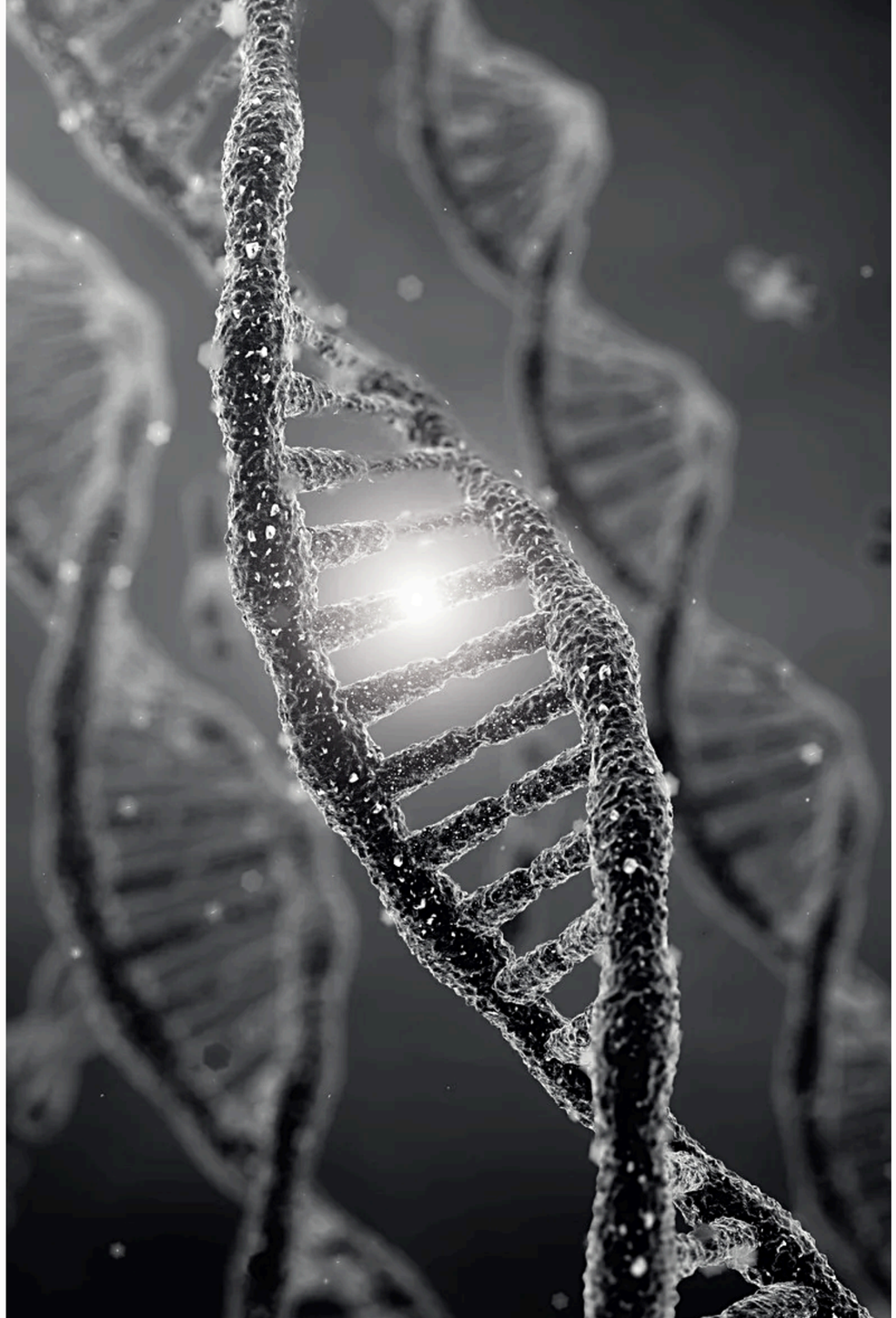


BIOINFORMATICS HACKATHON 2024

OLIVIA, MOANA, BAREERA, SAMA, SARINA

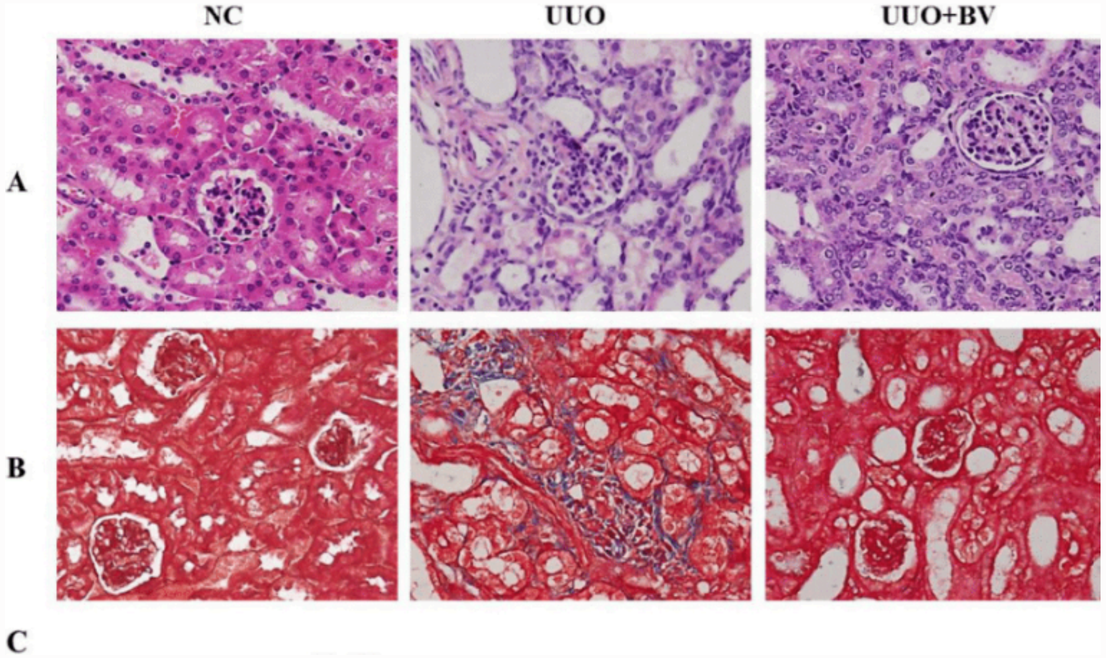
Key Biomarkers in Kidney Transplant

Investigating key differential gene expressions in kidney transplant

Our Agenda for Today

List of key concepts

- Research Question
- Problem Context + Motivation
- Methods & Model
- Discussion of Results
- Recommendations



Research Question

What are the **key differential gene expressions** driving kidney transplant **rejection** and **fibrosis**, and how can we investigate these biomarkers to **enhance patient outcome**?

Problem Context

- Kidney transplants face challenges, with ~40% failing within 10 years
- Genetic factors contribute to rejection
  - Allograft rejection (immune response)
  - Allograft fibrosis (excess collagen after chronic rejection)

