Chapter 12
Opening Research Biobanks: An Overview

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Abstract In biomedical research and translational medicine, the ancient war between the exclusive right (private control over information) and public access to information is struggling on a new battlefield: research biobanks. The latter are becoming increasingly important (one of the ten ideas changing the world, according to Time magazine) because they collect, store and distribute in a secure and professional way a critical mass of human biological samples for research purposes. Tissues and related data are fundamental for the development of biomedical research and the emerging field of translational medicine, because they represent the "raw material" for every kind of biomedical study. For this reason it is crucial to understand the boundaries of IP in this prickly context. After an overview of the complex interactions among the different stakeholders involved in the process of the production of knowledge, in this paper we will thin out some blurring of language concerning concepts often mixed up, such as "open source", "open access", and their precipitates. Then, the aim is to understand if we can use the concepts in the biomedical context, and which are the open models proposed in literature specifically for research biobanks in order to avoid the tragedy of anticommons.

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12.1 Introduction

In the last 30 years, we have witnessed an overgrowth of Intellectual Property Rights (IPRs) almost in every field of our daily life.[1] According to the traditional view, the protection of IP and the control of information are key to the strategy of many companies and both have been justified with well-known economic and utilitarian arguments[2]: patent, copyright, trademark and other forms of exclusive rights offer incentives to undertake risky projects, represent the main source of appropriating returns, can lead to a "more equitable distribution of profits across all stages of R&D"[3] and are the better antidote for corporate secrecy.

At the same time, the public domain has suffered slow but constant erosion. Legislators have supported this trend towards privatisation, progressively attributing to multiple owners a set of rights to exclude others.[4] Governments have been creating this dangerous dominance through some interventions in patent law and copyright law, such as the Bayh-Dole Act,[5] the Digital Millennium Copyright Act,[6] the Sonny Bono Copyright Extension Act[7] in the U.S. or Directives 91/250/EEC,[8] 96/9/EC,[9] 98/44/EC,[10] 2001/29/EC[11] or

[1] According to Robert Merges, IP law is like Shanghai or other megacities of the developing world, where new constructions and buildings proliferate everywhere without taking into account the urban planning of the old city. The author concludes his metaphor asserting that: "It's an exciting time, to be sure; but a confusing time too". Merges (2011).

[2] See also Ladas (1929), Plant (1934a, b), Nordhaus (1969), Mazzoleni and Nelson (1998), Menell (1999), and Landes and Posner (2003).

[3] Heller and Eisenberg (1998), p. 698.

[4] See Heller and Eisenberg (1998), Lessig (2004a, b), and Boyle (2008).

[5] Bayh–Dole Act is a watershed from the past patent regimes. First of all, it introduces the possibility of patenting results of publicly funded research. Secondly, it allows university and public laboratories to sell exclusive licences to private companies or to create partnership with them in order to economically exploit the research results and to translate their basic research into marketable products. See Rai and Eisenberg (2003) and Corian and Weinstein (2011).

[6] Digital Millennium Copyright Act, 17 U.S. Code. This statute has qualified as a criminally relevant behaviour the circumvention of technological protection measures and the distribution of tools to encompass DRM.

[7] Copyright Term Extension Act, 17 U.S. Code, also known as Mickey Mouse Protection Act, extended copyright terms in the U.S.A. as following: duration of copyright protection is raised from 50 to 70 years after the death of the author and it lasts 120 years after creation or 95 years after publication if it is a work of corporate authorship.

[8] Council Directive 91/250/EEC of 14 May 1991 on the legal protection of computer programs, in Official Journal L 122 of 17 May 1991.

[9] Directive 96/9/EC of the European Parliament and of the Council of 11 March 1996 on the legal protection of databases, in Official Journal L 077 of 27 March 1996.

[10] Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions, in Official Journal L 213 of 30 July1998.

[11] Directive 2001/29/EC of the European Parliament and of the Council on the harmonization of certain aspects of copyright and related rights in the information society, in Official Journal L 167 of 22 June 2001. The importance of IP protection is stressed in whereas 4 and 9.

2004/48/EC[12] in the European Union. Such national or regional legislation is reflected in a number of international provisions like the WTO's Agreement on Trade Related Aspects of Intellectual Property Rights (1994) or the World Intellectual Property Organization "Internet" Treaties (WIPO Copyright Treaty and the WIPO Performances and Phonograms Treaty), and it has also been confirmed by relevant judicial decisions.[13] This progressive transformation has been creating the conditions for new institutional complementarities between IPR and finance, opening *de facto* to capital the door of the "workshop" of knowledge.[14]

A set of interventions in the public and private sector has significantly contributed to this "second enclosure movement", shifting the balance of power towards private control and increasing the risk of non-use or under-utilisation of information.[15] In other words, we have such a wide range of Intellectual Property tools that we can no longer manage it.

In this perspective, many authors talk about the tragedy of anticommons. The tragedy of anticommons is a mirror-image of Hardin's tragedy of the commons.[16] According to the American ecologist Hardin, when multiple individuals can use a shared limited resource (in the original example it was an open-access pasture) without the right to exclude others, they tend to act independently and according to their self-interest, exploiting the resource as much as possible. In this way, the

[12] Directive 2004/48/EC of the European Parliament and of the Council on the enforcement of intellectual property rights, in Official Journal L 157 of 30 April 2004. See whereas 10: "The objective of this Directive is to approximate legislative systems so as to ensure a high, equivalent and homogeneous level of protection in the internal market".

