Free Access to Biological and Medical Knowledge: Scientific Imperative or Quixotic Pursuit

The ownership of knowledge in biology and medicine is one of the most controversial areas confronting biomedical researchers and health care practitioners. Although this controversy has been simmering for more than a decade, it is now beginning to boil as the fruits of the genomic revolution are becoming clinically useful [1]. Proponents of strong intellectual property laws such as the American Intellectual Property Law Association argue that the ability to patent biological and medical knowledge is an essential motivation for continued discovery and innovation [2]. In contrast, biomedical organizations such as the U.S. National Academy of Sciences, and the Nuffield Council on Bioethics argue that ownership of biological knowledge will stifle innovation because most biological discoveries are incremental and require the use of previous discoveries; and that patents on medical knowledge are antithetical to medical practice which requires the unrestricted dissemination of clinical knowledge [3,4].

As HIV researchers who are regular users of the Stanford HIV Drug Resistance Database, we read the Science News article "Tangled Patent Dispute Over 'Free' Drug-Resistance Database" with great interest but also with a certain perplexity. The article mainly focused on the tabloid aspects of the patent dispute between Advanced Biological Laboratories, Stanford University, and Robert Shafer, the creator and principal investigator of the Stanford Database. This dispute is indeed related to one of the most pressing ethical, social, and legal aspects of biomedical research.

The patents at the center of the dispute (U.S. patents 6,081,786 and 6,188,988) are described as: "Systems, methods and computer program products for guiding selection of a therapeutic treatment regimen for a known disease such as HIV infection are disclosed. The method comprises (a) providing patient information to a computing device (the computer device comprising: a first knowledge base comprising a plurality of different therapeutic treatment regimens for the disease; a second knowledge base comprising a plurality of expert rules for selecting a therapeutic treatment regimen for the disease; and a third knowledge base comprising advisory information useful for the treatment of a patient with different constituents of the different therapeutic treatment regimens; and (b) generating in the computing device a listing (preferably a ranked listing) of therapeutic treatment regimens for the patient; and (c) generating in the computing device advisory information for one or more treatment regimens in the listing based on the patient information and the expert rules.".

Although most scientists may be quite unfamiliar with patent lingo, it is immediately apparent that what was patented in US (but not in Europe indeed) is broad and vague. A press release issued by ABL itself in 2004 when it acquired the patents from Therapy Edge seems to confirm this impression: "We believe the patents will prove seminal to the diagnosis and treatment of *most chronic diseases*. The patents *broadly* cover the computer analysis of multiple databases, which lead to a report meant to guide physicians towards the optimal therapy for a given patient. Historically, such reports were principally associated with the treatment of HIV, but we envision that eventually the diagnosis and treatment of *most chronic diseases* will fall under the claims of these patents as well. We intend to *widely* license the patents to diagnostic companies, diagnostic service providers and therapeutic manufacturers." [5].

A second objection seems also obvious. Computer based medical expert systems assisting the choice of therapy have been around for years before the two ABL patents were issued. Innovation is a fundamental requirement for patenting and protecting new knowledge and intellectual property rights, however it is hard to find any novelty or creative contribution in these patents.

According to what is documented on the www.harmfulpatents.org web site recently launched by Robert Shafer, ABL filed lawsuits for patent infringement against five companies prior to threatening Stanford University with a similar lawsuit in 2007. While this was not noted in the *Science* article, it is suggestive of a rather aggressive patent litigation policy.

In conclusion, the dispute between ABL, Stanford, and Dr. Shafer reflects a disturbing trend in which biological knowledge and medical reasoning are increasingly considered property that can be bought and sold but not shared. How this trend is resolved has important implications for biomedical research and the practice of medicine. We are confident that *Science* can understand our point of view and that the proposed analogy with the Cervantes' 17th century novel "Don Quixote" will turn to be inappropriate since biomedical scientists do not represent a pursuit of idealistic but unreachable and impractical goals.

1. Soini S, Ayme S, Matthijs G (2008) Patenting and licensing in genetic testing: ethical, legal, and social issues. Eur J Hum Genet 16 Suppl 1: S10-50.

2. American Intellectual Property Law Association (2008) Brief of amicus curiae in support of appellant in Prometheus Laboratores Inc v. Mayo Collaborative Services in the United States Court of Appeals for the Federal Circuit. http://wwwlawumkcedu/events/PrometheusAmicuspdf (last accessed February 2009).

3. Nuffield Council on Bioethics (2002) The ethics of patenting DNA, a discussion paper. http://wwwnuffieldbioethicsorg.

4. National Research Council (U.S.) (2006) Committee on Intellectual Property Rights in Genomic and Protein Research and Innovation: Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health.: National Academies Press (http://www.nap.edu/catalog/11487.html).

5. Advanced Biological Laboratories (2004) Evidence Medical, LLC and Advanced Biological Laboratories SA complete licensing agreement of seminal IT related patents. http://wwwablsacom/site/en/press/2004-11-22_ABL_EvidenceMedical_Finalpdf (last accessed April 2009).

