## Press release

# Identification of a recurrent chromosomal anomaly in neural cells derived from pluripotent stem cells (ES and iPS).

Paris, 25 January 2012

**At a time when the first regenerative medicine clinical trials are being performed using pluripotent stem cells, teams from the I-Stem Institute, directed by Marc Peschanski (Inserm Research Director), are continuing to explore the quality criteria that must be adopted to best ensure patient safety.**
**Three years ago, an I-Stem team identified a genomic anomaly that very frequently appeared in undifferentiated cell lines when the latter were forced to perform too great a number of proliferation cycles[1]. The same team, directed by Nathalie Lefort (Inserm Research Engineer), has today demonstrated the systematic occurrence of a genomic anomaly in differentiated neural stem cells, beginning at these lines, after several dozen replication cycles. The details of this research are published in the Journal of Clinical Investigation, dated 24 January. This research received backing from Inserm and the AFM thanks to donations from a Telethon.**

Pluripotent stem cells can differentiate into any other cell in the body if they are subjected to a suitable environment. As such, they represent a major beacon of hope for the treatment of several degenerative diseases, since they can conceivably be used to replace sick or lost cells. Last year, the American Regulations Agency (FDA) authorized the launch of the first cell therapy clinical trials (based on differentiated cells using pluripotent stem cells). All the trials currently in progress use progenitor cells from the nervous system (central or retinal).

Nathalie Lefort's team has been focussing on neural progenitors of the same type, resulting from the differentiation of pluripotent stem cells of an "iPS" embryonic or lined origin (induced pluripotent through the genetic reprogramming of adult cells). The researchers were surprised to observe that they could be cultivated over very long periods – well over one hundred replication cycles – without ever reaching senescence. This is surprising since all cells in the body are programmed to fulfil a limited number of divisions before reaching senescence (generally to the order of a few dozen).

The occurrence of some chromosomal anomalies may lend mutated cells the capacity to divide up an infinite number of times. Nathalie Lefort and her collaborators thus concentrated their research on these anomalies. They found them in the neural progenitors that they cultivated. Interestingly, they were not random disorders. A single type of chromosomal rearrangement was observed: duplication of long arm chromosome 1 (arm 1q), accompanied by a translocation of this supernumerary arm to another chromosome (random). This type of chromosomal anomaly has already been described in haematological malignancies under the name of "jumping translocation", and sometimes in solid tumours (breast cancer, hepatocellular carcinoma, retinoblastoma, paediatric brain tumours). The presence of this chromosomal rearrangement is still associated with a poor prognosis for patients. Therefore, this new data demonstrates that, during the long-term cultivation of neural progenitors derived from pluripotent stem cells, the duplication of arm 1q provides a massive advantage, resulting in the selection of abnormal cells. An additional

[1] Lefort N et al., *Human embryonic stem cells reveal recurrent genomic instability at 20q11.21*. ***Nature Biotechnology*** 2008 ; 26 : 1364-6

interesting result of this research: it is not one of the chromosomal anomalies identified in the undifferentiated pluripotent stem cells, which means that it did not predate the differentiation of neural progenitors, it appeared afterwards.

This discovery provides researchers and clinical practitioners with the opportunity to identify this recurrent anomaly at each stage of cell therapy; thus systematically eliminating the preparations that would be likely to present a risk for the patient.

## For more information

## Source

*Recurrent genomic instability of chromosome 1q in neural derivatives of human embryonic stem cells.* ***Journal of Clinical Investigation*** 2012*; in press, sortie prévue le 24 janvier 2012.*
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