[13] Taking as an example the case law of the United States, because its parabola serves to illustrate the evolution of the trend towards enclosure, regarding patents we can mention Diamond v. Chakrabarty, 447 U.S. 303 (1980), affirming that, "anything under the sun made by man is patentable", and introducing the patent protection for micro-organism; State Street Bank and Trust Company v. Signature Financial Group Inc., 149 F. 3d 1368 (1998), establishing the patentability of business methods in the United States; Appeal from the United States District Court for the Southern District of New York in Case No. 09-CV-4515 (Association for Molecular Pathology v. UPO) overruling the revolutionary judgment of the NY District court which had invalidated the Myriad patents on BRCA gene in virtue of the "product of nature" doctrine. The Court of Appeal overruled the decision of the inferior court and confirmed the principle that isolated DNA is a distinct chemical entity with different physical characteristics from natural DNA, so eligible for patent protection under 35 USC §101. Meanwhile, with regard to copyright Eldred v. Ashcroft, 123 S.Ct 769 (2003) is significant, a decision that seems to attribute to Congress the possibility of extending the validity of copyright without apparently any limit (see Samuelson 2003; Lessig 2004a, b; Kranich 2006); more specifically on file sharing, see the famous ruling of A&M Records v. Napster, 239 F.3rd 1004 (9th Cir. 2001); MGM Studios Inc. v. Grokster Ltd, 545 U.S. 913 (2005)

[14] Corian and Weinstein (2011).

[15] Boyle (2003).

[16] Parisi et al. (2005).

common good is prone to be overgrazed[17]; meanwhile, in the tragedy of anticommons, the social dilemma is the opposite: the common resource risks being underused because individuals have a right to exclude others and no owner has effectively a privilege of use.[18]

The danger of the anticommons tragedy is particularly sharpened in the current biomedical research, the development of which depends inextricably on the opportunity to access and use data, materials, expertise and, consequently, on the possibility of cross-checking pre-competitive information and results.

The scenario described so far gives rise to the risk that rigid and centralised control of information based on many and strong IPRs, shaped on market considerations, invades the proper domain of the scientific community (which is, on the contrary, motivated by the logic of flexible and decentralised control, based on customs and informal norms), decreasing the possibility of access to scientific knowledge.

To counteract this risk, part of the scientific community is promoting the logic of "open intellectual property" to scientific knowledge. In fact, the emersion of initiatives based on contracts (licences) such as the Open source movement or Creative Commons reveals different perspectives with regard to the statutory regime of intellectual property. In the last years, the movement of "open intellectual property" is more and more active in the biomedical field.

In biomedical research and translational medicine, the ancient war between the exclusive right (private control over information) and public access to information is struggling on a new battlefield: research biobanks. The latter are becoming increasingly important (one of the ten ideas changing the world, according to *Time* magazine)[19] because they collect, store and distribute in a secure and professional way a critical mass of human biological samples for research purposes. Tissues and related data are fundamental for the development of biomedical research and the emerging field of translational medicine, because they represent the "raw material" for every kind of biomedical study. For this reason, it is crucial to understand the boundaries of IP in this prickly context.

After an overview of the complex interactions among the different stakeholders involved in the process of the production of knowledge, in this paper we will thin out some blurring of language concerning concepts often mixed up, such as "open source", "open access", and their precipitates. Then, the aim is to understand if we can use the concepts in the biomedical context, and which are the open models proposed in literature specifically for research biobanks in order to avoid the tragedy of anticommons.

[17] Hardin (1968).

[18] Michelman (1967) and Heller (1998, 1999).

[19] http://www.time.com/time/specials/packages/completelist/0,29569,1884779,00.html. Accessed 01.02.2012.

12.2 IP Law, Market and University: A Complex Relationship

The dominions of IP had been constantly expanding insomuch as undermining the flexibility of the scientific social norms. This is evident if we consider, for example, the patent race by academic institutions: there is a tension between the patent requirement of novelty and the need for the scientist to publish as soon as possible. Since the publication of the results frustrates the requirement of novelty, the scientists are prohibited from publishing until the patent is granted.[20] In the biomedical field, the formalism of law is looked on because it tends to encompass areas that were previously managed in a free and independent way by the whole scientific community, thus changing informal rules and attitudes. This passage is evident if we compare the famous cases of Henrietta Lacks and John Moore.[21] In the first case, scientists who discovered the "HeLa" cells—an immortal cell line derived from the biological samples of the woman—distributed them to all laboratories around the world. In the 1950s those scientists had understood the value of that discovery for the progress of science and they decided to share their results with other peers and potential competitors.[22] It was a farsighted choice, if we consider that HeLa cells were used in a huge amount of research fields: from polio vaccine to gene mapping; from the development of the first anti-cancer drugs (such as tamoxifen) to space experiments for testing the reactions of the human body to the absence of gravity. In the second case, two physicians at UCLA isolated a cell line from the spleen of John Moore and they did not have any hesitation: they rushed to find a patent application on that invention and the Regents of UCLA were designed as assignees of the patent. They immediately started to negotiate agreements with two big pharmaceutical companies for the commercial exploitation of the "Mo cell". Add to this that everything happened behind John Moore's back.[23]

Is it just a coincidence that within three decades researchers have acted so differently? The answer to this question can be given if we consider the different role that science has taken over the years. Since the beginning of the twentieth century, science has turned to market, replacing its old form based on the principles of universality and author's prestige with a new form of managerial science characterised by teamwork.[24] This change has been speeded up more recently by

[20] Streitz and Bennett (2003), Kinney et al. (2004), and Murray and Stern (2007).

