

## Intellectual Property Perspective on Biophotonics

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## Patent Overview

- Rights granted by a patent
- Rights NOT granted by a patent
- Strategies for new companies

### Case Studies

- Approaches taken to protect two different areas of technology related to biophotonics.

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## Patent Overview

- 1) Rights **GRANTED** by a patent:
  - In exchange for telling the world how to make and use your invention, the U.S. government grants, for a limited time, the right to exclude others from **making, using, or selling** that which is covered by the patent, in the US
- 2) Rights **NOT** granted by a patent:
  - The right to **make, use or sell** your patented invention
  - (Huh?)

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### What Can Be Patented?

- Compositions of matter
- Articles of manufacture
- Processes
  - methods of making or using something
  - methods of treatment

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### Requirements for Patentability

- **Useful** – low threshold
- **Novel** – low threshold
  - currently 1 year grace period (US only)
- **Non-obvious** – a tougher climb

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### Anatomy of a Patent

- **Specification:** Inventor's disclosure of how to make and use the invention
- **Claims:** The heart of the patent
  - Descriptions of what it is that others are excluded from making, using or selling
  - Claims must be supported by the invention disclosure in the specification

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**Strategic Thinking**

- Think broadly, but not *too* broadly....
  - What are all possible ways to do what your invention does?
  - What else can it be used for?

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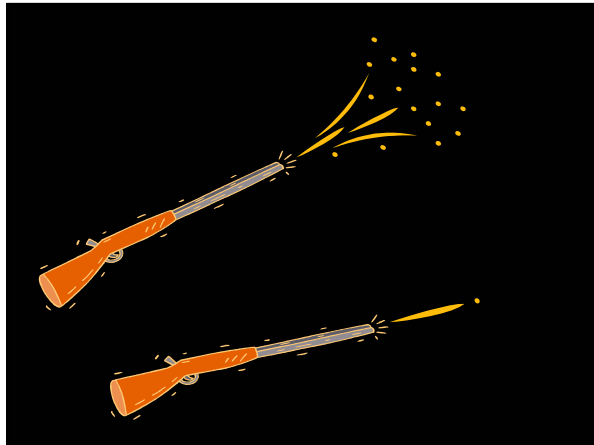
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**Strategic Thinking**

- What will you do with your patent?
  - a) license to others for \$?
  - b) sell the patent to make \$?
  - c) confound competitors?
  - d) bargaining chip?
  - e) make and sell covered item(s) / process(es) – become a market player?
- Answers should influence your patent approach(es)

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***"I plan to use the patent to generate licensing revenue or to sell outright"***

- Make the patent specification and claims attractive to potential licensees / assignees:
  - Slant the specification and claims towards the licensees / assignees
    - i) along with broader claims, include specific narrower claims that cover their likely uses of the technology, even if these are not *your* primary interests
    - ii) include specific examples in the specification that show how it would benefit the licensee / assignee – apply the examples to their technologies

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***"I do not plan to make or sell a product under this patent, but wish to hinder the competition"***

- Identify techniques the competition could use to avoid your protection for the products or processes you *do* intend to use, and file on them
- Keeps the competition from getting too close

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***"I plan to use the patent as a bargaining chip"***

- The competition has a patent covering an area of technology you need
  - Identify an area of technology they will need, and file on it
  - Helps if the specification and some claims include specific coverage of the area they will need
  - Can sometimes revise claims in a pending application to tailor them more towards a competitor's new approach
- The competition is threatening you with patent litigation
  - Show them your patent that covers some aspect of their technology

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**"I plan to make / sell products related to the patent(s)"**

Multiple layers of protection:

Claims covering product itself

Claims covering how to make product

Methods of using the product

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**"I plan to make / sell products related to the patent(s)"**

- q Patent claims covering your intended products / methods **broadly**
  - o Cover potential design-around approaches
- q Patent claims covering your intended products / methods **narrowly**
  - o When you're staying in the business, even marginal improvements add another valuable hurdle for competitors, and depth as well as breadth can be attractive to investors
  - o *contrast with:*
  - o If looking to license only, a narrow patent may not get much interest from potential licensees

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**Obtaining a Patent**

- q Cost
- q Timing

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**Case Studies Relating To:**

- 1) University of California's protection of Green Fluorescent Protein
- 2) CeramOptec's protection of Fiber Optic devices and Photodynamic Therapy products

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**Green Fluorescent Protein**

- q From Coelenterate species, e.g., *Aequorea victoria*, *Renilla reniformis*, *R. mulleri*
- q Uses
  - o "selectable" marker
  - o protein localization studies
  - o protein-protein interaction studies
  - o expression profiling
  - o analyte detection
  - o enzyme activity assays (and screens)
  - o (others?)

