Gene editing: Do we need a universal approach?*

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Only a few years ago, a new scientific discovery shocked not only the scientific community, but also society as a whole: gene editing using the CRISPR Cas9 technique. Similarly to what happened when it was reported that a mammal was obtained by means of an ingenious technique (transferring the nucleus of a somatic cell into a previously enucleated egg cell).

In contrast to cloning, whose spectrum of possibilities focused on reproduction and shortly afterwards on research to treat certain pathologies (the misleadingly misnamed "therapeutic cloning"), gene editing is proving much more promising than cloning was in the past. Gene editing is opening up an almost inexhaustible range of applications, not only in direct relation to human biology (the prevention of hereditary diseases, their treatment and possibly even procedures to improve or enhance already born human beings and their offspring), but also with respect to other non-human living beings. All agree that it is a relatively simple, cheap and efficient technique, although these are under discussion.

As in the past, scientists (and the institutions and companies behind the funding of the research) are pressing for applying this technique to human beings, both in the somatic and germ line. For their part, ethicists, lawyers and policy-makers face similar dilemmas to those of the past, based on different techniques: should gene editing be allowed in the human germ line, or should it be rejected altogether? What medical, moral and legal criteria should we keep in mind to distinguish and assess the permissibility of the use of gene editing for preventive, therapeutic or enhancement purposes?

The knowledge and experience gained in the more than twenty years since a similar dilemma arose with human reproductive cloning, both scientifically and in the field of normative sciences, mainly Bioethics and Law, has taught us some lessons; whether we have been able to learn them is another matter. It would suffice to recall reproductive cloning, at the time full of emergencies, as it could satisfy the supposedly pressing need of thousands of couples to have children. Finally, it was stopped when it was found that this technique was not so easy to apply to humans, unlike other mammals (without going into the significant side effects it had on them), that other reproductive techniques already known at the time were more efficient and safer. Cloning for research purposes was also abandoned because of its own technical difficulties; something similar happened with research with totipotent human embryonic cells.

Firstly, these issues have shown that extreme positions should be avoided, as they lead to closing the doors to further reflection and social dialogue. New information and new approaches are always emerging that can lead to a change of perspective, albeit in a moderate way.

Secondly, in this form of gene editing as in other genetic engineering techniques on germ-line and

* *This work is carried out within the framework of the Basque Government funding for Research Groups in the Basque University System (IT 1066-16).*

in reproductive cloning, the main problem that is (or was) to be solved is not to save the life of a patient, even in the foetal stage, nor to improve his or her health in any significant way. The aim of this technique is to ensure that a future child, not yet even conceived, will be engendered and born free of the diseases that his or her parents are carriers of. In other words, this is not a vital or urgent matter for specific individuals. Moreover, at the moment it does not seem foreseeable that the CRISPR Cas9 technique will be available in the short term to be applied to humans, at least in the germ line.

These facts should lead us to conduct ourselves with caution, reflection and in a measured manner.

Thirdly, as in other sectors of human productivity, the globalisation of scientific research has developed, with high-level scientific projects often being carried out with the concurrence of a plurality of research groups located in centres of excellence throughout the world. Consequently, what were known in the 1990s as "genetic paradises" are now less of a concern from the point of view of the regulatory framework. This term was intended to describe the risk for states with specific restrictive regulatory frameworks and even for international organisations (think of the important legal instruments adopted by UNESCO, the WHO and the Council of Europe, for example) that other countries without legislation, not characterised by their leadership in the fields of scientific research in human biotechnology, would welcome foreign scientists and companies to their territory, thus causing companies to translocate to these countries.

The current concern is to find regulatory frameworks or other procedures for monitoring and control of these activities that are generally and universally accepted and shared. It is also a matter of concern that some states that are particularly prominent and dominant in international politics refuse to apply international agreements to their respective research collectives, in view of the great economic importance that many of these activities promise in their industrialisation and commercialisation phase. We have examples of great powers with dictatorial regimes (e.g. P.R. China), or that do dubiously democratic (Russia) or ultra-liberal (occasionally the USA) practices that do not always respect agreements of various kinds or recommendations to limit certain activities until minimum points of international consensus are found.

Finally, society claims that the moral assessment of these matters and the establishment of regulatory frameworks, since they can have a radical impact on the essence of the human being as a moral entity and as holder of fundamental rights, cannot remain confined to the circle of reflections and decisions of researchers, health professionals or their respective scientific societies. The whole of society is concerned, both individuals and the political (states), cultural and other collectivities in which human beings are integrated.

There are issues under discussion which are of the utmost relevance, but for which cultural, ideological, religious and social diversity does not allow for global agreements to be reached without great difficulty. Thus, the meaning of human life, human beings' belonging to their species and the safeguarding of this in what may be their essence, the moral and legal aspects arising from these recognitions, such as the moral status of human life, the right to life and to physical and moral integrity, the rights related to the human species, our responsibilities towards future generations, the specification of the scope of human dignity in the context of the modification of one's own and individual genetic endowment as part of one's biology, etc. For the time being, it

seems that these issues should be left in the reserve of the debate, which will have to be long and will have to be broadened as progress is made in reaching important, but less ambitious, consensuses.