[21] Moore v. Regents of University of California, 51 Cal.3d 120, Supreme Court of California, 9 July 1990.

[22] Landecker (1999), O'Brien (2001), Lucey et al. (2009), Javitt (2010), and Skloot (2010).

[23] The Moore affair gave rise to a long and famous lawsuit: John Moore, after discovering the business built from his cell by Dr. Golde and Dr. Quan, his two physicians at UCLA, tried to sue them for breach of fiduciary duty in the doctor–patient relationship (both had acted without his informed consent), but above all for the recognition of property rights on the patented cell line (he claimed for conversion). About this case, see Annas (1988), Paganelli (1989), Hipkens (1992), Burrow (1997), and Campbell (2006).

[24] Johns (2009).

legislation which has strongly encouraged university and public research centres to patent discoveries and to transfer their technology to the industry, also through the use of exclusive licenses.[25] The initiative was welcomed, and has yielded significant benefits in the short term. Before 1980, fewer than 250 patents per year were issued to US universities. After the Bayh-Dole Act, the number of patents increased greatly and university licensing revenues had grown from $221 million in 1991, to $698 million in 1997.[26] Patents became a source of additional funding and income for universities; at the same time, the network between university and private sector also allowed companies to cut down the costs for research. Just to remain in the area of drug discovery, thanks to the basic research done by universities and the R&D realised by start-ups in order to bring to market academic results, pharmaceutical companies discovered and validated new drug targets in a faster and cheaper way.

This trend toward enclosure, consisting of an elephantiasis in patenting, arises parallel to another front: the access to knowledge commons. The prime example is represented by what happened in the United States after the Second World War. At the beginning, public funds were assigned for the creation of the first databases indexing military information, and then also medical and educational data.[27] Through these funds, it was possible to create new research centres and federal libraries. The wind changed when the Reagan administration decided to outsource governmental publications, and some federal programs related to libraries, to the private sector. Even academic institutions followed this path, outsourcing the publication of their journals to private companies. Moreover, the mergers in the 1970s between publishers created a situation of oligopoly, so almost all of the scientific production was in the hands of a few big international groups; and consequently the price of scientific journals soared. The conditions for triggering a vicious cycle had been created: at the end universities invested twice for the same thing. In the first instance, they had been investing to fund research that would subsequently be given away for free to publishers; and they invested a second time to regain that same publication, buying for their libraries the subscription to the journal at a higher price.[28]

This evolution in the 1980s is crucial because universities and big biotech/pharmaceutical companies started to colonise the area of pre-competitive research and to make access to knowledge more difficult. Such proliferation of IPRs upstream, while it had a positive effect in the short period, has hindered biomedical research in the long run.[29] Covering basic research discoveries, research materials and reagents with proprietary claims means to inhibit the use of those tools that are

[25] Heller and Eisenberg (1998), Mowery (1998), and Granieri (2010).

[26] Nelson (2001). Some authors downsized the importance of Bayh–Dole Act in the university patent process. See, for example, Mowery et al. (2004) and Mowery and Sampat (2005).

[27] Such as for example, Dialog System. See Summit (2002).

[28] Guedon (2004), Suber (2004a, b), Kranich (2006), and Caso (2009).

[29] Rai and Eisenberg (2003).

fundamental not only for downstream research but also for basic research itself.[30] This dangerous stalemate is confirmed by the decrease in the number of new patented drugs notwithstanding the growing public and private investments in drug discovery.[31] At the origin of this phenomenon there are factors such as the insufficient scientific understanding of biological and molecular mechanisms of diseases, the limited availability of data and biological samples, the lack of collaboration between researchers working in academia and industry and, above all, the complex landscape of IPRs.

12.3 Research Biobanks: Exclusive (or Para-Exclusive) Rights in a No-Man's Land

Data sharing and collaborative research have become an imperative in contemporary science, whose development depends inextricably on: the opportunities to access and use data, the possibility of sharing practices between communities, the cross-checking of information and results and, chiefly, interactions with experts in different fields of knowledge. Data sharing allows both to spread the costs of analytical results that researchers cannot achieve working individually and, if properly managed, to avoid the duplication of research. These advantages are crucial: access to a common pool of pre-competitive data and the possibility to endorse follow-on research projects are fundamental for the progress of biomedicine. This is why new institutions such as research biobanks have gained in importance.

