



# Juan Carlos I. Belmonte

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**“Our ultimate goal is to try to understand the molecular and cellular basis of organ and tissue regeneration.”**

Ever since the first adult cells were converted into induced pluripotent stem cells (iPSCs), they have generated excitement as an alternative to embryonic stem cells and a potential source for patient-specific stem cells. Unfortunately, reprogramming adult cells into iPSCs is a slow, inefficient, and costly process and carries the risk of cancer, limiting the cells' therapeutic value. Two recent studies in Izpisúa Belmonte's lab, however, offer the prospect of safer, faster, and more efficient approaches to coaxing cells back in time.

The most widely used technology involves the forced expression of four transcription factors in fully committed adult cells: Oct4, Sox2, Klf4, and c-Myc. Because only a tiny fraction of cells transdifferentiate into iPSCs that look and act like embryonic stem cells, Izpisúa Belmonte wondered whether the process used to reprogram the cells was inducing a response that stopped them from growing. Izpisúa Belmonte and his team showed that adding Klf4 and c-Myc, which are oncogenes, activated the pathway for the tumor suppressor p53. In cells genetically engineered to lack p53, reprogramming efficiency

increased at least tenfold, clearly demonstrating the important role that p53 played in reining in cells trying to revert back into a stem-like state. Because iPSCs generated with the full complement of reprogramming factors can turn malignant, Izpisúa Belmonte and his team also tried reprogramming mouse cells lacking p53 using only Oct4 and Sox2. The cells readily converted into iPSCs and gave rise to healthy, full-term mice that were able to reproduce, passing the ultimate test for pluripotent embryonic stem cells.

In related work, Izpisúa Belmonte's group set out to transform immunologically immature hematopoietic stem cells isolated from umbilical cord blood into iPSCs. They not only successfully converted them using only Oct4 and Sox2, but did so in less time than any previously published methodology. The resulting iPSCs were indistinguishable from human embryonic stem cells and passed all standard tests for pluripotency, establishing the possibility of a comprehensive bank of tissue-matched, cord blood-derived stem cells.

For more information, please visit  
[salk.edu/faculty/belmonte.html](http://salk.edu/faculty/belmonte.html)

**Left to right:**

*Back row:* Athanasia Panopoulos, Emmanuel Nivet, Jun Li, Leo Kurian, Sergio Menendez, Sunny Yang

*Front row:* Ilir Dubova, Basam Barkho, Guanghui Liu, Chris Walsh, Alex Bukrinsky, Concepcion Rodriguez Esteban, Juan Carlos Izpisúa Belmonte, May Schwarz, Scott Stewart

