

Computational integration of homolog and pathway gene module expression reveals general stemness signatures.

Journal: PLoS One

Publication Year: 2011

Authors: Martina Koeva, E Camilla Forsberg, Joshua M Stuart

PubMed link: 21559491

Funding Grants: Mechanisms of Stem Cell Fate Decisions , Training Program in Systems Biology of Stem Cells

Public Summary:

Because all stem cells are defined by their ability to give rise to both new stem cells and to more differentiated cells, we hypothesized that stem cells use similar mechanisms to regulate their function. This report describes the results from global gene expression analyses of 12 different stem cell types, focusing on gene families and regulatory units that are coordinately up- or downregulated in multiple stem cell types.

Scientific Abstract:

The stemness hypothesis states that all stem cells use common mechanisms to regulate self-renewal and multi-lineage potential. However, gene expression meta-analyses at the single gene level have failed to identify a significant number of genes selectively expressed by a broad range of stem cell types. We hypothesized that stemness may be regulated by modules of homologs. While the expression of any single gene within a module may vary from one stem cell type to the next, it is possible that the expression of the module as a whole is required so that the expression of different, yet functionally-synonymous, homologs is needed in different stem cells. Thus, we developed a computational method to test for stem cell-specific gene expression patterns from a comprehensive collection of 49 murine datasets covering 12 different stem cell types. We identified 40 individual genes and 224 stemness modules with reproducible and specific up-regulation across multiple stem cell types. The stemness modules included families regulating chromatin remodeling, DNA repair, and Wnt signaling. Strikingly, the majority of modules represent evolutionarily related homologs. Moreover, a score based on the discovered modules could accurately distinguish stem cell-like populations from other cell types in both normal and cancer tissues. This scoring system revealed that both mouse and human metastatic populations exhibit higher stemness indices than non-metastatic populations, providing further evidence for a stem cell-driven component underlying the transformation to metastatic disease.

Source URL: <https://www.cirm.ca.gov/about-cirm/publications/computational-integration-homolog-and-pathway-gene-module-expression-reveals>