Biobanks are powerful tools and organisational structures essential for translational medicine and biomedical research, because they are treasures of a pool of pre-competitive information and materials tempting both public research centres and BigPharma.[32] On the one hand, they are a source of human biological samples stored according to high standards of quality and safety. On the other hand, a biobank is also an informational "mine"; in its databases are classified clinical/diagnostic information, sample-derived genetic data, donor's personal data, and the type of consent given for the research. Such data have a surplus value for translational and biomedical research because they are constantly updated with donor's follow-up data: it is possible to follow the clinical history, the disease progression, the response to different therapies, etc. In some cases, research biobanks have also created additional resources such as archives of graphical elaborations of protein structure (in 2-D or 3-D).

[30] This recent trend towards the appropriation of data is posing serious obstacles to full and open access to data for scientific purposes. ICSU (2004).

[31] Booth and Zemmel (2004), Cuatrecasas (2006), and Weigelt (2009).

[32] Translational medicine is based on pre-clinical bio-molecular analysis of a critical mass of human biological samples in order to obtain results immediately usable in the clinical context. This allows the identification of biomarkers, i.e. those molecules that can predict the risk of cancer, the presence of a neoplasia and the possibility of identifying the most appropriate and effective drug or treatment for a particular patient. See FitzGerald (2005).

Thanks to technological and scientific progress, what until a few decades ago had been considered a worthless hospital waste (a *res derelictae*), nowadays has become an asset in a legal and economic sense. Thereby, the cloud of enclosure is gathering all over these research structures: biological samples are legal assets, subject to the bundle of property rights; genetic sequence derived from the sample could be patented or covered by a trade secret; biobanks' database is under the protection of copyright or EU sui generis right; also some contents of the databases are covered by copyright; the handling of personal data, health records and genetic information must preserve the donor's right to privacy.

Taking into account this panorama, we can distinguish two different levels in the biobank structure, based on the twofold nature of human biological samples. Biobanks, in fact, store a critical mass of tissues (leftover tissues, blood, saliva, urine, etc.) in their bio-repositories; but, however numerous they may be, biological samples are still exhaustible resources. They are scarce and rival assets that need to be efficiently allocated among stakeholders. On the contrary, data are "ubiquitous": they can be replicated *n* times and distributed to *n* researchers at the same time. Therefore, access to biological samples is crucial but access to the information embodied in the material support is even more critical to the improvement of data sharing. Thus, in biobanking activity two tragedies potentially coexist: firstly, the tragedy of commons with regards to human tissues; secondly, the tragedy of anticommons with respect to data and information related to the sample.

Regulatory gaps and the lack of common and shared reference points have been filled by privatisation trends, at the expense of the collective good and, in an increasing number of cases, at the expense also of private companies. In particular, traditional models seem to stifle a lot of potential for the biobank activities. For example, the tools ordinarily used for fruition of data and materials, the Material Transfer Agreement (MTA), are cause of unrest among researchers, because of the cumbersome nature of the mechanism, the length of the procedures and the high transaction costs.[33] Against this impasse some authors are invoking (and business models are moving towards) the "open" philosophy.[34]

12.4 Towards "Open Science": Some Basic Legal Tools

The vision that closed model systems, and patents in particular, encourage an efficient management of research, balancing the return on investments and the benefits for the whole community, has been strongly challenged in recent years.[35]

[33] Streitz and Bennett (2003), Ku (2007), Rodriguez (2008), Lei et al. (2009), and Noonan (2009). Specifically on the problems related to MTA and possible solutions offered by Science Commons, see Margoni (2012).

[34] Hess and Ostrom (2007), Hope (2008), Edwards et al. (2009), Weigelt (2009), Lei et al. (2009), and De Robbio and Corradi (2010).

[35] Kitch (1977) and Gallini and Scotchmer (2002).

This change is evidenced not only by the signal given by some "rebel" researchers (e.g. Ilaria Capua),[36] but even by big pharmaceutical companies (e.g. Novartis and Glaxo-SmithKline).[37] BigScience becomes "open" certainly not because of altruism, but simply because they realised that cooperation is more convenient than competition based on IPRs.

In order to understand how the "openness" is spreading to the realm of biotechnology, we have to contextualise the original concept of "open source" in the world of information technology and software. Afterwards, we will discuss whether such concepts work if applied to scientific research in the "bio-" fields.[38]

12.4.1 Opening Software

Open source is a revolutionary and provocative concept, developed since the early 1970s as part of computer science, and it represents a new way of thinking about computer programming and software in its entirety: from conception to final release and distribution. This movement is composed of two different souls: Free Software and Open Source Software. The first is linked to the name of Richard Stallman[39] and has an ethical aim. According to free software philosophy, proprietary software is a social problem that shakes the values of communality and sharing to its foundations. Software must be freely available and accessible without restraints as a desirable social outcome. On the contrary, Open Source Software is a definition created in 1998 on the occasion of the release of the source code of Netscape's browser by Eric Raymond. According to these alternative currents, open source is a more efficient choice if compared to the traditional closed model.[40] The collaboration of different programmers, who at the same time are users, and the decentralised production monitored by strong normative expectations and social sanctions are a synonym of quality, and they also reduce the time for development and the costs of production. Therefore, open source software shows a broad range of economic advantages.

