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Scientists announce human intestinal stem cell 'breakthrough' for regenerative medicine

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Human colon stem cells have been identified and grown in a lab-plate for the first time. This achievement, made by researchers of the Colorectal Cancer Lab at the Institute for Research in Biomedicine (IRB Barcelona) and published in Nature Medicine, is a crucial advance towards regenerative medicine.

Throughout life, stem cells of the colon regenerate the inner layer of our large intestine in a weekly basis. For decades scientists had evidences of the existence of these cells yet their identity remained elusive. Scientists led by the ICREA Professor and researcher at the Institute for Research in Biomedicine (IRB Barcelona, Spain) Eduard Batlle discovered the precise localization of the stem cells in the human colon and worked out a method that allows their isolation and in vitro expansion, that is their propagation in lab-plates. Growing cells outside the body generally requires providing the cells in a lab-plate with the right mix of nutrients, growth factors and hormones. But in the same way that each of the more than 200 types of cells in our body differs from the others so too do optimal growing conditions in the lab. Consequently, human adult stem cell culture in labs has been a truly impossible mission until now. Batlle's team has also established the conditions for maintain living human colon stem cells (CoSCs) outside of the human body: "This is the first time that it has been possible to grow single CoSCs in lab-plates and to derive human intestinal stem cell lines in defined conditions in a lab setting," explains the IRB Barcelona researcher Peter Jung, first author of the study together with Toshiro Sato, from the University Medical Center Utrecht in The Netherlands.

The development, published by Batlle's research group in the prestigious journal *Nature Medicine,* arrives after more than 10 years of intense research focused on the characterization of the biology of the intestinal stem cells and its connection with cancer. The research has been made possible by close collaboration between Batlle's team and the group led by Hans Clevers at the Hubretcht Institute and University Medical Center Utrecht in The Netherlands, and María A. Blasco at the Spanish National Cancer Research Centre in Madrid (Spain). "For years, scientists all over the world have been trying to grow intestinal tissue in lab-plates; testing different conditions; using different nutritive media. But because the vast majority of cells in this tissue are in a differentiated state in which they do not proliferate, they survived only for a few days", explains Jung. "The aim of this study was to find a way to identify and select individual CoSCs and to grow them while maintaining their undifferentiated and proliferative state in lab conditions. Thus, we would be able to model how they grow —in number— and differentiate into normal intestinal epithelial cells in lab-plates", continues Jung. The scientific community now has a defined 'recipe' for isolating CoSCs and deriving stable CoSCs lines, which have the capacity to grow undifferentiated for months. In fact, "now we can maintain stem cells in a plate up to 5 months or we can induce these cells to differentiate artificially, as they do inside our bodies".

"This achievement opens up an exciting new area of research with the potential to bring about a huge breakthrough in regenerative medicine", says Jung. Regenerative medicine — or the idea of repairing the body by developing new tissues and organs as the old ones wear out— involves growing new cells from patients into tissues and organs in a lab. However, the main element for making regenerative medicine a reality, namely adult stem cells, are just starting to be understood. "Now that guidelines for growing and maintaining colon stem cells in the lab are in place, we have an ideal platform that could help the scientific community to determine the molecular bases of gastrointestinal cell

proliferation and differentiation. It is also suspected that alterations in the biology of CoSCs are at origin of several diseases affecting the gastrointestinal tract, such as colorectal cancer or Crohn's disease, an autoimmune and inflammatory disorder. Our discovery also paves the way to start exploring this exciting field," finishes Jung.

Provided by IRB Barcelona