Pluripotency genes and their action in development and cell culture

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Introduction

The early stages of development are crucial for a proper formation of the embryo. Huge changes happen in a very small window of time, and pluripotency plays a key role in this process. Understanding the major genes responsible for pluripotency, as well as the factors that affect this process is essential not only to comprehend the changes that happen in the first days of development, but also to efficiently culture and derive stem cells.

Methodology

The material used has been obtained from primary research papers and reviews, reached using web search engines as Pubmed, and using key words as pluripotency, Oct4, Sox2, Nanog, embryo. Research has also been limited mainly to the past 5 years of publication and acquired from indexed journals such as: *Cell, Nature, Development,…*

Pluripotency

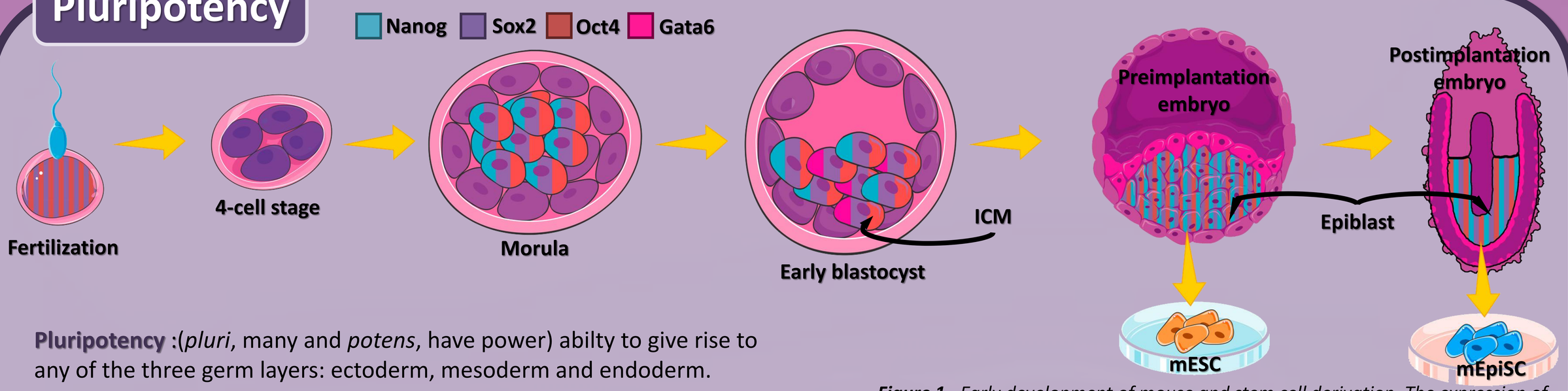


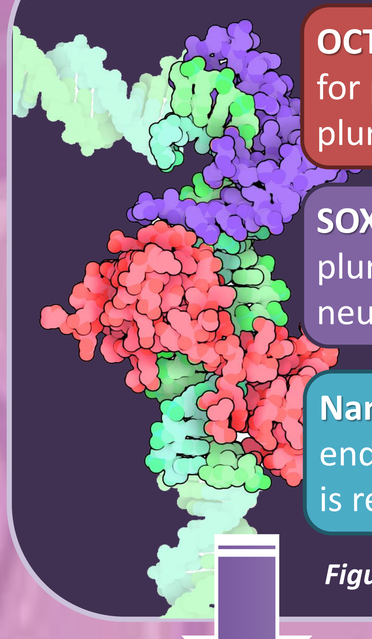
Figure 1. *Early development of mouse and stem cell derivation. The expression of the core transcription factors is showed aswell. Adapted from: Servier Medical Art (1)*

Pluripotency :(*pluri*, many and *potens*, have power) abilty to give rise to any of the three germ layers: ectoderm, mesoderm and endoderm.

Epiblast formation is the onset of pluripotency, but this potency is eventually lost: pluripotency in development is **transient** and **plastic**.

Embryonic Stem Cells (ESCs) are derived from **epiblast** . Preimplantation epiblast forms **ESC;** post-implantation epiblast derives **EpiESC** . Epiblast Embryonic Stem Cells posses similar characteristics to human ESC (hESC).

Pluripotency transcription core



OCT4. Expression restricted to ICM and epiblast. Essential for pluripotency maintenance. Pivotal role on the pluripotency transcription core.

SOX2. Expression at the ICM and epiblast, critical to sustain pluripotency, but not restricted to it. Also present in the neuroectoderm. Forms a complex with Oct4.