Unless the starting point is different (the former school has a more philosophical and political approach, whereas the latter has a more utilitarian vision), the

[36] The Italian virologist identified the genetic sequence of the avian flu virus and decided to make it available to the worldwide scientific community by uploading it to GenBank, disregarding the invitation of the WHO to file it in a limited-access database. See Enserink (2006).

[37] Strauss (2010).

[38] The following classifications were also illustrated by Prof. Richard Gold during the seminar "Models for Sharing Data" within the Biobank Lab, held at the University of Trento in May 2010.

[39] In 1983, he announced the GNU project, an operative system compatible with Unix, the proprietary software more widespread in research laboratories in American universities. Stallman's novel idea consisted in the creation of a licence (copyleft, "all rights reversed") giving much more power to the user than to the owner. About the origins of free software, see Stallman (2002).

[40] Raymond (2000).

pragmatic result is the same. In fact, according to both Free Software and Open Source Software, in addition to the object-code (the machine-readable format) the source code is also distributed (the "human language") to the public of user-programmers.[41] In this way, they cannot only use the software, but copy, modify and redistribute it.[42] According to the General Public License manifesto, free software gives users the four "fundamental freedoms": (1) run the program, for any purpose; (2) study how the program works, and change it to make it do what you wish; (3) redistribute copies; (4) distribute copies of your modified versions to others.

Both "open projects" are distinguished by a special legal regime that allows progressive development. The GNU GPL, in fact, is a viral licence because it "infects" all subsequent products containing the original code: the programmer gives up IP exploitation to follow-on users as the latter are not allowed to distribute the modified software with a proprietary licence.

It is hardly necessary to point out that this movement is not the negation of intellectual property, but rather represents a new way of interpreting it. It would be a mistake to think that copyleft means the absence of copyright. Viral licensing is properly designed under copyright law, but it allows users to modularise the availability and distribution of their works, while also posing some limits and obligations.

12.4.2 Opening Biotechnology

In the field of biomedicine, the open source philosophy has been transposed into "open source biotechnology".[43] Of course, such a transplant is not a trivial question because the open source model and open source licensing have been developed around the idea and the structure of copyright. Instead, in what we call open technology, we have to deal with patents.

At first sight, *open source patent* may seem a tautological expression, because the information related to the invention is already publicly accessible and available through the mechanisms of disclosure or deposit.[44] In fact, even though the invention is disclosed, it does not mean that the information and data embodied are non-excludable. Patent itself may inhibit the public use of that invention

[41] A way to overcome this problem is a particular technique called reverse engineering, where the reverser analyses the programs and tries to understand how they work without having the source code. See Lessig (1999) and Nichols and Twidale (2003).

[42] Stallman (2002).

[43] Gitter (2012).

[44] Dasgupta and David (1987).

through exclusive licences. In this context, "open source" refers to an issue of accessibility rather than disclosure.[45]

Taking ideals behind the free software movement, the open source patenting develops "the aspirational goal of biological scientists [to] closely track those of the open source community in desiring to keep information and discoveries communal and accessible".[46] Here, the "viral" licence works in the following terms: the licensees cannot appropriate the fundamental "kernel" of the technology and cannot improve it exclusively for themselves[47]; data and results of research should fall into the public domain, but only under certain conditions, for example, by waiving an "unfair" use of IPRs. The participants in the open source project, therefore, would agree to grant licences or to exercise their rights in order to make inventions and improvements available to the whole community.[48] In this scenario, the patent holder should license the invention with a licence that protects those technical solutions and improvements from possible attempts of appropriation, for example by commercial competitors.

That has already been done by the BIOS's CAMBIA, an Australian nonprofit research institute that has extended this model to the transfer of biological samples.[49] Users of the BIOS "concordance" do not assert IP rights against each other's use of the technology, materials and methods to do research, or to develop products either for profit or for the public good. Consequently, the improvements must be shared according to a BIOS license, while the products and inventions developed from the same technology can be patented. In the latter case, however, the improvements that have been patented must return (grant back clause) to the BIOS and to other licensees on the same terms of the original licence or must be freely cross-licensed.

Another example of this trend is represented by "HapMap Project",[50] an international consortium involving ten research centres located in Japan, the UK, Canada, Nigeria, China and the USA. The scope is to create a map of genetic variations in human beings in order to offer a valid instrument in support of biomedical and clinical research and make this information freely available. According to the Data Release Policies, in fact, all data generated must be released "quickly"[51] in the public domain. The user accepts the terms of this agreement

[45] Boettinger and Burk (2004).

[46] Ibid., p. 225.

[47] See BIOS concordance.

[48] About the adoption of the open source model in the biotech field, Hope (2008).

[49] http://www.bios.net/daisy/bios/home.html. Accessed 01.02.2012.

[50] Internation HapMap Project, http://hapmap.ncbi.nlm.nih.gov/. Accessed 01.02.2012. See also The International HapMap Project (2003).

[51] See http://hapmap.ncbi.nlm.nih.gov/datareleasepolicy.html. It is not well specified how quick the release into the public domain has to be.

through a "click-wrap" licence. In this way, the database is freely accessible to all bona fide researchers and users cannot tie down data and information by filing "patent parasite"[52] application over the resulting discoveries. They are forced to share information among the participants in the HapMap project, so bound by the same contractual provisions. In any case, the possibility of patenting is not excluded a priori: if it is possible to show a specific utility, researchers can apply for a patent "as long as this action does not prevent others from obtaining access to data from the Project",[53] licensing the invention so that the information used is still accessible to other participants.

