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STAT3 and BMP-receptor 1a functionally interact in different stem cell types

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Introduction:

Stem cell status is maintained and ended by mixtures of signals received and interpreted by the cells. The often referred to stem cell niche is such a mixture of signals and varies strongly for most stem cell types. Our approach to identifying the signaling mechanisms underlying these different effects include inter- as well as intraspecies comparison of signal-cascade statuses in stem cells.

Materials and Methods:

Using an array of different stem cell types from the lower vertebrate medaka (Oryzias latipes) and the mouse, we have compared the signalling activity as well as the signal-complex make-up and its consequences on upkeep of stemness versus differentiation. We used approaches such as co-immunoprecipitation, HPLC fractionation, immunofluorescence and real-time PCR as well as live-imaging of fluorescently tagged signal-mediators such as STAT3.

Results:

We were able to demonstrate that the pluripotency of medaka stem cells as well as medaka blastula embryos are independent of STAT3 activity. Furthermore, biochemical analyses of the signalling complexes downstream of BMP2 revealed the presence of STAT3. Next, we found STAT3 modified and re-located to the cytoplasm as a result of ligand-engagement of BR1a in embryonic stem cells. Alteration of the composition of the complex also changed differentiation behaviour of neural stem cells.

Discussion and Conclusions:

While our comparison between pathways necessary for pluripotency in both mouse and medaka revealed strong differences both in vivo and in vitro, all the systems analysed thus far share a common, huge signal-integrator complex. Amongst other proteins, this complex includes the BMP-receptor 1a and STAT3. Treatment of stem cells with different BMP ligands results in re-localisation and secondary modification of STAT3. The presented data a hence first evidence for a functional crosstalk between these pathways.