

COMMENTARY

Research on biological materials of human origin. Jurists and scientists face to face

Carlo Petrini¹ and Walter Ricciardi²

¹Unità di Bioetica, Presidenza, Istituto Superiore di Sanità, Rome, Italy

²President, Istituto Superiore di Sanità, Rome, Italy

Abstract

On 3rd October 2016 a convention was held in the Aldo Moro room of the Chamber of Deputies on “Research on biological materials of human origin. Jurists and scientists face to face”. The convention was organised by the Bioethics Unit of the Istituto Superiore di Sanità (ISS, Italian National Institute of Health) in conjunction with the Italian Academy of the Internet Code (IAIC) and the Fondazione Centro di Iniziativa Giuridica Piero Calamandrei. The present contribution reports the topics discussed and the key conclusions reached. As a follow-up to the discussion, the scientists, jurists and institutions concerned are resolved to take further steps towards the formulation of operational proposals intended to facilitate research using human biological materials within a framework of precise and strict regulations.

Key words

- bioethics
- human research
- informed consent
- legislation

Twenty-five years ago, on 19th September 1991, on the Italian side of the Similaun glacier in the Alps, 92 metres from the border between Austria and Italy, Erika and Helmut Simon found a mummified man. The man is now known as Ötzi, the “Man of the Similaun” or as the “Ice Man”. According to dating techniques, he lived approximately 5100 years ago. The discovery immediately sparked a debate as to the exact side of the border on which Ötzi had been found. He was first taken by helicopter to Vent, in Austria, and thence in a hearse to Innsbruck, where he was closely examined using several techniques. Claims that Ötzi had been found in Italy were subsequently shown to be correct and, following an agreement between the Austrian Government and the Italian district of Bolzano, the body was returned to Italy and housed at the South Tyrol Archaeological Museum. The ethnic origin of the mummy known as Ötzi has been the subject of contentious debate. He was discovered in a region of modern-day Italy that belonged to the Austro-Hungarian empire prior to its partitioning in the wake of World War I. Consequently, the majority of its inhabitants still feel a strong sense of Austro-Hungarian – or more specifically, Tyrolean – identity. The finding that Ötzi had been wounded in the shoulder by an arrow led to yet further debate. Had he been walking from North to South or from South to North? Had he been injured by an Austro-German or by an Italian?

Was his genetic inheritance Mediterranean or Northern European? And could he offer proof that South Tyroleans were of German stock and not Italian? In 1993 a group of researchers, none of whom was Italian, took tissue samples and analysed Ötzi’s mitochondrial DNA. The results were published in *Science* on 17th June 1994: “this sequence shows that the mitochondrial type of the Ice Man fits into the genetic variation of contemporary Europeans and that it was most closely related to mitochondrial types determined from central and northern European populations” [1]. On 28th February 2012 Andreas Keller and coauthors reported, in an article published in *Nature Communications*, “the complete genome sequence of the Iceman”, showing “100% concordance between the previously reported mitochondrial genome sequence and the consensus sequence generated from our genomic data”. They reported “indications for recent common ancestry between the Iceman and present-day inhabitants of the Tyrrhenian Sea, that the Iceman probably had brown eyes, belonged to blood group O and was lactose intolerant. His genetic predisposition shows an increased risk for coronary heart disease and may have contributed to the development of previously reported vascular calcifications” [2]. On 7th October 2012, Marek Janko, Robert W. Stark and Albert Zink, in the *Journal of The Royal Society Interface*, “show that RBCs [red blood cells] were preserved in Iceman tissue sam-

ples for more than 5000 years. The morphological and molecular composition of the blood corpuscle is verified by atomic force microscope and Raman spectroscopy measurements" [3].

From an ethical perspective, these genetic tests raise important questions. Since Ötzi clearly could not and did not consent to being transferred from Italy to Austria and back or to the storage and analysis of his biological tissues, how were the ethical requirements for biological sample transfer and use respected? We cannot imply consent from any significant social activity of his, nor can we apply the principle of proxy consent: not only are his descendants (in the broad biological sense) unknown and hotly contested, but the very purpose of the research is to identify them. The same circular scenario occurs if we try to identify a modern-day ethnic or cultural group that identifies with him historically: both the Italians and the Austrians would include Ötzi in their history, leading us once more right back to the initial point of contention. We might think to ask what Ötzi himself would have wanted, but our knowledge of his culture is so limited and the distance between ours and his so vast that the question would ultimately be meaningless. To make matters even more nebulous, the research provides no direct benefits to Ötzi.

So how should we judge these studies on Ötzi in ethical terms? Each of us is free to answer as he or she thinks fit, but the majority of ethicists would most probably agree that they are acceptable. The problem is, rather, whether or not some of those studies are perhaps a little "over the top" and of doubtful scientific value. This reference to the well known mummy Ötzi, with its mention of some of the difficulties encountered in reconciling the interests of scientific research, ethical values and legal regulations, introduced the discussions of the Convention on "Research on biological materials of human origin. Jurists and scientists face to face" in the Aldo Moro room of the Chamber of Deputies. The Convention was organised by the Bioethics Unit of the Istituto Superiore di Sanità (ISS, Italian National Institute of Health) together with the Italian Academy of the Internet Code (IAIC) and the Fondazione Centro di Iniziativa Giuridica Piero Calamandrei and was broadcast live via the Chamber of Deputies web tv.

