RareSeq Lit/ Reading

▼ John meeting notes/ points

> 1. Rare disease need. Foundations and companies wanting to find drugs for rare disease could benefit from any engine that predicts drug activity for a genetic disease.

> 2. Drug databases. A variety of accessible drug activity databases are out there (CMAP, L1000, Creeds, Recursion, etc) any of which would be valuable predictors of drug activity if it can be queried correctly.

3. Project RareSeq. Can we make a virtual screening tool that uses RNAseq profile to find which drugs may be therapeutic (multistep approach).

step 1. Can we develop a screening tool that takes RNAseq data from patient (DEG of patient vs control) to find the gene expression profile specific to disease, then use that to query a database for which drugs are best at reversing the patient RNAseq phenotype. (familial hypercholesterolemia and treatment with Statins as one positive control).

step 2. Can we figure out how to convert worm RNAseq into Human RNAseq (we have whole worm RNAseq for Milan rare disease model and now have access to fibroblast RNAseq from Milan patients -> can we see similar profile. soon we will have iPSC from neurons which will be better comparator since this is primarily a CNS disease)

Also, the demo concept that Chris mentioned was looking at expression response to statins for hypercholesterolemia. I think you'd want to find some literature on expression patterns associated with hypercholesterolemia, then use the response to statins to test the results from the system.

▼ FH- Familial Hypercholestrolemia

Gene Sets: LDL receptor gene (LDLR), apolipoprotein B gene (APOB), or proprotein convertase subtilisin/kexin type 9 gene (PCSK9).

Physiology: Impair the removal of LDL cholesterol from the bloodstream resulting in increased levels of LDL and heart problems.

Statin: Serves as a positive control. Statin medications, such as atorvastatin, simvastatin, and rosuvastatin, are commonly prescribed as a positive treatment for familial hypercholesterolemia. Statins act by inhibiting an enzyme called HMG-CoA reductase, which plays a crucial role in cholesterol synthesis. By blocking this enzyme, statins reduce the production of cholesterol in the liver, thereby lowering LDL cholesterol levels in the blood.

Links

- Enter a single gene and get a list of up and down regulated genes:

https://maayanlab.cloud/sigcom-lincs/#/SignatureSearch/UpDown

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