Editorial

Stem cells had already been the object of study and laboratory culture and had been used with growing effectiveness in a variety of therapeutic applications for more than 20 years, prior to the first isolation of human embryonic stem cells by Thomson in 1998. However, it has only been in the past few years that they have received considerable attention from the media, causing widespread interest in public opinion and moving enthusiasm among scientists. The hope of subsequently converting stem cells into differentiated cells of a target organ seemed to announce the imminent availability of a boundless source of replacement tissues, the era of regenerative medicine just around the corner, and a promised land for the economies of technologically advanced countries. Yet, the media themselves could not hide deep ethical concerns arising from the scientific world itself and more – from ethicists, politicians and opinion movements, with the debate bisecting public opinion and also being a matter for some national referenda.

Any future therapy using embryonic stem cells presumes that the cell lines are obtained by sacrificing lives of human embryos. Destruction of these live human embryos, which is implied by the procedures for the cells' extraction, would be ethically justified due to the great benefits promised by therapeutic applications of the stem cells. However, this pragmatic attitude conflicts also with traditional biomedical scientific research, which requires any experiment to be conducted in animals before in humans and any application in humans to be harmless, after having resolved in animals every foreseeable (and unforeseeable if possible) unwanted effect.

Over the past few years, some things have changed. On the one hand, stem cells extracted with destruction of human embryos, although easier to be cultured *in vitro*, are characterized by great, yet unsolved problems *in vivo*, such as development of tumours, the need for immune-compatible donors and/or possibility of infection from animal extracts used in human stem cell culture. On the other hand, scientific evidence has shown that stem cells from adults or from placental and umbilical cord blood cells after birth of a child, are much more abundant and easier to culture in laboratories than it had been previously believed. In addition, growing evidence, concerning possibility of transdifferentiation from one cell type to another, makes non-embryonic stem cells more attractive in terms of their ability to generate different types of tissue, and more effective for distinct types of therapy. At the time of this publication, there are at least 73 documented clinical trials or treatments using human adult or cord blood stem cells.

In order to provide an opportunity for profound reflection on these hot and popular topics, the World Federation of Catholic Medical Associations (FIAMC) and the Pontifical Academy for Life, in 2006, organized the International Congress '*STEM CELLS: WHAT FUTURE FOR THERAPY? Scientific aspects and bioethical problems*'. The Congress, which was held in Rome, Italy, 14–16 September 2006, was made possible thanks to a generous grant from the Jérôme Lejeune Foundation; it was intended to offer a forum for evaluating the current status of therapeutic applications of stem cells in different clinical fields. The impact of research into stem cells and subsequent applications to regenerative medicine, on the future of biotechnologies and on economy and politics themselves of developed countries, were also examined. In addition to the scientific updates, qualified experts in bio-ethics discussed the ethical problems arising from stem cell research and its clinical applications.

The invited lectures were presented by a faculty of distinguished speakers, coming from Europe, North America and Asia. In addition, a large arena was reserved for presentation of free oral communications and posters. For the 3 days of the Congress, more than 400 clinicians, scientists and ethicists, coming from 43 countries, had the possibility to share their experiences

and to enjoy the cosmopolitan flavour and warm hospitality of the Eternal City and the magical atmosphere of nearby St. Peter's Square. At the end of such an exciting event, it was spontaneously thought to compile a publication collecting the texts of the invited lectures together.

Sadly, time restrictions on some of the authors have not allowed this goal to be fully achieved; however, in a reasonable timeframe, we have been able to gather most of the contributions and to pass them through the necessary revision processes followed by papers submitted to such an internationally recognized journal as *Cell Proliferation*. Today, thanks to the invaluable cooperation of the Editor-in-Chief, Dr. Catherine Sarraf, we are proud to present these papers collected in a special supplement of the journal. We are confident that scholars and students will find it a useful instrument for a broad comprehensive view of the issues at stake.

The articles gathered in the supplement are grouped in three main sections. The first five examine the possibility of alternatives to embryonic stem cells in the search for pluripotent stem cells. In particular, in the first three, respectively, Condic discusses the two forms of altered nuclear transfer (ANT-OAR and ANT-GD), Brevini and Gandolfi present their studies on parthenotes, McGuckin and Forraz examine the potential and advantages of access to embryonic-like stem cells from human umbilical cord blood and Noia *et al.* demonstrate the longer persistence of human cord blood stem cells compared to human foetal bone marrow stem cells after xenotransplantation in the ovine recipient. In the fifth paper, Yamanaka presents his very innovative approach to induce pluripotent stem cells by dedifferentiating somatic cells.

