Response to the International Commission on the Clinical Use of Human Germline Genome Editing Call for Evidence

https://royalsociety.org/-/media/policy/projects/gene-tech/international-commission/Call-for-Evidence-Questions.pdf?la=en-GB&hash=3365D5CCF5C41C730CA483D743300E7D
Submitted September 27, 2019

The American Society of Gene & Cell Therapy (ASGCT) appreciates the opportunity to respond to the International Commission's call for evidence, which we commend as a first step in collecting input from a variety of stakeholders. The Society's position related to many of the questions posed is outlined below. Regarding the technical scientific questions, we recommend that the Commission extend the call for evidence, to allow for a comprehensive and meaningful response based on an internal compilation of the state of the science from our members.

ASGCT does not view any clinical application of germline genome editing to be appropriate and finds such uses at the present time to be a breach of international normative restrictions, as well as likely violations of regulatory and legal restrictions in many nations. The Society does not believe this status quo should be revisited unless or until the technical and ethical problems regarding such uses of germline gene editing are broadly and deeply discussed, and societal consensus is reached among all major diverse stakeholders, including members of patient, caregiver, scientific, medical, ethical, cultural, and other civil society organizations and communities. These stakeholders need to determine together whether, and under which conditions, clinical germline gene editing should take place in the years ahead, both through this call for evidence and additional dialogue.

From a scientific perspective, the issues that must be addressed before proceeding toward clinical applications of germline gene editing include, but are not limited to, optimizing the efficiency and precision of on-target modification; defining and minimizing off-target mutations; preventing on- and off-target mutation mosaicism; and understanding how novel on- and off-target mutations might interact with existing human genetic diversity when these new alterations are passed on to future generations.

In addition, the intergenerational medical and ethical implications of human germline genome editing should be a central concern in addressing this topic. Among those implications, research subjects would include not only embryos and children, but also future generations of descendants. Risks and potential harms to future generations are currently too high and/or insufficiently known to allow proceeding with use of this technology. Informed consent could not be obtained from modified embryos for their children to be genetically modified. Moreover, the results of clinical use of germline gene editing could not be analyzed for decades or generations, which make these applications incompatible with long-term evaluation in a scientifically reasonable time frame.

In terms of oversight, ASGCT encourages the identification of a fine balance between the strong international governance required to prevent abuses of gene editing technology and the sufficiently flexible regulatory environment necessary to allow groundbreaking treatments to be developed expeditiously for patients in need of them. Governance structures should not inhibit the great scientific advancement represented by gene editing technologies when used on somatic cells, and their potential value for an improved understanding and possible treatment of a variety

of diseases.

Additional exploration of attributes of effective governance frameworks is necessary before deciding whether the most appropriate oversight structures should be international, regional, national, or a combination of these levels of oversight; whether they should be voluntary or compulsory; and whether and what type of enforcement mechanisms should be enacted. The Society specifically recommends the development and use of formal, effective, easily accessible mechanisms for reporting potential violations of current societal norms.

The Society appreciates the International Commission's consideration of these comments, as well as our request for additional time to provide technical input. We look forward to working with you on these issues.