Some scholars have emphasised the advantages of this approach. In fact, the absence of IP income is counterbalanced by a social recognition for the participants.[54] This can also means economic rewards in terms of future job offers, proposals for collaboration in commercial open source companies and access to venture capital market.[55]

However, the adoption of this system does not dissolve some key issues. First of all, the translation of the open source model outside the field of information technology raises a series of challenges.[56] At first instance, it seems obvious that research equipment and laboratories in the biotechnological field are more advanced and costly rather than the resources necessary in the computer context.[57] Secondly, the timing and development are very different in the two sectors. While in software, you can quickly have a response by the whole community of programmers about the improvements made, in the biomedical field the process from discovery to marketing can take years. In addition, this model seems to ignore the exorbitant costs of drug discovery, clinical trials, intellectual property (e.g. the cost of patent application), and the length of regulatory procedures.[58] The adoption of open source in biotechnology would, therefore, run a high risk of rejection. Open source is a culture of sharing developed in the hacker community with different needs from the biotech world. Pharmaceutical companies want to get patents and license as much as possible, while the researchers want to have credit and reputation

[52] According to Daniel de Beer a "patent parasite" is a patent developed from the original material "to which just a tiny change has been made". De Beer (2005), p. 366.

[53] HapMap Project, Data Release Policies.

[54] von Hippel and von Krogh (2003).

[55] Hope (2008), Chakravarty et al. (2007).

[56] As pointed out by Gold (2010).

[57] Lerner and Tirole (2005).

[58] de Beer (2005).

for their works.[59] Open source, therefore, may not provide the right incentives for effective collaborative research.

12.4.3 Open Access Publishing

Open Access (OA) is the free online access. That means the freedom to access data without most copyright and licensing restrictions.[60] In the OA context two different routes have been distinguished, regularly labeled as gold road and green road. The first one refers to OA journals; the second one to self-archiving previous published works. In any case, they correspond to different phases of the same movement.[61]

The core of open access works as follows: the institution shall pay the cost of publication of its researcher, who retains some rights (authorship, in particular) and surrenders others—throughout licences such as Creative Commons[62]—in order to make the publication freely available.[63] Here, production costs are borne by the authors and institutions, while distribution costs—held down thanks to digitisation—are shared with new intermediaries.

At the end, OA reduces costs, circumvents the limits imposed by increasingly stringent regulations on copyright, licensing agreements and DRM. OA offers also reputational incentives, because it represents a means to disseminate authors' ideas, to disseminate their intellectual production, to promote themselves before other peers; but it is also a tool to get free and quick access to the literature necessary for implementing and deepening their own scientific production. OA is also an opportunity for libraries to mitigate the costs of journals and subscriptions.[64] Also, society and the progress of knowledge, in general, can benefit from such a system because the openness is the primary method for correcting errors and mistakes through the sociological mechanisms of peer review and citation.[65]

However, authors play the key role in building a system based on open access, as the fate (open or closed) of their works is in their hands. It is a cultural problem (in the sense that part of scientific community still ignores what OA is) but is also a challenge to remove the existing disincentives (such as the Ingelfinger rule) and to find those incentives that could propitiate this mentality.[66]

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[59] Gold and Nicol (2012).

[60] Suber (2004a, b).

[61] Guedon (2004).

[62] Creative Commons (CC) is a charitable corporation that promotes the sharing and circulation of knowledge in compliance with copyright law. Although it offers standardised models, its modular licenses (attribution, noncommercial, no derivative works, share alike) and their combinations can provide flexibility in setting the interests of parties. Source: http://creativecommons.org/.

[63] Caso (2009).

[64] De Robbio (2010).

[65] Boyle (1997).

[66] Suber (2004a, b).

12.5 Open Models in the Field of Research Biobanks

Research biobanks have been metaphorically described as a library. This comparison is not so abstract since biobanks have databases and digital archives. They are already digital libraries but, maybe, do not yet know it.

Digital databases of the biobanks may contain a variety of information. First of all, information related to the "owner" of the sample like personal and clinical data, and additional information such as eating, life or relationship habits. Biobanks' databases can also index information derived from the material support, i.e. genetic data or sensitive information that can reveal the health conditions of the patient. In particular, genetic data are a very peculiar category because they concern not only the person they belong to but also his entire biological family. Quite often biobanks proceed to aggregate the data and to make the first analysis. Therefore, the results of these analyses and the generated cohorts are included in digital files and stored in the archive for following research. Moreover, since the main purpose of a biobank is to provide samples and data to researchers, while one of the main bonds of the latter is the reporting of his activities and the grant back of analysis' results, biobanks also collect the research reports and, if available, the publication derived from the study of the biological and informational resources provided.

Within the digital archives of the biobank can therefore be stored copyrighted materials, and simple data. Regarding researchers' reports and publication, the new methods offered by the Open Access in the field of scientific and academic commons (OpenWetWare,[67] PLoS,[68] Open Archive Initiative,[69] etc.) represent a great chance to transform research biobanks into an invaluable resource and an Institution.

