Activity Report (Dnr: SNIC 2020/12-34)

Project Title: Context dependence of the co-transcriptional activators Yap/Taz in the lung epithelium of Idiopathic Pulmonary Fibrosis
Type: SNIC Small Storage
Start Date: 2020-09-10
End Date: 2021-10-1
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Summary

The aim of the project is to examine molecular mechanisms driving the lethal disease idiopathic pulmonary fibrosis (IPF). In specific, the context dependance and role of the hippo signaling pathway. To achieve this project several optimization steps of disease and culture models must be optimized to generate high quality data. The allocated resources from this project have been used to support two projects resulting in two primary research articles: one published and one in preparation.

Studying a complex disease such as IPF requires a culture system able to recapitulate such complexity. Precision cut lung slices (PCLS) offers such ability to mimic the native environment through generating culture slices from native tissue. However, the inability to obtain high quality RNA to perform advanced techniques such as RNAseq had been a limitation of this method. To this end, we have developed an RNA isolation protocol that produces high quality RNA from PCLS; and to validate it, RNAseq was performed in addition to advanced bioinformatic techniques (Stegmayer et al). In this study, to estimate the complexity of the PCLS in cell composition, we used deconvolution of bulk RNAseq thourgh using a reference single cell dataset. The reference dataset was huge and required high computational power. RNAseq analysis, scRNAseq analysis, and BisqueRNA deconvolution were done using the resources allocated for this SNIC project.

Moreover, to be able to study the context dependence of the hippo signaling pathway in the lung epithelium, we have developed a cell isolation protocol that allows for the simultaneous isolation of proximal and distal lung epithelial cells. To validate these isolated cells and their differentiation capacities, we have performed RNAseq. The SNIC resources were instrumental in the analysis of these samples. This data will be part of the near-submission to the American journal of respiratory cell and molecular biology (Alsafadi et al).

SNIC resources have been advantageous through-out this project and will continue to be.

Publications list

- Stegmayr, J., Alsafadi, H.N., et al. "Isolation of high yield and quality RNA from human precision-cut lung slices for RNA-sequencing and computational integration with larger patient cohorts." (2020) *American Journal of Physiology-Lung Cellular and Molecular Physiology*. https://doi.org/10.1152/ajplung.00401.2020
- Alsafadi, H.N. et al. "Simultaneous isolation of murine proximal and distal lung epithelial progenitor cells from individual mice". Manuscript in preparation.

Academic achievements

The use of SNIC resources have aided me during my half-time review. While this is not a major academic achievement, it is a huge milestone in the PhD at Lund University.

The use of this SNIC resources aided in the graduation of international bachelor student:

Laura Martinez (UNIVERSIDAD FRANCISCO DE VITORIA, Madrid, **Spain**): *In silico* identification of Yap/Taz bound transcription factors in the lung epithelium of Idiopathic Pulmonary Fibrosis

E-infrastructure related developments

Bulk RNAseq deconvolution pipelines were implemented using the SNIC resources. However, no new resources have been developed during this process.

Grants and patents

No grants or patents have been produced in relation to this SNIC project. However, plans for grants are in order.

The use of SNIC resources at Lunarc have been acknowledged in the aforementioned publications.