pAM92 and pTrcBM3-14-G4. FIGS. **5**B-C depict the mass spectra of artemisinic-11S, 12-epoxide synthesized chemically (B) or produced by an *Escherichia coli* DH1 host strain (C).

FIGS. **6**A-C depict ^{1}H-NMR spectra (500 Mhz) of an amorphadiene standard (A), chemically synthesized artemisinic-11S,12-epoxide (B), and artemisinic-11S,12-epoxide produced by an *Escherichia coli* DH1 host strain (C).

D. DEFINITIONS

Legal documents such as patents have to be very precise in defining the scope of the invention. Thus, it is critical to define what exactly various terms used in the description of the invention entail. Some of the terms defined in this section include the following: "substantially pure," "melavonate pathway," "nucleic acid," and "recombinant."

Not all patents include a definition section. You should note that unless they are specifically defined, the terms used in the claims are typically their "plain and ordinary meaning" (7).

E. DETAILED DESCRIPTION

This section is a much longer version of the summary. As the title implies, there is much more detail given on the invention and how it works. It is generally required that the inventor describe the invention is such a way that someone of ordinary skill in the art can practice the invention (7). In addition, the inventor is supposed to describe what he or she believes is the best way to practice the invention as of the date of filing (see 35 U.S.C. §112) (4,13). Here are some examples of the further information provided on the invention: suitable eukaryotic host cells (column 14 line 59), suitable plant host cells (column 15 line 4), suitable prokaryotic host cells (column 15 line 30), suitable eukaryotic promoters [both constitutive and inducible] (column 24 line 31), suitable prokaryotic promoters [both constitutive and inducible] (column 26 line 40), and variant P450 enzymes (column 30 line 18).

F. EXAMPLES

The paragraph shown below is part of the introduction to the examples section of the patent. It does a pretty good job of explaining the purpose of this section: "to provide those of ordinary skill in the art with a complete disclosure and description of how to make and use the present invention" (column 46 lines 16-18). In other words, these sections explain how to build the genetically modified host cells, with the disclaimer that the scope of the invention is not meant to be given here (see the next section for that).

Example one explains how to generate the expression constructs for various enzymes of the melavonate pathway and for amorpha-4,11-diene. Example 2 explains how the inventors created constructs coding for a modified cytochrome P450 enzyme. Example 3 details how artemisinic epoxide is produced in E. coli through the melavonate pathway.

Finally, Example 4 discusses the methodology for knocking out Tryptophanase A from E. coli host cells, which increased the yield of amorpha-4,11-diene and artemisinic epoxide.

EXAMPLES

The following examples are put forth so as to provide those of ordinary skill in the art with a complete disclosure and description of how to make and use the present invention, and are not intended to limit the scope of what the inventors regard as their invention nor are they intended to represent that the experiments below are all or the only experiments performed.

G. CLAIMS

You know what they always say: "Save the best for last." Well, the claims are definitely the proverbial meat of the patent, regardless of being located at the very end of the document itself. These numbered statements, simply put, define the scope of the patented invention. Section §112 requires that the inventors conclude their specification with one or more claims that particularly designate the subject matter that the inventors regard as their invention (7). In other words, they define what characteristics of the invention or method—in the laws surrounding a patent—cannot be used, sold, or imported into the U.S.

A claim can be designated as independent or dependent. The definitions are pretty self-explanatory: independent claims do not reference other claims, while dependent claims reference either an independent claim or another dependent claim (7). Both types are numbered statements. The independent claims define the broadest scope of the invention, while the dependent claims narrow things down a bit. The key, however, is to note that what actually is patented is much more defined than what the abstract would have you believe, or what could be gleaned just from the drawings. As you will see in the methods section, this is the reason that the claims are the most important statements to read in the body of the patent.

What is claimed is:

1. A genetically modified host cell, wherein the genetically modified host cell produces amorpha-4,11-diene, wherein the genetically modified host cell comprises a heterologous cytochrome P450 enzyme that converts the produced amorpha-4,11-diene into amorpha-4-ene-11,12-epoxide, and wherein the genetically modified host cell is a yeast cell or a bacterial cell.

2. The genetically modified host cell of claim **1**, wherein the amorpha-4,11-diene is produced via a 1-deoxy-D-xylulose 5-diphosphate (DXP) pathway.

3. The genetically modified host cell of claim **1**, wherein the host cell comprises a heterologous nucleotide sequence encoding one or more enzymes of the DXP pathway.