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**University of California GFP Protection – First Layer**

A. victoria GFP mutants with altered fluorescence characteristics

Claims to basic GFP mutant protein compositions, fusion proteins, nucleic acids encoding them, etc.

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### University of California GFP Patents – First Layer

**Basic protein compositions, nucleic acids encoding them, etc.**

Family 1: **"Modified Green Fluorescent Proteins"**

- **U.S. 5,625,048** April 29, 1997  
Mutants at position 65 in combination with other specific sites of mutation, having altered fluorescent characteristics.
- **U.S. 5,777,079** July 7, 1998  
Specific mutants at AA position 65, having altered fluorescence characteristics.
- **U.S. 6,319,669** November 20, 2001  
Specific mutants at AA position 65, having altered fluorescence characteristics.
- **U.S. 6,066,476** April 25, 2000  
GFP mutated at AA position 65 (substitutions not specified). Includes mutants, fusion proteins comprising them.
- **U.S. 6,800,733** October 5, 2004  
Compositions with modified GFPs, claim language includes sequence *homology* plus some specific mutations.
- **Pending applications this family:** *Broader composition claims in pending family members do not specify sites of modification – obviously more valuable if they issue.*

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### University of California GFP Patents – First Layer

**Basic protein compositions, nucleic acids encoding them, etc.**

Family 2: **"Long Wavelength Engineered Fluorescent Proteins"**

- **U.S. 6,054,321** April 25, 2000  
Methods of rational mutant design based on crystal structure of GFP.
- **U.S. 6,077,707** June 20, 2000  
Mutants at positions F64 and Y66.
- **U.S. 6,403,374** June 11, 2002  
Specific mutants with altered fluorescence characteristics.
- **U.S. 6,780,975** August 24, 2004  
Narrower specific mutants with altered fluorescence characteristics.

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### University of California GFP Protection – First Layer

**A. victoria GFP mutants with altered fluorescence characteristics**

Claims to basic GFP mutant protein compositions, fusion proteins, nucleic acids encoding them, etc.

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**University of California GFP Protection – Second Layer**

Claims to specific GFP fusion constructs and methods and assays based upon them

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**University of California GFP Patents – Second Layer**

**Specific constructs and fusions and assays based upon them**

- U.S. 5,998,204 "Fluorescent protein sensors for detection of analytes" (1999)  
Methods based on detection of protein conformational change upon binding analyte, by change in FRET signal.
- U.S. 6,046,925 "Photochromic fluorescent proteins and optical memory storage devices based on fluorescent proteins" (2000)  
Exposure of fluorescent protein to a given wavelength induces a stable shift in fluorescence characteristic, permitting writing to a memory.
- U.S. 6,248,550 "Assays for protein kinases using fluorescent protein substrates" (2001)  
Difference in phosphorylation state of GFP fusion results in different fluorescent characteristics.  
Adapted for screening for modulators of the kinases.

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**University of California GFP Patents – Second Layer**

**Specific constructs and fusions and assays based upon them**

- U.S. 6,803,188 "Tandem fluorescent protein constructs" (2004)  
Fusions of donor and acceptor versions of mutant GFP – permit, e.g., protease assays based on change in FRET.  
Family members claim screening methods for protease, e.g., HIV protease, and screens for agents that modify that activity.
- U.S. 6,448,807 "Method for determining and modifying protein/peptide solubility" (2002)  
GFP fusion proteins used to analyze solubility of fusion partners.
- U.S. 6,511,829 "GFP-annexin fusion proteins" (2003)  
Annexin-GFP fusions, useful for selective labeling of, e.g., apoptotic cells.
- U.S. 20050079525 "Long Wavelength Engineered Fluorescent Proteins"  
Screening method based on alteration of fluorescence upon binding of a test agent.

