The power of cell autonomous growth in the absence of ERK signalling is gained just before implantation

Summary
One of the defining features of naïve pluripotent mouse embryonic stem cells (ESCs) is their ability to thrive in the absence of Erk signaling. Dual inhibition of Gsk3 and Mekk (2i) has been proposed to “capture” cells in a naïve ground state directly from late preimplantation epiblast.

We set out to identify at which stage ICM/epiblast cells become responsive to 2i plus LIF during early embryonic development at a single cell level. We found that only cells isolated from E3.75-E4.5 embryos were able to give rise to germline competent ESCs in these minimal conditions. In contrast, earlier ICM cells had a tendency to remain in culture for prolonged periods of time, without undergoing apoptosis or cell division. Finally, by mimicking the in vivo environment with a defined matrix, a protocol was established to routinely derive 10 clonal ESC lines per embryo.

This supports the hypothesis that naïve pluripotency is a transient state, which can be directly captured in vitro.