PATENTS

Patenting DNA sequences

Questions to ask when building your patent portfolio.

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It is essential that all patentable subject matter be recited in the claims of a patent in order to have the most advantageous marketing position since in many startup biotechnology ventures, the patent portfolio is one of the largest and sometimes only asset. The claims located at the end of every patent specification measure the protection afforded by a patent[1]. For example, if one isolates a protein, it is not enough to claim the protein itself; methods for obtaining the protein, methods of using the protein, and a nucleic acid sequence encoding the protein must all be claimed as well. A number of articles have appeared in this journal and other publications exploring what constitutes patentable subject matter. However, it is equally important to know what to claim for various types of biotechnology inventions.

Advances in recombinant DNA and DNA sequencing techniques, as well as the advent of bioinformatics, have spurred a number of public and private groups to sequence the human genome. There is little doubt that the isolation and characterization of DNA sequences will have vast implications for the development of therapeutic agents. However, protecting inventions based on DNA sequences is not as clear-cut. Every inventor seeking to capitalize on his or her DNA discovery must accurately answer two questions in order to lay the foundation for intellectual property protection: First, is this particular isolated DNA sequence patentable? Second, what should be included in the claims? As the topic of whether a DNA sequence is patentable has been covered extensively[2], this column will be devoted to which claims are necessary and appropriate for DNA sequences.

What to claim?

Claims are analogous to a deed to a house[3]. They describe the metes and bounds of the legal rights of the patent owner against a potential infringer. Claims should be drafted that are as broad in scope and depth as possible in order to preclude a competing entity from encroaching upon one's "niche." Claiming the DNA sequence itself is not enough.

How does one start? One claim will most likely be drafted to the DNA sequence itself. For example, "An isolated polynucleotide sequence depicted in SEQ ID No. 1." A claim may be drafted to a polynucleotide sequence that hybridizes to the isolated DNA sequence under certain conditions, depending on what DNA sequences have previously been isolated, as well as on what is described in the patent application, for example, ". . .hybridization in 5× SSC, 2% SDS, and washing with 0.5% SDS at 42°C." In addition, a patent claim for a homologous DNA sequence having a certain percent identity to the DNA sequence may be drafted to cover homologs that do not necessarily hybridize to the DNA sequence. In such cases, it is important to include a description of the method or algorithm used to determine the sequence's identity in the application.

Table 1. Possible types of claims that should be drafted for DNA used as a therapeutic.

Method of use	Claims to be drafted
Vaccine	Vaccine formulation Mechanism of action Method of preparation
Gene therapy	Viral vectors Formulation Method of treatment (in vitro or in vivo)
Antisense oligonucleotides	Formulation Method of use

Next, one should consider any known function of the DNA sequence. If, for example, it is discovered that the DNA sequence encodes a peptide or protein, a claim may be drafted to reflect this. For example, "An isolated polynucleotide comprising a polynucleotide encoding a polypeptide having at least X% identity to the polypeptide depicted in SEQ ID No. 1."[4]

What other functions of the DNA sequence may be claimed? If the DNA is a control sequence because it functions as a promoter, signal sequence enhancer, or terminator, this function can be included as part of the claim. For example, the claim might state, "A nucleic acid promoter fragment isolated from the 5′ flanking region upstream of the coding region of gene X, which is inducible by application of compound class Y."[5]

Claims should also be drafted to means and methods for expressing the claimed DNA sequence. For example, if a DNA sequence is introduced into a host cell, claims should be drafted to a nucleic acid construct or expression vector containing the DNA sequence and to a host cell into which the DNA sequence, alone, or in any construct or expression vector has been introduced.

Finally, one should also examine whether the DNA sequence has possible commercial uses (e.g., its possible use as a probe in a diagnostic kit, or as a therapeutic). Here again, context should be considered: if claiming use as a probe, it is important to claim not only the method of use, but also all of the elements needed to be used in the claimed method. For example, if the probe is being used to detect the presence or absence of bacteria X in a sample, claims should be drafted not only to a method for detecting the presence or absence of the bacteria X in a sample but also a biological detection kit for detecting bacteria X comprising, for example, primers A, B, C, restriction enzymes 1, 2, 3, Taq DNA Polymerase[6].

If the DNA sequence may be used as a therapeutic agent, then one must consider whether it will be used in vaccines, in gene therapy or as antisense oligonucleotides. If the DNA sequence encodes an antigenic protein, it may be used in live vaccine formulations[7]. Alternatively, if the DNA sequence encodes a protein that may be used to treat a disease, it may be used in gene therapy[8]. A DNA sequence that hybridizes to mRNA transcribed from a gene of interest and inhibit expression of the gene, it can be used in an "antisense" formulation[9].

Conclusion

Once the determination that a DNA sequence is patentable has been made, it is important to draft claims that not only cover the sequence itself, but also related sequences, constructs, vectors, and host cells that may contain the sequence and possible uses of the sequence. If such claims are included, the owner of the patent should have protection of appropriate scope and depth against potential infringers.

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1. See 35 USC 112 and 37 CFR 1.75.
2. Agris, C.H. 1996. *Nature Biotechnology* **14**:1309–1310; Chahine, K. 1998. *Nature Biotechnology* **16**:683–684.
3. Faber, R.C. 1997. In *Landis on Mechanics of Patent Claim Drafting, 4th Ed.* Practicing Law Institute, NY.
4. See, for example, US Patent No. 5,506,133.
5. See, for example, US Patent No. 5,654,414.
6. See, for example, US Patent No. 5,654,144.
7. See, for example, US Patent No. 5,599,544.
8. See, for example, US Patent No. 5,593,974.
9. See, for example, US Patent No. 5,652,274.