The authors of the present article, the Head of the Bioethics Unit (CP) and the President (WR) of the ISS, respectively opened and concluded the discussions. Opening addresses were also given by representatives of the other two institutions responsible for organising the Convention, namely Professor Alberto Gambino (President of the IAIC and Deputy Chancellor of the European University of Rome) and Professor Giorgio Resta (Associate Professor of Comparative Private Law at the Faculty of Jurisprudence of Roma Tre University).

The morning session of the Convention was moderated by Professor Marialuisa Lavitrano (co-Chair of the Management Committee of the Biobanking and Biomolecular Research Infrastructure – BBMRI and co-Director of the Common Service Ethical Legal Societal Issues of the same institution), and the afternoon session was moderated by Professor Vincenzo Zeno-

Zencovich, full Professor of Comparative Law at Roma Tre University.

Other contributions were received from the Hon. Paola Binetti of the Chamber of Deputies Social Affairs Committee, and from Professor Pietro Rescigno, one of the most authoritative representatives of Italian jurisprudence. In the wake of the discussion, the scientists, jurists and institutions concerned are resolved to move ahead towards the formulation of practical proposals to facilitate research using human biological materials within a framework of clear and rigorous regulations. This initiative is largely inspired by the considerations voiced in the three concluding addresses, of which the following paragraphs are a summary.

The final addresses followed on from the topics discussed during the day, which touched on all the stages through which human biological materials pass when they are used for research purposes, from their isolation and preservation to their examination. These stages comprise numerous aspects: the organisation of biobanks (the requisites for their establishment and accreditation); approval of the research projects (the responsibility of ethics committees and the Italian Data Protection Authority); the acquisition of biological materials (problems involving consent, management and communication of possible incidental findings, non-monetary incentives, the principle of finality, research on material from deceased subjects); the preservation of biological materials (problems concerning the notion of "identifiability" of samples, requisites of anonymity, safety measures); the uses of biological materials (range of consent and types of permissible research, secondary uses of materials, patentability); the appropriation of samples and data (ownership conflicts between researchers and patients or between researchers, legal protection of data banks and individual contributions of single research units); the transfer and sharing of data and samples (regulations for transfer abroad, data sharing models).

The President of the ISS placed particular emphasis on the following aspects:

- in the field of research, aspects of ethics should receive the same consideration as scientific aspects, which means that a constant dialogue between ethicists, researchers and jurists is indispensable;
- there is a need for exhaustive and strict regulations, which should nonetheless not suffocate research efforts;
- there is also a need for financial backing by the State in order to ensure the viability of the system of biobanks for research. The situation in Italy is not encouraging, with unofficial figures suggesting that 85% of global public financing for research is accounted for by the US, about 5% by Japan, 4% by China, and the rest by Europe;
- Italy should aim to have a national research agency that combines funding for both research and governance;
- notwithstanding the generally unfavourable economic situation, there are signs of recovery and excitement in the Italian research field. Two events deserve mention in this respect: the re-organisation of the ISS [4] and the launching of Human Technopole.

The honourable Paola Binetti began her contribution by remarking on the great promise currently offered by several lines of research and recalled, in particular, innovative drugs and precision medicine. She then submitted the following points to the attention of participants:

- Italy still lacks comprehensive legislation covering research with human biological materials and no bills on this topic are currently in the pipeline, though some aspects are addressed in various other laws;
- of particular interest to legislators – who are constantly in touch with the Italian Data Protection Authority – is the question of informed consent: biological samples should be used only for the purposes specified by the donor. However, the need for a long-term view makes it difficult to establish limits to the possible uses of biological materials, and no checklist for use in assessing the precise nature of informed consent could ever contemplate all the possibilities. There is thus a need to ensure mutual trust between researchers and donors;
- the need to promote research of real quality suggests the usefulness of careful vetting procedures for new projects;
- the transparency of results is essential and implies – among other things – the obligation to publish negative as well as positive findings;
- biobanks are essential for the future development of biomedicine: after decades of studying the general features of diseases, research is now focusing more on individual peculiarities, so that biobanks are a valuable resource enabling comparisons between different individuals, as well as between samples from the same individual;

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- it is therefore the duty of legislators not to obstruct, but rather to facilitate research, while being constantly on the alert for situations that could lead insidiously to ethically unacceptable deviations. Sectors such as the donation of gametes for research are particularly sensitive in this sense.

Professor Pietro Rescigno recalled episodes from his many years of academic experience and offered some comments from a broad legal point of view:

- legislators should not invade the bioethics sector: it is to be hoped that the relevant legislation will effectively be directed above all to social and community education (of professionals, patients and the general public);
- the notions of ownership, consent and non-remuneration are of particular importance;
- a balance needs to be struck between the interests of research and the rights of the individual from whom the material is taken.

On the basis of these contributions the organisers are resolved to promote cooperation between researchers, jurists, ethicists and the community in general to formulate practicable proposals to define a legislative framework, the limits of informed consent, and the sustainability of biobanks for research.

Conflict of interest statement

There are no potential conflicts of interest or any financial or personal relationships with other people or organizations that could inappropriately bias conduct and findings of this study.

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