Advanced Patent Prosecution Workshop 2021:

*Claim Drafting & Amendment Writing*

**Biotechnology**

In-Class Problems 1-7

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**PLI Biotech Practice****In Class Problem 1**

Scientists at McAteer University invented a chimeric antibody to TNF-α. The antibody included a mouse variable region and a human constant region. The chimeric antibody was less immunogenic than previously made mouse antibodies.

McAteer University filed a patent application in 2008 directed to chimeric anti-TNF-α antibodies. The patent application also described antibodies having both human variable and constant regions. The patent application, however, only exemplified the preparation of one chimeric TNF-α antibody. The patent application described difficulties associated with making a fully-human antibody to a human protein like TNF-α.

McAteer University obtained a patent having the claims below. The claims cover both chimeric and fully human antibodies.

1. An isolated recombinant anti-TNF-α anti-body or antigen-binding fragment thereof, said antibody or antigen-binding fragment comprising a human constant region, wherein said antibody or antigen binding fragment (i) competitively inhibits binding of A2 (ATCC Accession No. PTA-7045) to human TNF-α, and (ii) binds to a neutralizing epitope of human TNF-α *in vivo* with an affinity of at least 1 × 108 liter/mole, measured as an association constant (Ka), as determined by Scatchard analysis.

2. The antibody or antigen-binding fragment of claim 1, wherein the anti-body or antigen binding fragment comprises a human constant region and a human variable region.

**Do the claims meet the written description requirement?**

**What if the patent application was filed in 2015?**

**PLI Biotech Practice****In Class Problem 2**

YoYo Pharma develops an oligonucleotide (8 nucleotides in length) that, when intravenously administered, induces growth of eyelashes. Yo Yo Pharma quickly files a patent application to protect this valuable discovery. Claim 1-4 of the application read:

1. An oligonucleotide having the sequence of SEQ ID NO:1.

2. An oligonucleotide consisting of the sequence of SEQ ID NO:1.

3. An isolated oligonucleotide consisting of the sequence of SEQ ID NO:1.

4. A pharmaceutical composition comprising an oligonucleotide having the sequence of SEQ ID NO:1.

5. A method of inducing growth of eyelashes in a human subject in need thereof comprising administering the oligonucleotide of claim 1.

The patent application is rejected under 35 U.S.C. §101 as directed to non-patentable subject matter. The Examiner found that the oligonucleotide is present in chromosome 22 of humans who have incredibly large eyes. The Examiner argues that pursuant to the Supreme Court decision *Association for Molecular Pathology v. Myriad Genetics*, the oligonucleotide is not patent eligible as it is a product of nature.

**Please prepare a response to this rejection.**

**PLI Biotech Practice****In Class Problem 3**

ABC Labs developed a method for differentiating between whole (1-84) parathyroid hormone (PTH) and interfering non-(1-84) PTH fragments.

ABC Labs obtained a patent directed to its method for measuring whole PTH. Claim 1 reads:

1. A method for measuring an amount of whole parathyroid hormone in a sample comprising:

a) adding to a sample a labeled antibody or antibody fragment specific for an initial peptide sequence of whole parathyroid hormone wherein said initial peptide sequence consists of VAL-SER-GLU-ILE-GLN-LEU-MET (SEQ ID NO: 3), and wherein at least four amino acids in said initial peptide sequence are part of a reactive portion to said labeled antibody;

b) allowing said labeled antibody to bind to whole parathyroid hormone present, thereby forming a complex; and

c) measuring the amount of said labeled complex to measure the amount of whole parathyroid hormone in said sample while not detecting an interfering non-(1-84) parathyroid hormone fragment.

Cheap Labs sells a kit with a labeled antibody that binds, but at relatively low affinity, to interfering non-(1-84) PTH fragments. The labeled antibody has high affinity to whole PTH.

Does the Cheap Labs kit induce infringement of the claimed method?

**PLI Biotech Practice****In Class Problem 4**

A patent includes the following claim to an oligonucleotide:

1. An oligonucleotide containing a nucleotide having the structure:

wherein

B represents a 7-deazapurine or a pyrimidine moiety;

A comprises at least three carbon atoms and represents at least one component of a signaling moiety capable of producing a detectable signal;

B and A are covalently attached directly or through a linkage group that *does not substantially interfere* with the characteristic ability of the oligonucleotide to hybridize with a nucleic acid and *does not substantially interfere with* formation of the signalling moiety or detection of the detectable signal;

one of x and y is a –OP(O)(OH)O- or –OP(O)(O-)O-, and the other of x and y is absent or represents OH or H; and z represents H or HO.

The specification provides examples of suitable linkage groups between B and A such as -CH=CH-CH2-NH-. The specification further states that:

The linkage group may include any of the well known bonds including carbon-carbon single bonds, carbon-carbon double bonds, carbon-nitrogen single bonds, or carbon-oxygen single bonds. It is even more preferred that the chemical linkage group be derived from a primary amine, and have the structure -CH2-NH-, since such linkages are easily formed utilizing any of the well known amine modification reactions. One of the essential criteria of a modified polynucleotide is that the linkage that attaches the probe moiety should withstand all experimental conditions to which normal nucleotides and polynucleotides are routinely subjected, e.g., extended hybridization times at elevated temperatures, phenol and organic solvent extraction, electrophoresis, etc.

The polynucleotides' thermal denaturation profiles and hybridization properties can be used to measure the degree to which a linkage group interferes with hybridization.