Motivation

- Analyzing gene expression in fibrotic and rejected tissues identifies failure pathways
- Tailoring treatment plans to genetic profiles for improving transplant success

Methods

Data Analysis Approach: From Question to Results

Research Question Formulation

Formulated the research question to guide data selection.

Dataset Identification

Preliminary data analysis involved finding suitable datasets with relevant genetic parameters.

Analysis Method Selection

Selected Limma differential expression analysis using RStudio.

PCA was not viable due to time constraints and dataset complexity.

Data Analysis Execution

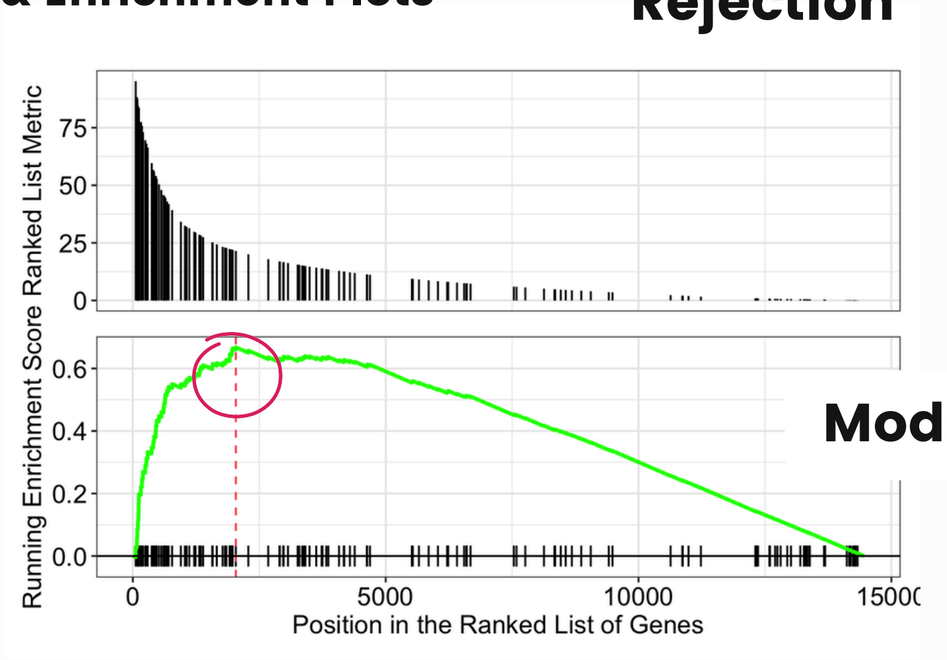
Perform gene analysis with the largest sample size data frame

Conducted Limma differential gene analysis to identify relevant genes.

