Cellular Programs

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Summer Semester 2025 — Chair of Computational Biology

Assignment 4

Handed out: 27.05.25

Due: 03.06.2025 10.00 am

Submit your solutions by e-mail with a single PDF attachment

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Label your pdf solution as MATRICULATIONNR_YOURNAME.pdf.

Every student should submit his/her own solution. Plagiarism of solutions will be penalized. Indicate whether you used AI tools. Label your assignment sheet with your name and matriculation number. Don't exceed specified page lengths by more than 0.25 pages.

All problems refer to paper #8: Lilja Li et al. Science, 382, eadi5516 (2023).

Problem 1:

Immediately after fertilization, the zygotic genome is transcriptionally inert. The initiation of gene expression by the zygotic genome is called zygotic gene activation (ZGA), which occurs according to species-specific timing. In Medaka (topic of assignment 3), zygotic genome activation occurred at the 4000-cell stage. Interestingly, mice undergo transcription initiation much earlier, namely already during the S phase of the 1-cell stage. (PMID: 35034936). In mouse, implantation occurs at E4.5.
2i ESC and EpiLC are two cell lines that enable developmental biologists to study cell differentiation *in vitro* instead of via animal experiments.

Fig. 1A bottom panel shows RPKM levels for Sox2 from RNAseq measurements for different stages of mouse development. Sox2 seems to be active during 5 stages, both before and during implantation and after implantation. Also shown are data for 2i ESC and EpiLC cells. Clustering of the joint data gave 8 clusters. Explain which sorts of SOX2-related differentiation processes can also be studied in vitro using 2i ESC and EpiLC cells instead of using mouse embryos? (0.25 page).

Problem 2:

ATAC-seq (Assay for Transposase-Accessible Chromatin with sequencing) is a technique used to assess genome-wide chromatin accessibility.
What is the role of ATACseq experiments in characterizing “pre-access” sites as shown in Fig. 3? Describe the ATACseq results for E3.5 ICM specific sites and for E4.5 Epi specific sites. Which sites (E3.5 ICM specific sites or E4.5 Epi specific sites) correspond to “settler” sites, which ones to “pioneer” sites? Explain your answer using the evidence of Fig. 3, e.g. “panel X shows … Hence, … sites can be classified as settler sites.” (0.25 page).

Problem 3:
(a) Use the evidence of Fig. 4A to describe the mechanistic role of the transcription factor TFAP2C (0.1 page)

(b) Does Fig. 4B suggest that TFAP2C is a pioneer transcription factor itself? Explain your answer. (0.1 page)

(c) The left-most column of Fig. 4D shows that Sox2 binds in many “pre-access” sites in a TFAP2C-knock-out mouse. How does this compare with the two “8C ATAC” columns “ctrl” and “Tfap2C KO”? (0.1 page)