4. The genetically modified host cell of claim **1**, wherein the amorpha-4,11-diene is produced via a mevalonate pathway.

5. The genetically modified host cell of claim **1**, wherein the host cell comprises a heterologous nucleotide sequence encoding one or more enzymes of the mevalonate pathway.

6. The genetically modified host cell of claim **1**, wherein the host cell is a yeast cell.

7. The genetically modified host cell of claim **6**, wherein the yeast cell is *Saccharomyces cerevisiae*.

8. The genetically modified host cell of claim **1**, wherein the host cell is a bacterial cell.

9. The genetically modified host cell of claim **8**, wherein the host cell is *Escherichia coli*.

* * * * *

As shown above, there are nine claims in the patent on artemisinin. Can you spot which ones are independent and which ones are dependent?

Claim 1 is the only independent claim, and claims 2-9 are thus dependent. So what is actually patented? The inventors have created a genetically modified host cell—either yeast or bacterial—which produces amorpha-4,11-diene through a DXP pathway or a melavonate pathway. Furthermore, the host cell contains a modified cytochrome P450 enzyme that converts the amorpha-4,11-diene into amorpha-4-ene-11,12-epoxide.

4. How should one read a patent?

Reading a patent is tedious work. In many ways, the work is even more tedious than reading a scientific paper because of the legal language. Many of you might have been taught a way to read scientific papers in your course work. What if there was an ideal way to read patents as well?

Method adopted from advice of Kevin Jackson

1. LOCATE THE FILING DATE ON THE VERY FIRST PAGE OF THE PATENT.

For the artemisinin patent considered above, we saw that the filing date was Dec. 12, 2007. As referenced in section 2, recall that a patent filed after June 8, 1995 expires 20 years after the earliest filing date. Thus, the Dietrich et al. patent expires on Dec. 12, 2027. Why is this the most important thing to do? Well, it tells you right off the bat whether you should be worried about infringement. If the patent has expired, you can be pretty sure that the claimed invention is now in the public domain.

2. DETERMINE WHO "OWNS" THE PATENT, I.E. LOCATE THE "ASSIGNEE" ON THE FIRST PAGE OF THE PATENT.

It could be the inventors, a company, or a university. There are a few tidbits of advice to keep in mind here. If the inventors are the owners of the patent, they MIGHT be less likely to sue a large corporation or a university for infringement. Corporations vary in terms of how litigious there are with others, which should be apparent from web searches (i.e. how many competitors have they ever sued for infringement?). To be very sure that the patent has not been sold to another entity, you should get in the habit of checking http://assignments.uspto.gov/assignments/q?db=pat for the most up to date information on who owns a patent.

3. NEXT, IT'S TIME TO EXAMINE THE CLAIMS AT THE END OF THE PATENT.

Specifically, the independent claims are where the money is at. Do not make the mistake of thinking that you know what invention is specifically being patented by reading the abstract and looking at the figures (notice that those two have not even come up in the method yet!). Only the claims define exactly what is patented. Reading them prior to any other material in the body is critical.

4. STILL UNSURE ABOUT WHAT'S BEEN PATENTED?

If you believe that some of the claims require further clarification, or you want to know more about how the invention specifically works, then it's time to peruse the rest of the patent. Given the huge range of material that an invention could entail, there is no set order in which to read the rest of the body. Dive right in!

5. IF YOU STILL THINK THIS PATENT CONTAINS MATERIAL RELATED TO YOUR WORK, IT IS OFTEN USEFUL TO FIGURE OUT WHAT OTHER COUNTRIES THE PATENT IS ISSUED IN.

Check out this website (it's free): http://worldwide.espacenet.com/?locale=en_EP, and enter the patent number [for the artemisinin patent, you would enter US8101399B2 into the search box]. This should spit out patents on the invention in other countries. Note that the claims in other countries could possibly be different than those in the U.S. patent, but that the patent again remains valid until 20 years after the filing date.

6. THE END-ALL-BE-ALL

If the patent is really relevant to your work, you should **consider consulting with an intellectual property attorney** on the matter. Some useful topics that could be brought up in such a consultation are how to design around a patent, how to file a patent on an invention that designs around the patent in question, finding references to invalidate the patent, and even exploring licensing opportunities with the patent owner.