The Patent Office rejected claim 1 as indefinite (35 U.S.C. §112(b)) due to the phrase “does not substantially interfere.” The Examiner argues that he patent does not explain how to measure interference or how to determine whether it is substantial. Because even a minor alteration of a single nucleotide may have profound effects on the ability of a DNA strand to hybridize, depending on the length and sequence of the strand, the Examienr argues that identical linkage groups may cause interference in some strands but not in others, thus rendering the claims hopelessly ambiguous.

**Please prepare a response to the rejection.**

**Is the “not interfering substantially” language definite (35 U.S.C. §112(b))?PLI Biotech Practice****In Class Problem 5**

CMU invented a new method for preparing DNA polymerase I (Pol I). Prior to the present invention, scientists encountered difficulties in cloning the gene *E. coli polA* into multicopy plasmids because the increase in the expression of DNA polymerase I above the natural level of expression was found to be lethal to a host bacterium. CMU overcame this problem by constructing a plasmid containing the entire polA gene coding region which contains essentially none of or at most only a portion of the activity of its natural promoter. According to the inventors, severely damaging the natural *polA* promoter sequence constituted a significant discover since it eliminates or greatly reduces the unregulated expression of Pol I, which would otherwise be lethal to the cell. By cloning the gene for Pol I into a vector along with a foreign promoter whose activity is conditionally controlled, one can obtain an amplified amount of Pol I.

CMU filed a patent application based on this discovery. Claim 1 of the patent application reads:

1. A recombinant plasmid containing a cloned complete structural gene coding region isolated *from a bacterial source* for the expression of DNA polymerase I, under operable control of a conditionally controllable foreign promoter functionally linked to said structural gene coding region, said foreign promoter being functional to express said DNA polymerase I in a suitable bacterial or yeast host system.

Throughout the specification, the application teaches that the bacterial strain used is *E. coli*. Notably, at the time the application was filed, three bacterial *polA* genes had been cloned (*E. coli*, *K. aerogenes*, and *K. pneumonia*).

The application is rejected as lacking written description. The Examiner contends that the specification has only shown possession for plasmids isolated from *E. coli*.

**Please draft a response to the rejection.**

**Does claim 1 meet the written description requirement?**

**PLI Biotech Practice****In Class Problem 6**

SeedCo obtained a patent on a process for producing transgenic corn (known as GA21) that is resistant to glyphosate, a nonselective herbicide. The patent includes the following claims:

1. A process for producing a fertile transgenic *Zea mays* plant comprising the steps of (i) bombarding intact regenerable *Zea mays* cells with DNA-coated microprojectiles, (ii) identifying or selecting a population of transformed cells, and (iii) regenerating a fertile transgenic plant therefrom, wherein said DNA is transmitted through a complete sexual cycle of said transgenic plant to its progeny, and imparts herbicide resistance thereto.

….

4. A process comprising obtaining progeny from a fertile transgenic plant obtained by the process of claim 1 which comprise said DNA.

5. The process of claim 4 wherein said progeny are obtained by crossing said fertile transgenic plant with an inbred line.

6. The process of claim 4 comprising obtaining seed form said progeny plants comprising said DNA from said seed.

7. The process of claim 5 wherein the progeny obtained are crossed back to the inbred line, to obtain further progeny which comprise said DNA.

8. The process of claim 6 wherein said seed are obtained from said further progeny plants and plants comprising said DNA are recovered from said seed.

9. The process of claim 7 wherein said seed further progeny are crossed back to the inbred line to obtain further progeny which comprise said DNA.

S. Alec Co. (SAC) bought GA21 seed from a company who was licensed by SeedCo.. SAC used the seed to produce further progeny containing the GA21 trait. SeedCo sued SAC asserting infringement of claims 4-9 of the patent.

**Which claim(s) are infringed by SAC?**

**Would the result change if the plant was produced by SAC before the patent issued?**

**Would you draft the claims differently? If so, how?**

**PLI Biotech Practice****In Class Problem 7**

Professor DeGreat of First University and his graduate student Jason DeNormal invented a new class of fusion proteins. First University, having invested millions of dollars into Professor DeGreat’s research, filed a patent application (the ‘111 Application) directed to this new class of fusion proteins listing DeGreat and DeNormal as inventors. Claims 18-20 of First University’s application reads:

18. A bidomain protein or peptide comprising a transglutaminase substrate domain and a polypeptide growth factor.

19. The bidomain protein of claim 18, wherein the trans glutaminase substrate domain is a Factor XlIIa substrate domain.

20. The bidomain protein of claim 18, wherein the polypeptide growth factor is TGFβ.

Shortly after inventing the new class of fusion proteins, Professor DeGreat left First University for Second University. At Second University, Professor DeGreat made certain bidomain proteins containing a transglutaminase substrate domain (such as a Factor XIIIa substrate domain) and a growth factor (such as vascular endothelial growth factor (VEGF)). Second University filed a patent application and obtained the ‘222 Patent which includes the following claim:

1. A fusion protein, comprising:

(i) a first protein domain selected from the group consisting of the platelet derived growth factor superfamily and the transforming growth factor beta (TGFβ) superfamily;

(ii) a second protein domain, which is a crosslinking Factor XIIIa substrate domain; and

(iii) an enzymatic or hydrolytic cleavage site between the first and second domains.

Claims 18-20 of the ‘111 Application have now been rejected for obviousness-type double patenting over claim 1 of the ‘222 Patent.

**Questions**

Does obviousness-type double patent patenting apply when an application and a patent have one or more inventors in common but inventive entities are not identical and the application and the patent were never commonly owned?

Can a terminal disclaimer be filed to overcome the rejection?