Submitted Proposal

This proposal has been submitted by Hani Alsafadi (#11497).
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Proposal Information

Dnr:	LU 2021/7-1
Project Title:	Context dependence of the co-transcriptional activators Yap/Taz in the lung epithelium of Idiopathic Pulmonary Fibrosis
Round:	LU Local small, 2021
Principal Investigator:	Hani Alsafadi (#11497)
State:	Submitted
Requested Start Date:	2021-01-01
Requested Duration:	12 months
Abstract:	Idiopathic pulmonary fibrosis (IPF) is a devastating chronic lung disease with no cure or effective treatments. The only available drugs for IPF can only slow down disease but a treatment that stops or reverses disease is non-existence. Thus, there is an unment need for new novel therapeutic targets. IPF is characterized by epithelial injury, subsequent deranged repair and excessive deposition of the extracellular matrix. Reactivation of developmental pathways is emerging as a potential mechanism driving the development of lung fibrosis. One pathway which has been largely unexplored in IPF is the Hippo pathway. The Hippo pathway plays a central role in regulating organ size during development and controls stem/progenitor cell proliferation and differentiation in the adult organism and has been more recently explored in cancer. Our novel data indicates that a number of Hippo pathway components are decreased in IPF and that YAP/TAZ are active in both proximal and distal IPF epithelium. Nuclear YAP/TAZ is present in epithelial cells which express known phenotypic markers of proximal and distal lung epithelial progenitor cells (KRT5+ and SPC+, respectively). Interestingly, we have observed that there is a dysregulation of genes known to be downstream of YAP/TAZ (i.e. known downstream targets are both up and down-regulated in IPF). YAP/TAZ cannot directly bind to DNA and must interact with transcription factors to induce changes in gene transcription. This indicates changes in transcriptional complexes in diseased epithelium as compared to normal epithelium. The aim of the Phd project project is to identify pro-fibrotic YAP/TAZ transcriptional complexes in proximal and distal airway epithelium. And thus, the aim of the SNIC proposal is perform all required analysis for this project. The ability to identify disease-relevant transcriptional interactions will provide us with new targets for therapy for IPF.

Resource Usage:	1. Bulk RNA seq analysis workflows: 1a. Alignment with HISAT2, Stringtie, STAR 1b. Pseudoalignment with Kallisto 1c. Rsubread with featureCounts. 2. Single-cell data analysis: Mostly done on re-analysis of published data sets and potential analysis of some 10X runs. R-studio will be used to perform analysis on single cell data (Seurat, t-SNE clustering, UMAPs, ...etc) 3. Deconvolution of bulkRNA seq using single cell RNAseq as a reference: example softwares: BisqueRNA, SCDC. 4. ChIP seq data anlaysis workflows. Currently, there are no special hardware requirements.
Affiliation:	Lunds universitet
Continuation of Project:	SNIC 2019/6-85
Primary Classification Code:	30108

Principal Investigator

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Co-Investigators

Requested Resources

Aurora

Requested:	5 x 1000 core-h/month

Documents

End of Proposal