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**CeramOptec Patent Protection –  
First Layer: Devices / Fiber Optic Core**

Fiber optic fibers and devices incorporating them

Claims covering laser delivery devices with fiber optic core

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**CeramOptec Patent Protection –  
First Layer**

Specific fiber optic materials and devices incorporating them

- U.S. 5,292,320, "Radial medical laser delivery device" (1994)  
Claims cover laser delivery devices with specific fiber optic core.
- U.S. 5,309,543, "Multiple effect laser delivery device and system for medical procedures Method of making infrared crystalline fiber and product" (1994)  
Claims cover silver halide core fiber material and methods of making it.
- U.S. 5,370,643, "Multiple effect laser delivery device and system for medical procedures." (1994)  
Claims cover medical laser delivery device with a fiber optic core having specific properties, and methods of manufacturing them.
- U.S. 5,647,867, "Laser assisted device and method for resectoscopes" (1997)  
Claims center on device that can be used with standard resectoscopes, but incorporates side-firing laser delivery through fiber optic core.
- U.S. 5,658,148, "Dental laser brushing or cleaning device" (1997)  
Claims cover a laser toothbrush, plus photosensitizer pastes that generate singlet oxygen upon laser irradiation.
- U.S. 6,527,764 "Device and method for laser biomodulation in PDT/surgery" (2003)  
Claims cover laser device with two laser energy sources, one a high power laser for surgery, the second a lower power laser for biomodulation (PDT) at surgery site.

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**CeramOptec Patent Protection –  
First Layer: Devices / Fiber Optic Core**

Fiber optic fibers and devices incorporating them

Claims covering laser delivery devices with fiber optic core

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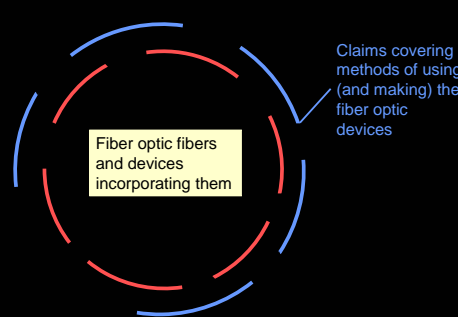
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**CeramOptec Patent Protection –  
Second Layer: Methods of Making and Using**



Claims covering methods of using (and making) the fiber optic devices

Fiber optic fibers and devices incorporating them

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**CeramOptec Patent Protection –  
Second Layer**

**Methods of Using the Fiber Optic Delivery Devices**

- U.S. 5,292,320 "Radial medical laser delivery device" (1994)  
Claims also cover method of prostatectomy, method of photodynamic therapy.
- U.S. 5,647,867, "Laser assisted device and method for resectoscopes" (1997)  
Claims also cover method of tissue ablation using the described device.
- U.S. 6,056,548, "Hygienic dental laser photo treatment method" (2000)  
Claims cover dental hygiene uses of a "laser toothbrush."
- U.S. 6,165,205, "Method for improved wound healing" (2000)  
Claims cover use of a non-ablative laser system to promote wound healing – minor papillary dermal injury by the laser promotes fibroblast and collagen production.
- U.S. 6,200,332, "Device and method for underskin laser treatments" (2001)  
Claims cover methods of laser treatment under the skin (e.g., for treating vascular abnormalities such as spider veins and varicosities, as well as other treatments).

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**CeramOptec Patent Protection –  
Second Layer**

**Methods of Using the Fiber Optic Delivery Devices**

- U.S. 6,454,790, "Treatment for Barrett's syndrome" (2002)  
Claims cover PDT treatment of Barrett's syndrome (esophageal scarring disorder) – uses fiber optic delivery of diffuse light to activate photosensitizer agent restricted to specific area with balloons.
- U.S. 6,494,878, "System and method for accurate optical treatment of an eye's fundus" (2002)  
Claims cover methods of fiber optic/laser treatment of, e.g., macular degeneration.
- U.S. 6,527,764, "Device and method for laser biomodulation in PDT/surgery" (2003)  
Claims cover use of laser device with two laser energy sources, one a high power laser for surgery, the second a lower power laser for biomodulation (PDT) at surgery site.

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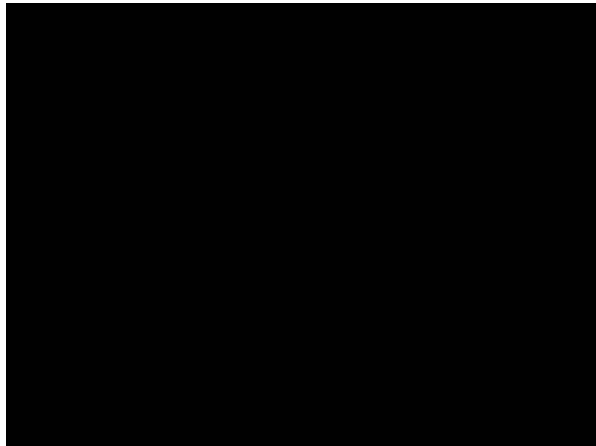
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