Concerning the diffusion of raw data, things may be a little bit different. Science Commons, for example, has been developing a protocol for the circulation of scientific data.[70] Moving from the awareness of the need of data's interoperability, the OA database protocol aims to provide the legal functions necessary to create a legal tool for the legal integration of different databases or data products.[71] The key principles at the base of the initiative are the promotion of legal predictability and certainty, the user-friendly approach and the reduction of transaction costs. The protocol suggests converging on public domain by: waiving statutory or intellectual

[67] http://www.openwetware.org/. Accessed 01.02.2012.

[68] http://www.plos.org/. Accessed 01.02.2012.

[69] http://www.openarchives.org/. Accessed 01.02.2012.

[70] http://sciencecommons.org/projects/publishing/open-access-data-protocol/. Accessed 01.02.2012.

[71] At first, Science Commons encouraged database licensing under the CC licences or the GNU Free Documentation Licence. The initial approach was abandoned for three main reasons (category errors, false expectations, attribution staking) and now the scope is to converge on public domain. http://sciencecommons.org/projects/publishing/open-access-data-protocol/. Accessed 01.02.2012.

property, deleting the contract control, implementing the interoperability with databases and data not available under the Science Commons Open Access Data Protocol through metadata, simplifying the citation requirements.[72]

In any case, these initiatives are lame and are likely to be abandoned if appropriate structures of governance are not established in order to allow their sustainability. It is necessary to involve all stakeholders in the design and management of these innovative projects, facilitating dialogue, participation and transparency.[73]

In response to this gap, new paradigms are emerging for access to pre-competitive information, such as collaborative partnerships. Many new cases of private-public collaboration are demonstrating their value and biobanks may claim their intellectual power on them.

It is the case, for example, of the Structural Genomic Consortium (SGC),[74] Sage Bionetworks,[75] the European Bioinformatics Institute (EBI) Industry Programme,[76] the Predictive Safety Testing Consortium (PSTC),[77] the International Union of Basic and Clinical Pharmacology (IUPHAR).[78] Life Science Grid—Eli Lilly, Pistoia[79] and Innovative Medicines Initiative (IMI).[80]

These new business models are developing in the area of biomedical research the idea of open innovation.[81] That was expressly declared by Weigelt and Edwards when they launched SGC, an innovative project to foster the free circulation of pre-competitive data, based on the osmosis between private and public sector and the adoption of open access structures.[82] According to SGC Data Policies, all products and results (material and expertise) are released into the public domain, but the enforcement of this system is secured by a participatory and transparent governance

[72] Ibidem.

[73] Kranich (2006).

[74] http://www.thesgc.org/. Accessed 01.02.2012. SGC is a non-profit organisation founded in 2004 with the aim of promoting the development of new drugs, investing in basic research and releasing to the public every type of information (from reagents to know-how) The SGC's primary goal is to determine the three-dimensional structure of proteins, in order to understand the molecular mechanisms of their biological function. Then, the data obtained are deposited in the Protein Data Bank (PDB), a freely accessible archive, which since 1971 collects information about 3D structures of large molecules, including proteins and nucleic acids (http://www.pdb.org/pdb/home/home.do).

[75] http://sagebase.org/. Accessed 01.02.2012.

[76] http://www.ebi.ac.uk/. Accessed 01.02.2012.

[77] http://c-path.org/pstc.cfm. Accessed 01.02.2012.

[78] http://www.iuphar.org/. Accessed 01.02.2012.

[79] http://www.pistoiaalliance.org/. Accessed 01.02.2012.

[80] http://www.imi.europa.eu/. Accessed 01.02.2012.

[81] Chesbrough (2003).

[82] Weigelt (2009) and Edwards et al. (2009).

structure, a number of clear operational rules and legal instruments, such as the adoption of CC licenses for the exchange of pre-competitive information.[83]

Sage Bionetworks is another example in this sense. It is a not-for-profit organisation founded in Seattle in 2009 with an ambitious goal: to create a Commons where computational biologists can improve an integrative bionetwork in order to expedite the pathway to knowledge, treatment, and prevention of disease (1st Sage Bionetworks Commons principle). The purpose is to build an innovation space where scientists are not limited to aseptically exchange data, but, as active participants, they are calling to create new tools (models disease) or improve those developed by other colleagues.[84] So through an open IT infrastructure (the Sage Bionetworks Platform), standard tool-sharing mechanisms, secure measures and a cloud computing system, this model aims to become a powerful resource for data sharing and interoperability of different data sets. Thanks to its governance structure,[85] Sage Bionetworks aims to protect the rights of patients in terms of privacy and self-determination expressed in the informed consent, ensuring participation and transparency. Probably this model is the one which better interprets the democratisation of innovation imagined by von Hippel.[86]

The list of examples could go on longer. In brief, what all these projects have in common is the recognition of the need for a community-based approach and for the widest possible access to data. However, they assume that public domain might not be the most efficient response for their purposes. For this reason, such partnerships pay attention also to the subsequent steps of circulation such as the licensing.

