INFRASTRUCTURE INGESTEM PLURIPOTENCY and CELL DIFFERENTIATION for DISEASE MODELLING and REGENERATIVE MEDICINE

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The last decade has witnessed major developments in the area of stem cell research which culminated with the demonstration of programming adult cells into a pluripotent stem cell state (Shinya Yamanaka, 2006). This demonstration is currently revolutionizing biomedical research and encourages optimism for future medical applications in all fields.

Extensive research under way has shown that the induced pluripotent stem cells (hIPSC) are very close to human embryonic stem cells (hESC) but compared to the latter they have some differences inherent, to the target cells which have been programmed, the methods of programming and the potential of differentiation. iPSC have several advantages as compared to hESC from the ethical point of view and with regards to the autologous nature of the cells in potential cell therapy applications.

One of the major applications, which have been envisioned, is the use of iPSC technology in modeling genetic or non-genetic diseases with the goal of generating differentiated cells of three germ layers with the hope of unraveling the pathophysiology of diseases which cannot be studied in vivo. Several disease-modeling examples are already available showing the major potential of this technology in this field but also their pitfalls in terms of efficiency of cell programming and induction of differentiation programs.

Several hurdles need to be resolved before clinical applications of the hIPSC-derived differentiated cells, the outset being the efficiency of standardized differentiation protocols. Similarly, due to the nature of the cell programming protocols and the pluripotency genes used, the problems concerning genetic instability of these cells need to be addressed before their use in biomedical research. Similarly, several aspects of the programming process remain poorly understood, especially in terms of recurrent genetic and epigenetic changes, suggesting that basic research efforts need to be performed in this field concomitant to permanent and rapid transfer to the biomedical applications.

The french national consortium “INGESTEM” will provide to the biomedical and research community, a major implementing condition for the development of translational research and clinical applications nationwide by building a national biobank of pluripotent stem cells and their derivatives generated from both normal and diseased tissues including cancer. The proof of concept of cell programming from hematopoietic malignancies will be extended to other cancers with the objective of generating cancer-initiating stem cells. The availability of pluripotent stem cell adapted high throughput screening strategies will allow the rapid assessment of highly purified stem cell populations with regard to their drug sensitivity in the context of cancer stem cells and other diseases. The optimal technique for generation of large amounts of clinical-grade iPSC and their differentiated derivatives will be tested as a prerequisite for their potential clinical use.