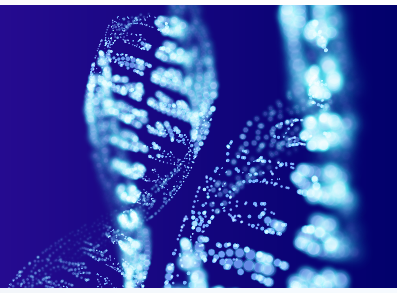
excelra

Where data means more

CASE STUDY

Leveraging WES data to identify biomarker signatures



Client

Industry
Pharma

Location
US

Therapeutic Area
Immuno-oncology

Specification

To identify biomarker signatures for efficacy/resistance to immunotherapy using gene expression profiles and somatic mutations in the Small Cell Carcinoma and Renal Cell Carcinoma patients.

Client challenges

- Parameter optimization
- Running computationally intensive tools on XOP
- Extensive troubleshooting

Key activities

Activity 1:

Identification of biological themes for tumor and tumor microenvironment from gene expression profiles.

Building of gene expression networks using WGCNA and detecting co-expression modules

- WGCNA co-expression networks were constructed using multiple parameters, testing various sample and gene filtering criteria.
- The results from avelumab Javelin 101 RCC & avelumab Javelin 100 1L UC studies (Nature Medicine papers) were reproduced with the developed code.
- After validation of code by reproducing the results, boostrapped amalgamations of 1000 networks were generated (multiple times) to perform "consensus" network analysis and identify robust modules that could be repeatedly identified.

Associating modules to clinical and other sample characteristics and perfrom enrichment analysis

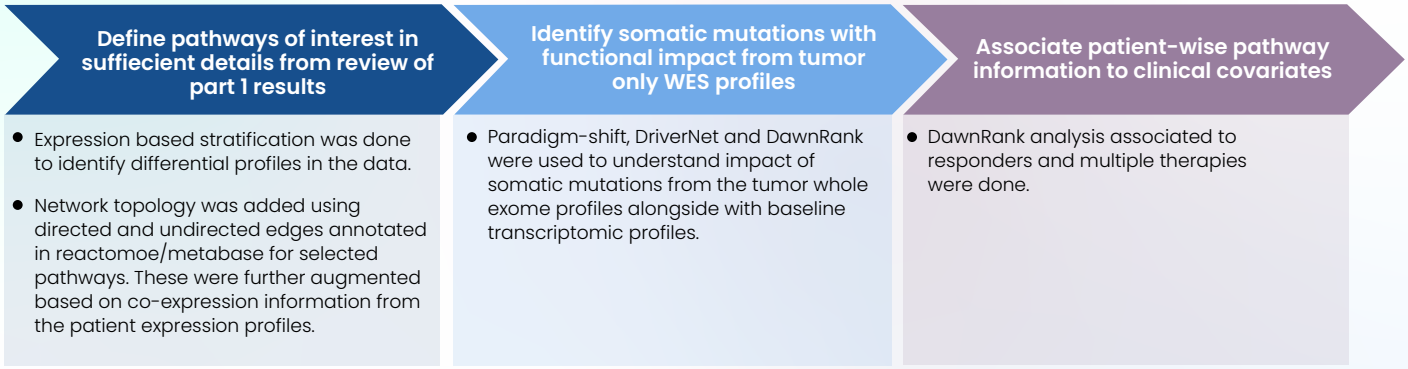
- Modules were annotated and correlated with clinical traits such as progression free and overall survival times.
- Gene set enrichment analysis was performed for modules using mSigDB collections.

Reduce the module of interest to signatures of biological significance

- Reduced the module of interest to signatures using a combination of biological knowledge about pathways/ immune signatures as well as methods like elastic net.

Activity 2:

Integration of mutation profiles with gene expression and identification of mechanisms for efficacy/resistance.



Deliverables

Analysis code in notebook format, network modules, gene signatures, augmented pathway definitions, and filtered functional mutations.

Results

- Developed an understanding of an approach to identify biomarker signatures within clinical data and related it to the IP of the client.
- Validated and optimized code was shared with the client.
- Network modules, gene signatures, augmented pathway definitions, and filtered functional mutations were shared from the analysis.