12.6 Conclusions: Governing the Components of the Research Biobanks

The English word "biobank" has in itself a theme connected to the world of finance (bank). In Italian, we use the term "bioteca" which clearly has a resonance with the word "biblioteca" (library). It is a terminological choice suggesting a paradigm shift. The enclosure movement is dramatically expanding its borders to crucial sectors of innovation such as the pre-competitive area and is trying to colonise strategic structures like research biobanks. In this sense, the latter, like real banks, risk being transformed into a *caveau*.[87] Scholars have warned against this dangerous drift, underling the institutional and public role of biobanks: the latter is the steward of a critical mass of material and information, fundamental for biomedicine and translation medicine, which have to be used in a far-seeing and efficient way.

[83] Ibidem.

[84] Derry et al. (2011).

[85] http://sagebase.org/downloads/SageBio_Governance.pdf. Accessed 01.02.2012.

[86] von Hippel (2005).

[87] De Robbio (2010).

How to build this knowledge commons of the twenty-first century?

First of all, lawyers and policy makers should consider how the components of IP, technology, social norm and contracts interact in the specific context of research biobanks. As we have already emphasised, the biobank has a dual nature: a material and informational one. Therefore, the exchange of biological materials will be managed through an MTA, while for the data appropriate access policies must be created.[88]

Why should researchers share information with others? Although the benefits of data sharing are universally recognised, the development of this process still faces technical and, above all, cultural problems. Obviously, we must play on reputation and authorship, the unmoved mover of the openness of information. Scientific data sharing must be encouraged by creating appropriate reputational incentives, like a sort of h-index. The more you share with biobanks and the scientific community, the more you are cited and the more are the benefits. A researcher with a higher h-index could have priority access to material resources (biological samples) over other colleagues. Of course, access to immaterial resources of the biobanks should be granted for any research purposes, as broadly as possible, to all bona fide scientists, just after an online registration.

The same "feedback" incentive could be a valid tool also for the biobank itself and can address its funding problems. Anne Cambon-Thomsen has proposed the creation of a BIF (*Biobank Impact Factor*), a sort of citation impact factor for biobanks.[89] The tool should quantify the biobank's use, view the number of access, calculate the range and the impact of the research obtained, giving credit to those who created and maintained a valid resource. A high number of citations means research funds for both the biobank, the laboratory and the research group.

Funding, of course, is another relevant issue for biobanks. How can they finance themselves? Through public funds? Private funds? Access fees? Other data?

For example, O+ehun,[90] the network biobank of the Basque Country (Spain), is growing thanks to public and private funds but also thanks to grant back clauses. In a nutshell, the Basque biobank "obliges" researchers who access its biological resources to submit periodical reports on their results. Here, trust is an important element, because scientists collaborate actively feeling themselves a part of the

[88] The contractual component is the ideal solution in order to settle the parties' interests, but in the biobank context MTA is more the problem than the cure. Collaborative initiatives such as Science Commons have offered contractual models to make the transfer of research materials easier, thanks to a flexible, modular, web-based and user-friendly tool. However, this MTA has the usual disadvantages of standard agreement and its modularity partially alleviates the problem by providing a limited space for autonomy. On the one hand, standardisation helps to reduce transaction costs and to facilitate circulation, but on the other hand, it creates difficulties in the field of open licences. Furthermore, a standard contract is always deficient in participatory aspects, because the contents of the agreement do not result from a negotiation, but it is unilaterally imposed. On the problems related to the standardisation of contracts, see Roppo (1975), Boggiano (1991), and Alpa and Bessone (1997).

[89] Cambon-Thomsen (2003).

[90] http://www.basquebiobank.com/. Accessed 01.02.2012.

same network: they use the samples and data collected by their colleagues and they want to create a common resource in the interest of the local research community. This provision also reflects the principles of altruism and reciprocity, which ideally should underlie scientific research. Furthermore, feeding the findings back reduces the risk of duplication of research. It is crucial to grant back the results of the analysis (other pre-competitive information) to the biobank, and to return not only the complete analysis (in order to permit the scientific review process) but, especially, the "blind alley", that is the negative findings that can orient next developments and efforts.

Someone could argue that a grant back clause could discourage researchers interested in publication from taking part. In order to address this problem, for example, the NIH grants a period of exclusivity for the data producer. In fact, the Policy for Sharing of Data Obtained in NIH Supported or Conducted GWAS Studies declares that investigators who contribute data to a NIH GWAS data repository retain exclusive right to publish analyses of dataset for a maximum of 12 months following its release via the NIH GWAS data repository. During this period of exclusivity, NIH grants data access through Data Access Committees (DAC) to other investigators, who may analyse the data, but are expected not to submit their analyses or conclusions for publication until expiration of the exclusivity period.[91]

These recent trends towards openness show fascinating perspectives but may paradoxically become a closure unless we learn to handle all these new possibilities. Lawyers must return to being the finest interpreters of contract law, in order to modulate a system of incentives that take into account the following steps: defining the organisation (public, private or partnership); establishing the governance structure and transparent data access policies; types of contracts and licences, considering the dual nature of the biobank and consequently the different object (digital information or biological material). The complexity lies in the management of the interface between copyright and patent. It represents the main challenge of this contractual drafting where lawyers still have something to say.

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