5. What is infringement?

According to the USPTO website, "infringement of a patent consists of the unauthorized making, using, offering for sale, or selling any patented invention within the United States or U.S., or importing into the United States of any patented invention during the term of the patent" (3). Whether infringement is actually occurring depends on the language of the claims of the patent. Thus, the most important thing to look at when examining a patent is the claims. If nothing else, that will tell you what you cannot do (sound familiar?).

So now you know what infringing a patent means, but what are the consequences? If a patent is infringed, the patentee can sue in federal court. The patentee can ask for an injunction, which requires the cessation of infringement and sometimes payment of damages (3). The defendant, however, can attempt to deny the validity of the patent or argue that the actions committed do not qualify as infringement based on the claims (3). If the court decides that the patent is invalid, then the document is thrown out (3).

"Thus, the most important thing to look at when examining a patent is the claims. If nothing else, that will tell you what you cannot do (sound familiar?)."

6. How does one search for a patent?

1. GOOGLE PATENTS

www.google.com/patents

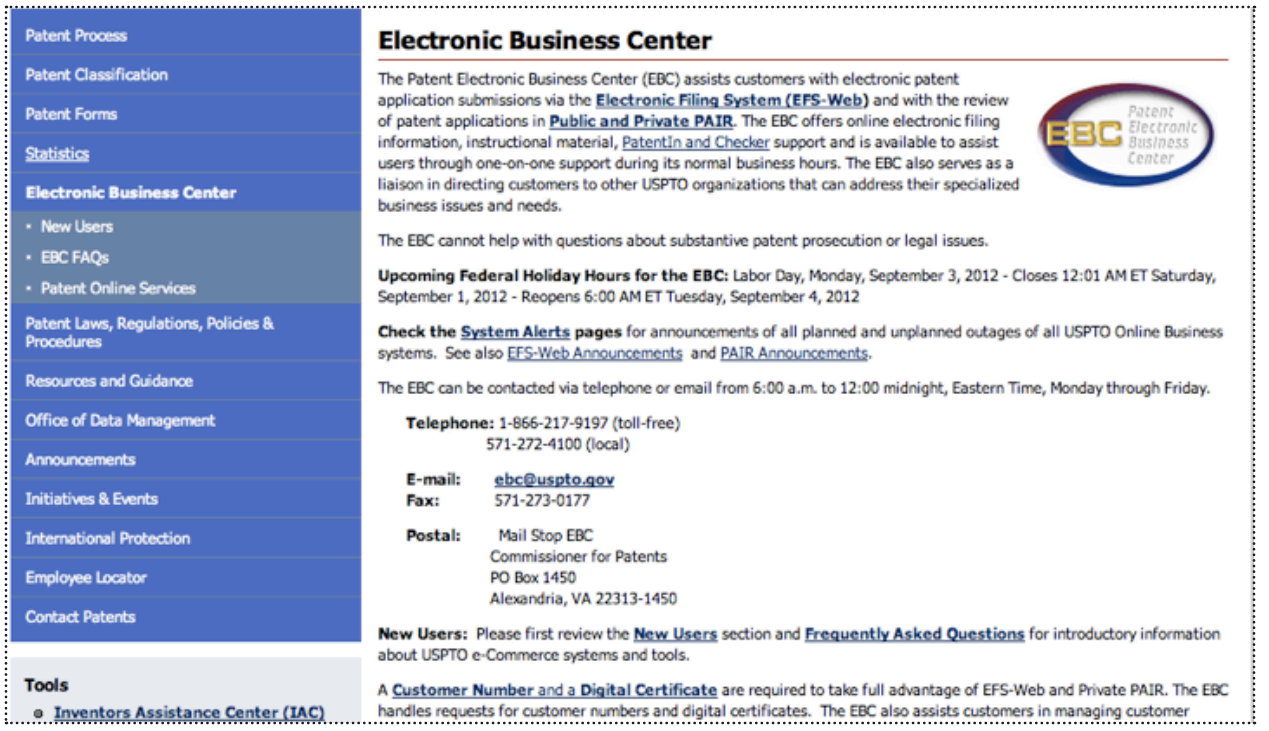
Google search does patents! Just enter the web address above and you can start searching for patents in the particular area of interest. If you enter "Green fluorescent protein" into the search box, Google spits out 50,400 results. Yeah, that's a lot of patents. You can then fine-tune the search with a few options along the left-hand side of the page, such as restricting by filing date, showing only applications or issued patents, or searching by patent type. These options include the following:

Google Patents does more than just keyword search as well. You can enter the patent number and search that way, or you can enter the name of a company or an inventor. Once you find the patent that you are looking for, you can click on the link and click "Download PDF" in the top right corner.