Given this current scenario, as opposed to the maximalisms of the past, there are controversies for which it seems easier to reach consensus. For the time being, it seems advisable that points of discussion focus on specific issues, on which agreement is easier to reach in the early stages of the global dialogue. For example, the safety of the gene-editing technique, its reliability, the occurrence of anticipated or unanticipated side effects, is of general concern, as it has been shown that there are aspects related to it that are still far from being resolved: the side effects that may result from its specific application in human beings (in their reproductive cells, in the zygote and in the early embryo). This is a crucial issue at the moment, although there are always those who argue that it is only a question of time, of researchers finding a safe way to prevent major risks for the new being. It is also claimed that reliability and efficiency is just a matter of time, of continuing research. This is probably the case, but it does not exempt us from paying due attention to it and taking whatever measures are necessary, even if they are provisional and revisable, to prevent risks and ensure a reasonable level of efficiency, so as to prevent guinea pig behaviours.

Consequently, proposals for universal dialogue are increasingly being made by numerous international organisations, as well as international or supranational conferences, expert groups and ethics committees. The Council of Europe's Bioethics Committee (DH BIO) and the European Commission's European Group on Ethics in Science and New Technologies (EGE) (Opinion on the Ethics of Genome Editing), for example, are committed to this approach. This is notwithstanding the fact that the Council of Europe Convention on Human Rights and Biomedicine (Oviedo Convention) states that "an intervention seeking to modify the human genome may only be undertaken for preventive, diagnostic or therapeutic purposes and only if its aim is not to introduce any modification in the genome of any descendants" (art. 13). UNESCO has also openly declared its rejection of this type of intervention ("[...] in particular regarding the identification of practices that could be contrary to human dignity, such as germ-line interventions", art. 24).

The wording of Article 13 of the Oviedo Convention has generated intense debate over the last few years, and has given rise to various proposals, including: maintaining it in its current wording; reaching a consensus on a more open interpretation of this provision, with the risk of distorting its current legal meaning, whether one likes it or not; and amending this article (e.g. by means of an Additional Protocol to the Convention), in such a way as to allow certain interventions on the human germ line, for example for preventive or therapeutic purposes against serious or very serious diseases, subject to the necessary controls, even if it means modifying the genome of the unborn human being.

It appears to me that it is still premature to examine the need to revisit in short-term the permanence of article 13 in its current wording, given that we still do not know very well what the development of this technique applied to the germ line may be, in particular its reliability and efficiency, to the point that it may one day be applied with sufficient margins of success and safety, without going into the more fundamental issues mentioned above. This is a clear example of the fact that Law must follow Science, there is no need to rush, notwithstanding to maintain an open dialogue on this issue.

This perception of how to deliberate and make decisions or, where appropriate, propose recommendations to authorities and legislators has been understood and practised for several decades through standing committees and ad hoc working groups, ensuring that their composition is multidisciplinary, independent and ideologically and culturally pluralistic and inclusive. However, the application of gene editing in humans (and other living beings) is now regarded as a global issue, which requires global governance, although achieving this goal seems still far from being achievable. Various proposals point towards the creation of an independent global committee that for the time being would limit itself to giving recommendations to researchers on what would be acceptable or objectionable from an ethical and scientific point of view, even proposing moratoria.

We already have expert group initiatives, such as the *Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing*, which was set up in 2018 by the WHO to examine the scientific, ethical, social and legal challenges associated with human genome editing (both somatic and germ cell), which in 2020 published the document *Human Genome Editing: A DRAFT Framework for Governance*, the annex to which raised numerous questions that needed to be answered or resolved in order to implement international governance of gene editing in humans. However, although it is a multidisciplinary committee, it does not seem sufficient to reinforce this requirement and its recognition as a universal independent body.

Another proposal consisting of an international regulatory commission agreed by scientific academies has been considered a premature and problematic approach to governing human germline genome editing; deferring to a single commission to set the agenda for global governance raises troublesome questions of framing and representation.

A worldwide pluralistic and democratic governance calls for a new process of active and sustained dialogue among stakeholders as well as public authorities and society as a whole. However, there are numerous and important problems that would have to be resolved for this hypothetical world committee to be able to work efficiently: defining its structure and composition, its non-binding nature, but its exhortative nature through its recommendations. It would also be necessary to decide to which international body it would be associated or whether it should be detached from any of them, but with the material and moral support of several bodies at the same time (consortium of bodies such as UNESCO, the WHO, the Council of Europe, the European Union, the OAS, the OAU, ASEAN and others like them).

It is true that a formula such as the one proposed here still needs reflection, dialogue and maturation, so that its moral authority to impose its criteria and proposals is recognised.

ISSN 2284-4503