Nanog. Heterogeneous expression at ICM, prevents endoderm differentiation. Downregulated at implantation is re-expressed at postimplantation epiblast.

Figure 2. *Oct4-Sox2 complex binding to DNA. Adapted from PDB (2).*

Pluripotency gene targets

Oct4, Sox2 and Nanog share over 350 targets, they act synergistically (with the help of other TF) to activate genes as chromatin remodeling and histone modifying complex, signaling pathway proteins, pluripotency TF, and repress tissue differentiating factors.

Stem cell derivation

Pluripotency can be propagated *in vitro* using ESC. Pluripotency genes used to induce pluripotency on somatic cells, as well as to support ESC in culture. ESC present a heterogeneous expression of the genes, thought to make culture more stable.

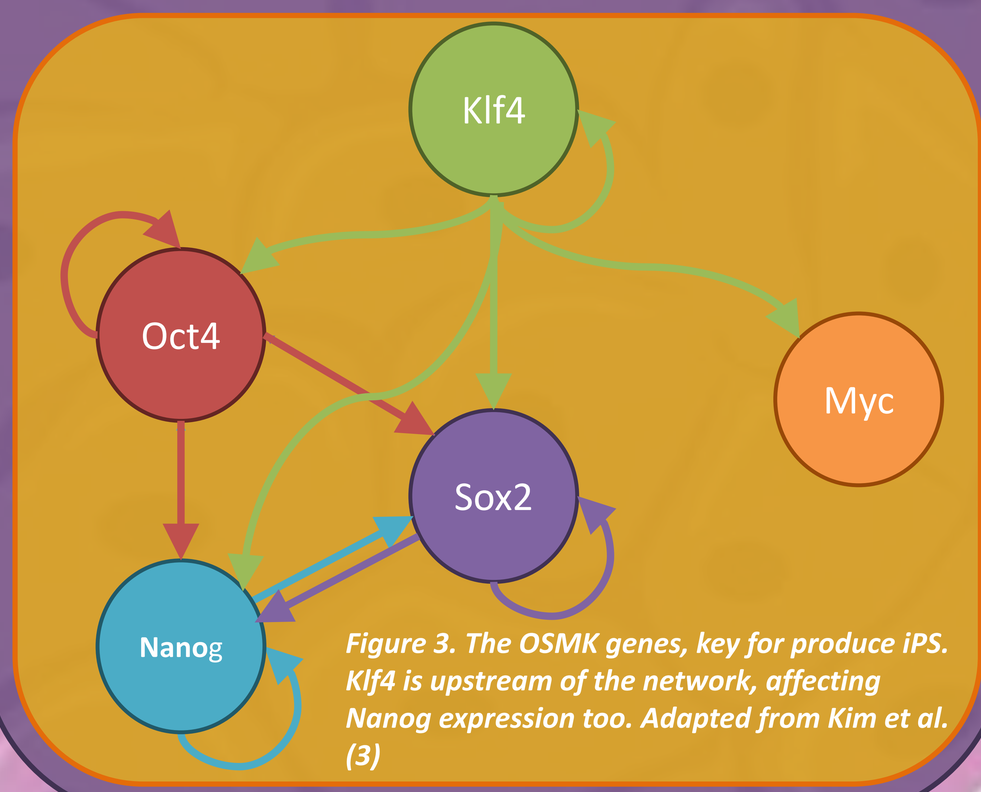


Figure 3. The OSMK genes, key for produce iPS. Klf4 is upstream of the network, affecting Nanog expression too. Adapted from Kim et al. (3)

Conclusions

This review represents a small contribution to the vast field of pluripotency and stem cells. Understanding the processes and genes behind pluripotency is essential to properly culture embryonic stem cells. Several questions remain unanswered. Why ESC present a heterogeneous expression is still not fully understood. Epigenetics –through histone modification and non-coding RNAs– plays a huge a yet fully unknown paper on pluripotency, and more research is needed on this area.

1. SERVIER LABORATORIES. Slide kit. Cell culture and microbiology [Internet]. 2012 [cited 2015 May 30]. Available from: http://www.servier.es/content/slide-kit?item=27
2. Reményi A, Lins K, Nissen LJ, Reinbold R, Schöler HR, Wilmanns M. Crystal structure of a POU/HMG/DNA ternary complex suggests differential assembly of Oct4 and Sox2 on two enhancers. Genes Dev. 2003 Aug 15;17(16):2048–59.
3. Kim J, Chu J, Shen X, Wang J, Orkin SH. An extended transcriptional network for pluripotency of embryonic stem cells. Cell. 2008 Mar 21;132(6):1049–61.