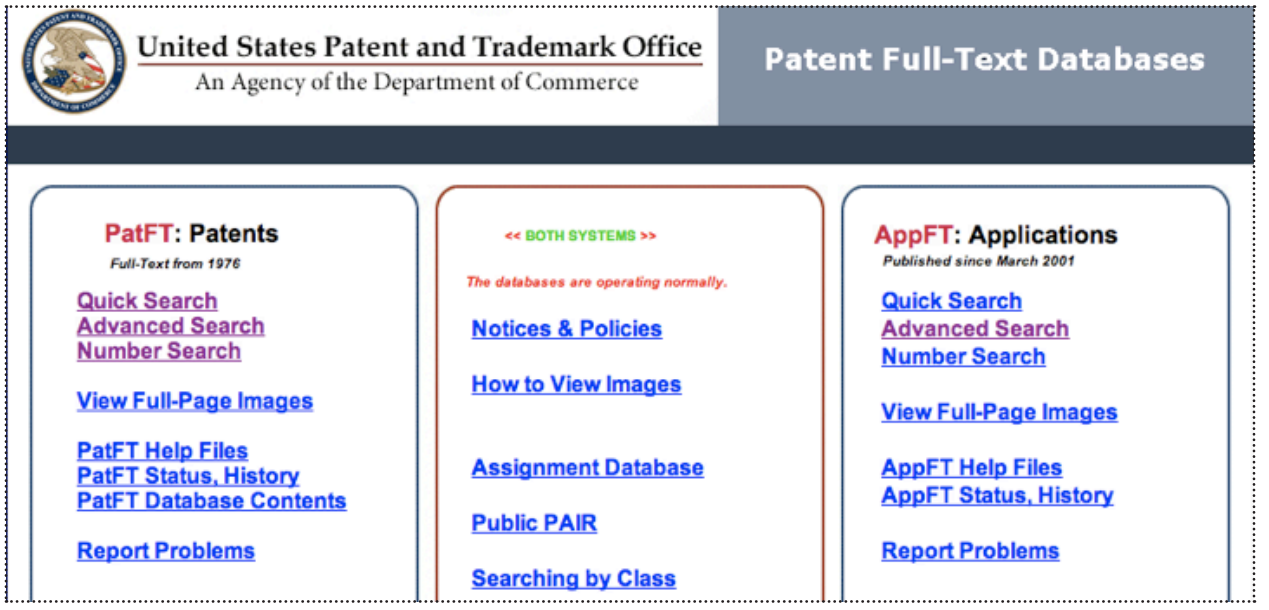
2. THE USPTO'S PATENT FULL TEXT DATABASES