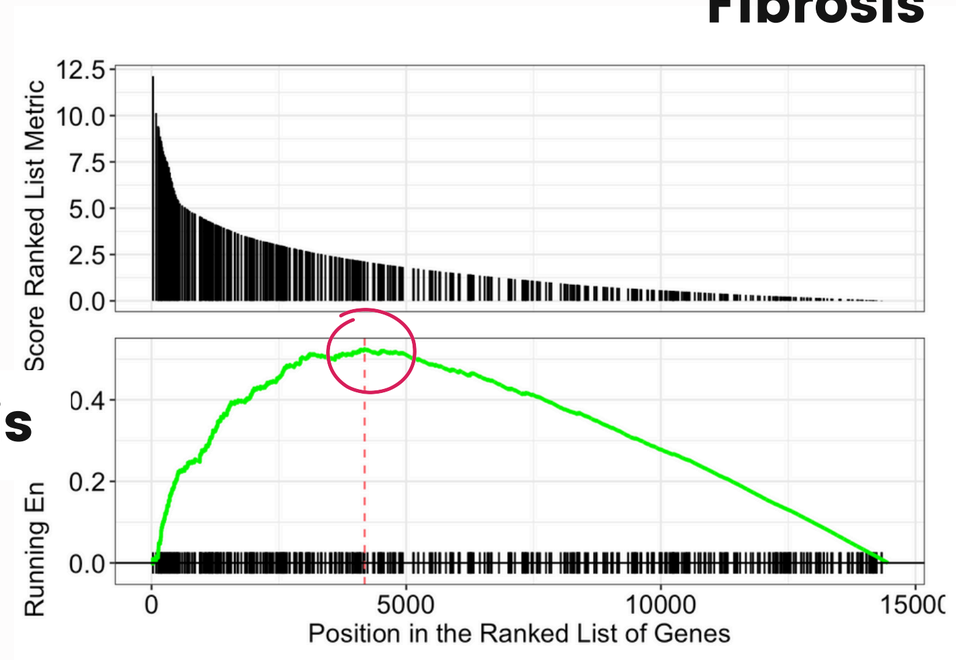
Model

GSEA & Enrichment Plots

Rejection



Fibrosis



Model Analysis

2 GSCE

2.1 Enrichment plot for all rejection, fibrosis genes

Show

Show 10 entries Search:

	ID	Description	setSize	enrichmentScore	NES	pvalue	p.adjust	qvalue	rank	leading_edge	core_enrichment
GO:0009060	GO:0009060	aerobic respiration	138	0.6776373991865908	1.46781210844373	8.847573266983e-9	0.00002720771494234679	0.00002371116785545207	2036	tags=37%, list=14%, signal=32%	UCN/FXN/MLXIPL/COX7C/NDUFA4/MDH1/COX
GO:0009896	GO:0009896	positive regulation of catabolic process	454	0.5684940088372488	1.275697809576093	9.364210959334636e-9	0.00002720771494234679	0.00002371116785545207	3109	tags=37%, list=22%, signal=30%	DEPDC5/MLXIPL/CD81/SLC25A5/DDB1/BCAP3
GO:0045333	GO:0045333	cellular respiration	177	0.6271276617283454	1.385335243743897	5.820182110560451e-8	0.00005636846374077797	0.00004912437918229182	2036	tags=33%, list=14%, signal=29%	VPS54/UCN/FXN/MLXIPL/COX7C/NDUFA4/MDH
GO:0043086	GO:0043086	negative regulation of catalytic activity	373	0.5761654304580911	1.29060461730824	4.095821146957343e-8	0.00005636846374077797	0.00004912437918229182	2551	tags=31%, list=18%, signal=26%	ZNF675/GSTP1/CST3/TIMP1/SERPING1/CDKN1
GO:0006914	GO:0006914	autophagy	486	0.560123977734811	1.257722720795278	5.505586425620765e-8	0.00005636846374077797	0.00004912437918229182	4124	tags=43%, list=29%, signal=32%	DEPDC5/WDFY4/ATP6V0E1/CALR/PHB2/SLC25

Visualization Process

GSEA Enrichment plots for overall vizualisations.

