CBCB SEMINAR 9/28/2020

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BIOINFORMATICS SEMINAR

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RNASEQ IN SEY MICE SUGGESTS KEY PATHWAYS IN ANIRIDIC CATARACT

Pax6 haploinsufficiency in humans leads to a constellation of blinding ocular defects known as Aniridia. This occurs when an individual has only one functional copy of the Pax6 gene due to either a spontaneous or an inherited mutation. Individuals with this condition are predisposed to ocular fibrosis and tend to develop cataracts far earlier than their wildtype peers. While the role of Pax6 in early eye development is very well characterized, it's continued necessity for lens homeostasis requires further study. We conducted RNA Sequencing studies on lens cells harvested from wildtype and Pax6 haploinsufficient (Sey) mice at 20 weeks of age. RNA Isolates from lens epithelial cells (LEC) and lens fiber cells (LFC) were sequenced separately, from ribo-depleted libraries. Reads were aligned to the mouse genome for transcriptomic quantification; separate alignments against the Rn45s mouse ribosomal RNA precursor were used to assess ribodepletion efficiency. Ribodepletion was generally more efficient for LEC than LFC. Library characteristics were consistent across both LEC genotypes, and between wildtype LFC samples however some variability was observed in samples from Sey mutants. In LEC, we observed 1920 differentially expressed genes (DEG), that in addition to meeting statistical criteria also met minimum abundance thresholds for biological significance. In LFC we identified 134 such DEG with all samples and 291 with all homogenous samples. This study revealed substantial Pax6 dependent transcriptomic remodeling, particularly in pathways known to contribute to lens fiber cell maturation and fibrotic disease. Disruptions in the fiber cell maturation process can influence the total RNA composition of fiber cells, which may contribute to the variation we observed in fiber cell samples. Experimental validation of this study's findings may eventually lead to therapies that help Aniridia patients preserve the clear lenses they are born with.

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PREDICTIVE MODELLING OF OPIOID EPIDEMIC IN UNITED STATES

Historically, drug abuse and addiction has been thought of as a failing of the moral character. But recent studies have demonstrated that contrary to the prevailing thought, it is a disease of the brain. Hence, like any other disease it must to be studied and those suffering from it must be given access to proper care and treatment. In recent years opioid abuse in the U.S has reached epidemic proportions and has given rise to a widespread crisis of opioid addiction. The current opioid epidemic continues to deepen despite significant interventions by federal agencies such as the Drug Enforcement Agency (DEA), Center for Diseases Control (CDC), and Department of Health and Social Services (DHSS). The factors underlying opioid abuse and addiction are varied and complex and include a wide array of individual and socio-contextual factors. Understanding the diverse manner in which these factors interact is the key to formulating effective intervention strategies to combat this epidemic on a larger scale. To this goal, I have been developing computational methods to build predictive models to predict the regions that are at an increased risk of opioid abuse. In this presentation I will give a brief overview of the history of drug abuse and addiction in general and our motivation to use machine learning to tackle this problem. I will also talk about an initial pilot study in the state of Delaware to evaluate the utility of existing machine learning algorithms to predict neighborhoods that are at an increased risk of opioid abuse. Further, I will talk about the challenges we faced during the initial study and my proposal to develop a novel machine learning framework to make better use of the existing opioid related data and provide robust predictions in the face of incomplete or missing data.

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