www.patft.uspto.gov/

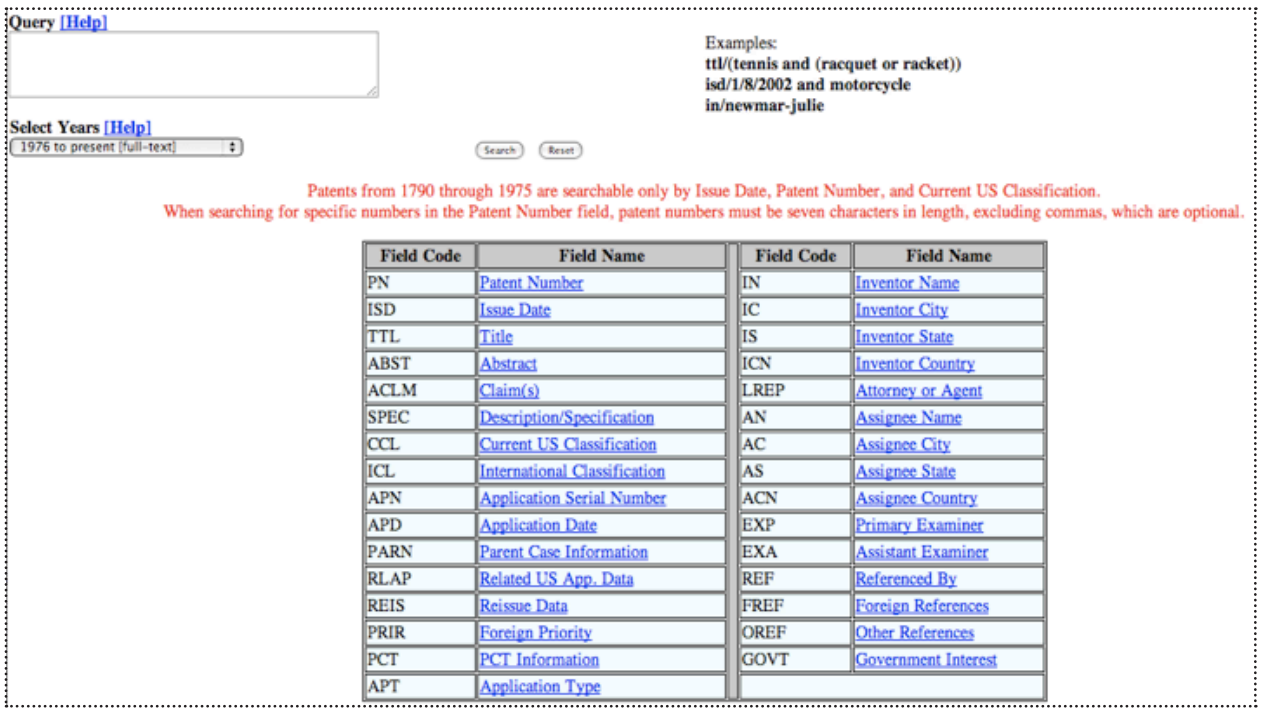
This is the official database of U.S. patents and patent applications on the web. The site is also accessible through the homepage, www.uspto.gov. On this page, go to the drop down menu called "PATENTS" in the top left-hand corner of the page, and click on "Electronic Business Center." Finally, go to the gray box on the bottom of the page called "Tools," and select the fourth bullet point from the top.



Now you should be on a page that looks like this:



The leftmost column links to a database of all U.S. patents issued after 1976. The three options of note are Quick Search, Advanced Search, and Number Search. Quick Search allows you to enter two terms with the connectors AND, OR, and ANDNOT. You can also limit these terms to specific fields of the patent (e.g. abstract, issue date). Advanced Search gives you more options that are not very hard to use either. Let's click on it and see for ourselves:



Field Code	Field Name	Field Code	Field Name
PN	Patent Number	IN	Inventor Name
ISD	Issue Date	IC	Inventor City
TTL	Title	IS	Inventor State
ABST	Abstract	ICN	Inventor Country
ACLM	Claim(s)	LREP	Attorney or Agent
SPEC	Description/Specification	AN	Assignee Name
CCL	Current US Classification	AC	Assignee City
ICL	International Classification	AS	Assignee State
APN	Application Serial Number	ACN	Assignee Country
APD	Application Date	EXP	Primary Examiner
PARN	Parent Case Information	EXA	Assistant Examiner
RLAP	Related US App. Data	REF	Referenced By
REIS	Reissue Data	FREF	Foreign References
PRIR	Foreign Priority	OREF	Other References
PCT	PCT Information	GOVT	Government Interest
APT	Application Type		

In the box that says query, enter text in the following format: field code/designation. The page shows examples at the top. If you wanted to search for patents assigned to Sangamo Biosciences, simply query AN/"Sangamo Biosciences." How about patents with Craig Venter as the inventor: IN/Venter-Craig.

Finally, Number Search allows you to simply enter the number of the patent in the search box. For the Dietrich et al. artemisinin patent examined above, the number is US 8,101,399. To search for the patent, you would enter 8101399.

3. ESPACENET

www./worldwide.espacenet.com/?locale=en_EP

As mentioned above, this is the free website to search for patents issued worldwide. Number Search searches by the patent number (try searching US8101399). Advanced Search gives similar options as the USPTO with examples provided. The neat thing here is that you can limit your search to the worldwide or strictly European databases. Quick Search only allows you to search for keywords in the title and abstract or for specific people or organizations. Smart Search is very similar to Google search in that it will accept pretty much any query.

These three websites are free. Many more exist that require hefty fees.

Conclusion

I hope many of you will find this guide useful in your iGEM endeavors, and that you make patent searches an integral part of your research phase. Patent law is a tough subject to grasp, but it is also a critical skill if you work in a burgeoning field of technology. Synthetic Biology is on the cusp of changing the world. You are now armed with very useful knowledge on how to make your innovations legal and non-infringing. So what are you waiting for?

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Keasling pic: http://pbd.lbl.gov/people/keasling.html