The following four articles review crucial ethical problems in the field of research regarding stem cells.

In his article, Sherley reviews several key aspects of newly emerging embryonic and non-embryonic stem cell technologies as they relate to the debate over the use of human embryos for medical research; convinced that without valid disclosure, misinformation can erode the legitimacy of any public debate. Following the recent disturbing fact that three major scientific journals had to retract significant claims about progress in this field, Doerflinger, responsible for one of the debates on scientific correctness, discusses the problem of deception in embryonic stem cell research. Finally, anthropological and ethical reflections on the production and use of embryonic and, alternatively, adult stem cells, are presented in the articles of Faggioni and, respectively, of Carrasco de Paula.

The third part of this supplement is more specifically devoted to presentation of some clinical applications of stem cells. Unfortunately, not all the contributions presented during the Congress in Rome could be gathered in time, nevertheless the reader will find up-to-date and interesting articles regarding human stem cells in genetic (Mackay-Sim and Silburn), neurological (Hess and Borlongan), hepatic (Levičar *et al.*), cardiac (Strauer *et al.*) and vascular (Jevon *et al.*) diseases, all contributions coming from most experienced and scientifically active centres.

The debate on stem cells is, of course, still open, but its most recent developments demonstrate how sound was the approach taken in the Congress and how innovative and authoritative were some of the contributions presented in Rome. One resounding example will be sufficient for all.

Just a few days before writing this editorial, after Dr. Shoukhrat Mitalipov and colleagues at Oregon Health & Science University, Beaverton, OR, USA, announced a breakthrough in the cloning of primate embryos, Prof. Jan Wilmut, the scientific father of Dolly the sheep, working at Edinburgh University, declared that the method pioneered in Japan by Prof. Yamanaka (presented for the first time in Europe just on the occasion of the Congress in Rome!) has better potential for making human stem cells that can be used to grow a patient's own cells and tissues for a vast range of treatments and will be less controversial than the nuclear transfer.

The press immediately realized the concept of his announcement would mark the beginning of the end for therapeutic cloning, on which tens of millions of euros have been spent worldwide

over the past decade. The research (Prof. Shinya Yamanaka, University of Kyoto, Japan), which inspired Wilmut's declaration, suggests a way to revert adult skin and connective tissue cells to an embryonic state (dedifferentiation). This new method would allow generation of patient-specific stem cell lines that would not need the use of human eggs. Cloning is too wasteful of precious human eggs, which are in great demand for fertility treatment, to consider creating embryonic stem cells. In addition, Yamanaka's method does not require creation and destruction of human cloned embryos, which would raise serious ethical concerns. Finally, stem cells produced by Yamanaka would also solve problems of immunological rejection, because they are the recipient's own cells.

The pioneering work of Yamanaka, recently published in *Cell* and reproduced independently for foetal and neonatal epidermal cells by the Wisconsin-based team of James Thomson (results published in *Science*), has the potential to bring all sides of the human cloning debate together, in a common quest for aggressive, yet ethical stem cell research. In addition, it should also mark the end of proposals to create animal/human hybrid embryos, made to overcome difficulties of obtaining sufficient human eggs, as this now could become irrelevant.

On the last day of the Congress, the speakers and the participants were received in Castelgandolfo by Pope Benedict XVI, who addressed them in an important speech in which he manifested strong appreciation for scientific advancements in the field of stem cell research and encouraged further development of studies able to combine 'scientific knowledge, the most advanced technologies in the biological field and ethics that postulate respect for the human being at every stage of his or her existence'. The complete text of the papal speech is reported immediately after this editorial.

At the end of this editorial, we would like to thank Dr. Sarraf once again, Editor-in-Chief of *Cell Proliferation*, for her continuous guidance and support, all the reviewers who promptly examined the manuscripts and offered their precious comments, Dr. Anna Serafini for her editorial assistance and the entire staff of Blackwell publishing for their competent commitment in facilitating (in respect of time schedules and high technical standard achieved) of the entire supplement.

Supplement Editors, this issue of *Cell Proliferation*:

Gian Luigi Gigli
Professor of Neurology
University of Udine, Udine, Italy
Past-President of FIAMC

Elio Sgreccia
Former Professor of Bioethics
Catholic University Medical School, Rome, Italy
President of the Pontifical Academy for Life