Activity Report

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Summary

In the year 2022, we got a SNIC project with 14 x 1000 core-h/month computing allocation and 12500 GiB storage allocation from Castor and 12500 GiB from Cygnus. We used around 13.6% of the computing allocation and 72.1% of the Caster and 69.6% from Cygnus storage allocation.

The major scientific achievements are we mapped 14 samples with the 10x snRNA-seq data of placentas from normal weight control and women with obesity.

Our study delves into the distinctive responses of placental cell types to maternal obesity and their correlation with infant birth weight. Using single-nuclei RNA sequencing, we analyzed human placental samples from a Chilean cohort, stratified into three groups: normal maternal BMI and appropriate baby birthweight for gestational age (N-AGA, n=4); obese AGA (O-AGA, n=4) with maternal BMI 30≤ BMI<35; and obese with large baby birthweight for gestational age (O-LAGA, n=4).

Thirteen major cell types were identified and all cell types presented differentially expressed genes (DEGs). Notably, in syncytiotrophoblast, gene expression increased in both obese groups, with a more pronounced effect in the O-AGA group. Conversely, in cytotrophoblast cells, the gene expression decreased in obese groups, with a more significant decrease in the O-AGA group. Fibroblasts from the O-LAGA group exhibited 87 DEGs compared to N-AGA, while the O-AGA group had 43 DEGs.

Pathway analysis revealed perturbations in hormonal response and secretion in syncytiotrophoblasts, modulation of nutrient sensing and tissue growth regulating pathways in cytotrophoblasts and altered responses to oxygen-containing molecules in fibroblasts from placentas of obese mothers. These results help advance our understanding of the placenta's role in fetal development and shed light on the potential adverse effects of maternal obesity on both maternal and fetal health.

Our next major analysis workload is:

- To integrate with recent public data from term placentas of healthy controls.
- To analyze placentas from women with PCOS treated with a placebo, PCOS treated with metformin and healthy controls
- To analyze the placentas of women with T1D and healthy controls.

Using this progress, we have applied for several grants to further validate the upcoming results in organoids, further mouse models, and humane samples. We have collected all planned PCOS samples and started sample collection from patients with type 1 diabetes and healthy controls for further translation of our results into clinical usage.

Publications list

As of this date, no papers have been published as the project started last year. The manuscripts originating from this project are under draft.

Academic achievements

The PhD student responsible for this project passed her half-time examination majorly presenting the progress of this project. She presented this project in the seminar in the department at KI. She submitted the abstract to attend the annual meeting of the Society of the Study of Reproduction. She plans to submit the abstract to the ECCB2024 and single-cell genomics in 2024. For these meetings, she applied for the grant from KI travel grant, the Högre stipendier from Gålöstiftelsen, and ELIXIR.

E-infrastructure related developments

A GitHub repo: https://github.com/brainfo/omics_utils for temporary developments related to code optimization and visualization from this SNIC project. A snakemake pipeline for snRNA-seq downstream analysis: https://github.com/brainfo/snRNAsnake. A bookdown discussing the snRNA-seq analysis: https://brainfo.github.io/book/ and a manuscript discussing principles of snRNA-seq analysis: https://brainfo.github.io/portfolio/pdfs/snRNAseqPrinciple-HongJiang.pdf

Grants and patents

This research is supported by a grant from Barndiabetesfonden (2022) and Diabetesfonden (2022), as well as a. CSC from China to cover a PhD student salary (2021-2025).

Acknowledging SNIC

Yes, whenever we have research output as publications or patents, we will give SNIC credit.