Pluripotent cells in developing embryos

Pluripotency is a transient state in vivo. It is acquired within the ICN of developing pre-implantation blastocysts, when cells of the ICN aggregate into a pluripotent pre-implantation naive epiblast, and is gradually lost during early post-implantation development, before cells differentiate somatic lineages. This transition from a pre-implantation pluripotent state to a post-implantation pluripotent state, which are referred to as naive and primed states, respectively, is associated with changes in molecular and functional characteristics.

Differences between human and mouse pre- and post-implantation pluripotent cells in vitro are due to the different requirements for their maintenance.

Gene expression in pre-implantation embryos

**Epiplastic**

<table>
<thead>
<tr>
<th>Gene expression</th>
<th>Human</th>
<th>Mouse</th>
</tr>
</thead>
<tbody>
<tr>
<td>KLF2</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>KLF17</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>ERK5</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>NOD1</td>
<td>High</td>
<td>Low</td>
</tr>
</tbody>
</table>

**Post-implantation embryonic (E-E2.5)**

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**Naive and primed properties of pluripotent cells in vitro**

Naive and primed states can be classified by the basis of multiple characteristics and can be distinguished from each other. Differences in the expression of endogenous factors confer distinct characteristics to pluripotent stem cells in vitro. As a result, cells acquire a distinct set of naive and primed properties. In mice, ESCs cultured in a medium supplemented with 2i (two inhibitors of MEK and GSK3) and LIF, and EpiSCs cultured in a medium containing FGF2 and LIF, constitute the two extremes of the naive and primed pluripotency spectrum maintained in various media and in different culture conditions.

**Naive ESCs**

- Nansig (NANOG), KLFs, ESRRb
- High expression of OCT4
- High expression of β-catenin
- High expression of prolactin

**Primed EpiSCs**

- Low expression of OCT4
- Low expression of β-catenin
- Low expression of prolactin
- High expression of FBS

**Additional regulatory pathways**

- MEK/ERK signaling
- TGFβ, GSK3, and β-catenin
- β-catenin-mediated transcription
- Wnt/b-catenin signaling
- JNK signaling
- p38 signaling
- PKC signaling
- FGF signaling

**Naive state**

- High expression of β-catenin
- High expression of prolactin
- High expression of FBS

**Primed state**

- Low expression of β-catenin
- Low expression of prolactin
- Low expression of FBS

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**Generation of human-induced pluripotent stem cells (iPSCs)**

- 504–511 (2011) | Tesar, P. J.

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**References**

- http://www.nature.com/nrm/posters/pluripotency