1 LIMA

1.1 Rejection

Show 10 entries Search:

	Gene	logFC	AveExpr	t	P.Value	adj.P.Val	B
9531	HIST1H3G	1.982549484600638	4.915668985541066	37.91240260852265	2.213814946269681e-185	4.446668701077282e-181	413.2802308373775
12264	TNFAIP8L1	1.925122748473844	3.734656095522456	34.30993979687642	5.583696366998917e-163	5.607706261377012e-159	361.9048676214131
8046	OTOP2	1.348847856407174	2.968136368073806	34.27625369852815	9.087836781557421e-163	6.084609653145412e-159	361.419644947342
8442	C17orf78	2.816934722404124	3.901817149560136	33.23474868524843	3.267830225566703e-156	1.64094094776832e-152	346.3813947491962
5590	CTAGE15 /// CTAGE6	1.738522023979315	5.527258499935407	32.73689272526584	4.546728650818368e-153	1.826511833606755e-149	339.1702444945044

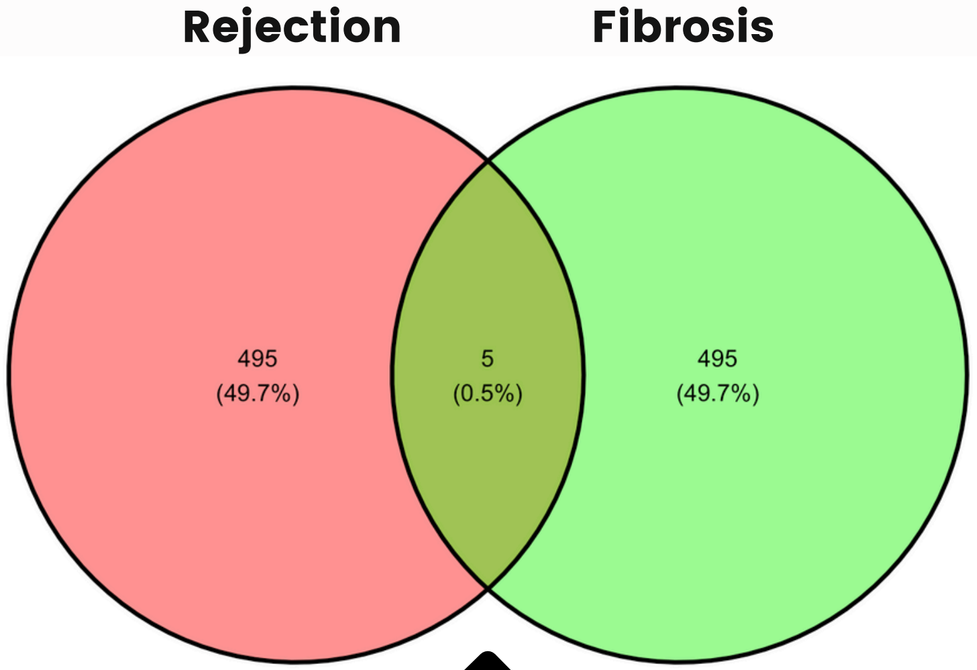
1.2 Fibrosis

Show 10 entries Search:

	Gene	logFC	AveExpr	t	P.Value	adj.P.Val	B
3973	DDR1	1.645778229867059	5.00765666163674	10.42108597396659	2.968682143157505e-19	5.213599579813211e-15	33.00842032653121
6894	RFC2	0.7310549879238177	4.614060786932247	9.673942168765798	2.50458243944278e-17	2.199273840074705e-13	28.73426133116459
2691	HSPA6	1.420879084896585	6.76786066193853	9.192046771322872	4.237519453024293e-16	2.480643887800421e-12	26.00735082134179
7801	PAX8	2.679836130044114	8.16667748755093	9.086433524903445	7.842422599097466e-16	3.040901961317383e-12	25.41382896015894
7756	UBA7	3.460415938769658	9.10971630979327	9.069439137960938	8.657618612109619e-16	3.040901961317383e-12	25.31847862321175

Model

LIMA & Venn diagram



Top 5 expressed overlapping genes: "UTS2R" "C15orf40" "NXNL2" "UBA1" "CYB5R3"

Model Analysis

Top 5/500 genes by overlapping genes between allograft fibrosis and rejection.
Venn Diagram for visualising LIMA findings

What do the genes say?

UTS2R
Reduces blood flow to the kidney

C15orf40
Causes inflammation, scarring, and immunity attack.

NXNL2
Long-term kidney failure when damaged.

UBA1
Enzyme that accumulates unnecessary proteins when damaged.

CYB53
Causes oxidative stress and impaired function when damaged.

Recommendation

In-depth Study of Genetic Pathways

Focus on genes involved in rejection processes during and after kidney transplants.

Enhanced Genetic Screening

Advocate for improved and regulated genetic screenings in kidney donor processes.
Leverage AI to advance screening techniques.

Future Approaches

Explore CRISPR for targeted gene regulation.
Develop targeted drug delivery systems using nanotechnology.

Conclusion

Genetic **Pathway** Understanding

In-depth understanding of genes and pathways is crucial to addressing rejection processes in kidney transplants.

AI and Genetic Screening

The growing medical AI industry highlights the need for improved, regulated genetic screenings in kidney donor processes.

Attention to Genetic Factors

Despite advancements, meticulous attention to genetic factors remains essential in transplant success.

Any Questions? Thank you! :)