2011.02.21-25 FANTOM 5 UME BLOSSOM MEETING

FUNCTIONAL ANNOTATION OF THE MAMMALIAN GENOME

Main Paper 2:
Specific and general transcriptome hallmarks of cell differentiation

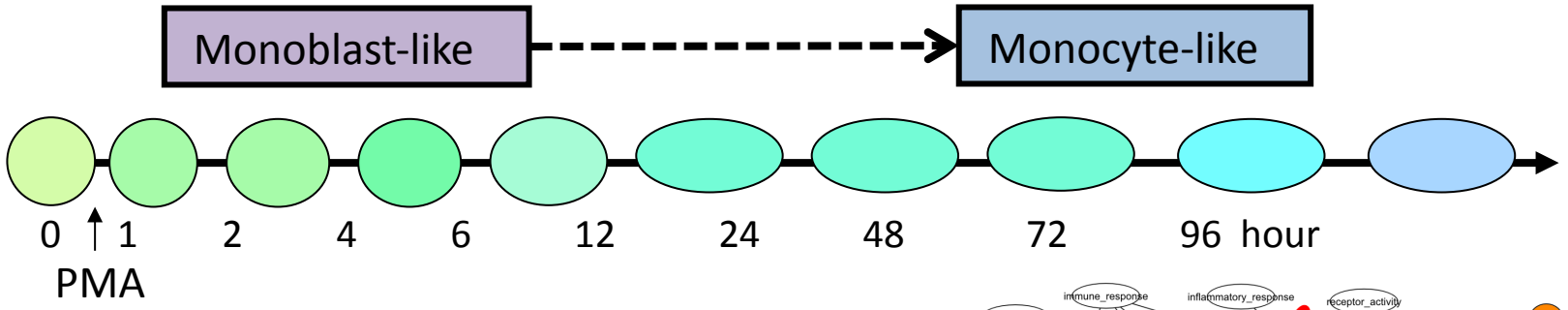
Carsten O. Daub

RIKEN OSC

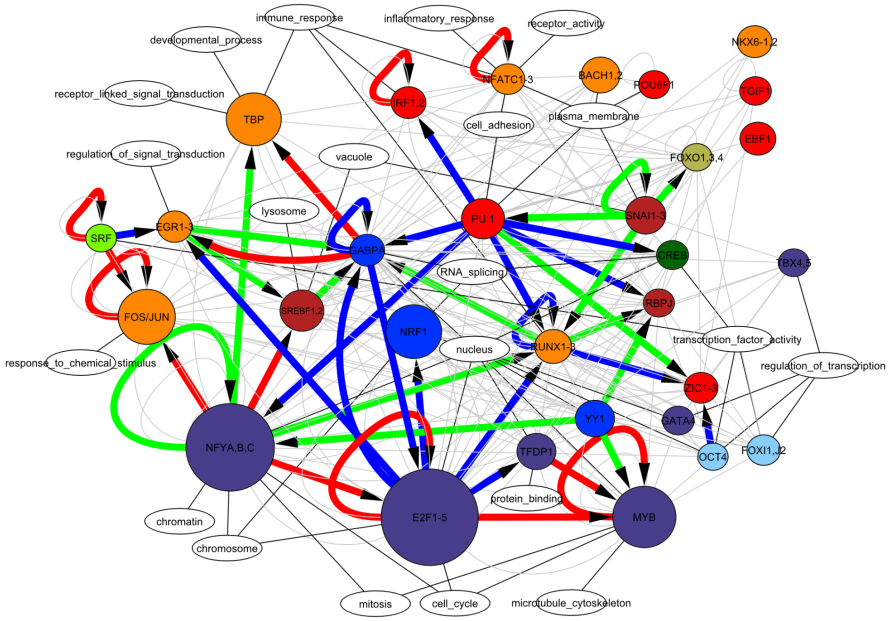
2011-02-20

FANTOM4 – Cell Differentiation

- THP-1 differentiation time course



- Regulatory network
- Basin (stable state) characterization
- Key factors *de-novo*



Time courses

Human

David Hume/Kenneth Baillie/Geoff Faulkner – Human macrophage LPS response timecourse

Mariko Okada – MCF7 response to Heregulin and epidermal growth factor timecourses

Levon Khachigian – Aortic SMC response to FGF2 and IL1b timecourses

Peter Arner/Niklas Mejhert – differentiation of primary preadipocytes, hMADs differentiation timecourse to adipocyte

Kim Summers – Calcification time course using Saos2 cells

Michael Detmar - lymphatic endothelial cells response to VEGFC

Peter Klinken/Louise Winteringham – Erythroid differentaion of K562 cells upon hemin treatment

Christine Wells – iPS to neurons timecourses (Down's patients and matched controls), CD34 differentiation timecourse to monocyte and granulocyte

Meenhard Herlyn/Susan Zabierowski – Differentiation of ES cells to melanocyte

Christine Mummery/Robert Passier - Differentiation of ES cells to cardiomyocyte

Mouse

Dan Goldowitz/Thomas Ha – cerebellum development time course

Peter Klinken/Louise Winteringham – Erythroid differentaion of J2E cells upon erythropoietin treatment

Yasushi Okazaki – ST2 mesenchymal stem cells differentiating towards osteoblast and adipocyte

Kawamoto/Tomokatsu Ikawa – EBF KO model of T cell differentiation timecourse

Slide borrowed from Al Forrest

Punch Lines

- General principles of cell differentiation
  - General key elements (genes + others) involved in all differentiations
    - Including basic human and mouse comparison
    - There are always some *agitator type* factors?
  - Specific key elements (genes + others) for each of the differentiation time courses
    - Elements specific for each germ layer?
  - Promoter cell map (Paper 1) required for this step

Punch lines (2)

- What is specific for early responses?
- Present & validate specific novel key elements for one of the time courses
- Pave the way for systematic cell conversion

Factors in addition to HeliscopeCAGE

- Distal regulatory elements
  - Enhancers, insulators
- Recognize ncRNAs involved in differentiation
- Epigenetic factors
- DNA structure

Roadmap

- Map time course to differentiation tree
- Draw the regulatory networks for each differentiation system
- Integrate enhancers, miRNA, etc.
- Characterize the stable state networks (basin)
- Characterize the transitions between start end end state
  - Based on network

Required for Paper

- Continuous stable data production
- Close collaboration with all time-course samples providers
  - Understand the available differentiation systems
  - Maybe consider additional time courses
- Consistent analysis for all time courses
- Systematic analysis and interesting findings
- Reliable validations