6. European Patent Office. Decision to refuse a European Patent application. The Examining Division - at the oral proceedings dated 28.02.2006 - has decided: European Patent Publication No. 99 916 262.1 is refused. Title: Systems, methods, and computer program products for guiding the selection of therapeutic treatment regimens. http://tiny.cc/YiH7x 2006.

Jan Albert, M.D., Professor of Microbiology, Tumor, and Cell Biology, Karolinska Institute, Stockholm, Sweden

Birgitta Asjo, Ph.D. Professor, Center for Research in Virology, Gades Institute, University of Bergen, Bergen, Norway

Claudia Balotta, M.D. Professor of Medicine, Institute of Infectious and Tropical Diseases, Univeristy of Milan, Italy

Marina Bobkova, Ph.D. Head of Laboratory, Scientific Research for Virology, Moscow Russia

Francoise Brun-Vezinet, Ph.D., Professor of Virology, University Bichat-Claude Bernard Hospital, Paris, France

Vincent Calvez, M.D., Head Division of Infectious Diseases, Pitié-Salpêtrière Hospital, Paris, France

Ricardo Camacho, M.D., Professor, Molecular Biology Laboratory, Center for Malaria and Tropical Diseases, Lisbon, Protugal

Dominique Costagliola, Ph.D., Directeure de l'U943 INSERM et Université Pierre et Marie Curie, Epidémiologie, stratégies thérapeutiques et virologie cliniques

Suzie Coughlan, Ph.D, Senior Scientist, National Virus Reference Laboratory, University College, Dublin, Ireland

Andrea De Luca, M.D., Associate Professor, Infectious Diseases, Catholic University, Rome, Italy

Diane Descamps, M.D., Professor of Microbiology, University Bichat-Claude Bernard Hospital, Paris, France

Philippe Flandre, Ph.D., Professor of Statistics, INSERM, Hospital Pitié-Salpêtrière, Paris, France

Herve Fleury, Ph.D., Director of Virology, Bordeaux University, Bordeaux, France

Rolf Kaiser, M.D., Professor of Medicine, Institute for Virology, Cologne University, Cologne, Germany

Thomas Klimkait, Ph,D, Professor of Biomedicine at the Institute of Medical Microbiology, University of Basel, Basel, Switzerland

Claudia Kücherer, Ph.D, Director of Project HIV Variability and Molecular Epidemiology, Robert Koch Institute, Berlin, Germany

Carlo Giaquinto, M.D., Professor of Pediatrics, Padua University, Padua, Italy

Huldrych Günthard, M.D., Professor of Medicine, Division of Infectious Diseases, University Hospital Zurich, Zurich Switzerland.

Thomas Lengauer, Ph.D., Professor of Computational Biology and Applied Algorithmics, Max Planck Institute for Informatics, Saarbrücken, Germany

Clive Loveday, M.D., Clinical Director / NHS Consultant, ICVC Charitable Trust HQ Buckinghamshire, U.K.

Jens Lundgren, M.D., Director of the Copenhagen HIV Programme and EuroSIDA, University of Copenhagen, Copenhagen, Denmark

Anne-Geneviève Marcelin, M.D., Professor of Infectious Diseases, Pitié-Salpêtrière Hospital, Paris, France

Bernard Masquelier, Ph.D., Associate Professor, Virology Laboratory, Hôpital Pellegrin, Bordeaux, France

Carlo Federico Perno, M.D., Professor of Virology, University of Rome Tor Vergata, Rome, Italy

Luc Perrin, M.D., Professor of Medicine, Hospital Cantonal University of Geneva, Geneva, Switzerland

Kholoud Porter, Ph.D. MRC Clinical Tirials Unit, University College Medical School, London, U.K.

Jorg Schupbach, Ph.D., Professor of Virology, University of Zurich, Zurich, Switzerland

Barbara Schmidt, Ph.D., German National Reference Center for Retroviruses, University of Erlangen, Erlangen, Germany

Janusz Stanczak, M.D., Hospital for Infectious Diseases, AIDS Diagnosis and Therapy, Warsaw, Poland

Stephen Taylor, M.D., Director of Sexual Medicine and HIV, NHS Foundation Trust, Birmingham, UK

Carlo Torti, M.D., Professor of Medicine, Institute of Infectious and Tropical Diseases, University of Brescia, Brescia, Italy

Kristel Van Laethem, Ph.D., Associate Professor, Clinical and Epidemiological Virology, Katholieke Universiteit Leuven, Rega Institute, Leuven, Belgium

Anne-Mieke Vandamme, Ph.D Professor of Clinical and Epidemiological Virology, Katholieke Universiteit Leuven, Rega Institute, Leuven, Belgium

Eric Van Wijngaerden, M.D., Professor of Medicine. Katholieke Universiteit Leuven, Rega Institute, Leuven, Belgium

Sabine Yerly, Ph.D., Professor of Virology, Geneva University Hospital, Geneva, Switzerland

Maurizio Zazzi, Ph,D., Professor of Microbiologo, University of Siena, Siena, Italy