TEAM-AI
Translational AI Excellence and Applications in Medicine

Exploring O-GlcNAcylation Dysregulation's Role in Cancer Progression: A Network-Level Analysis Across TCGA Datasets

Rastko Stojšin MSc

UT System 2025
AI Symposium in Healthcare

TMC | TEXAS MEDICAL CENTER

UTHealth Houston
McWilliams School of Biomedical Informatics

O-GlcNAcylation

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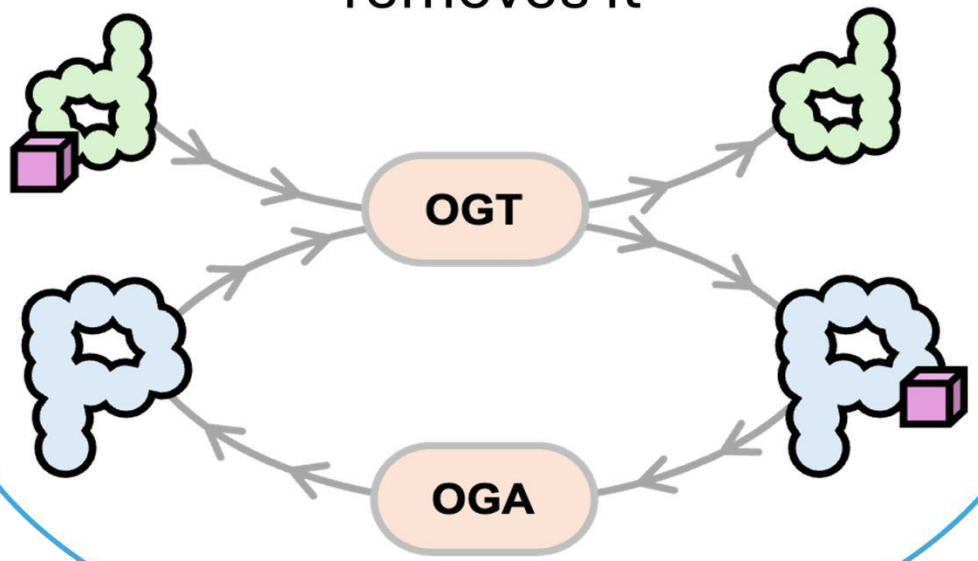
A post translational modification of proteins where **OGT** attaches a specific **sugar** (GlcNAc) from a glycosyl donor while **OGA** removes it



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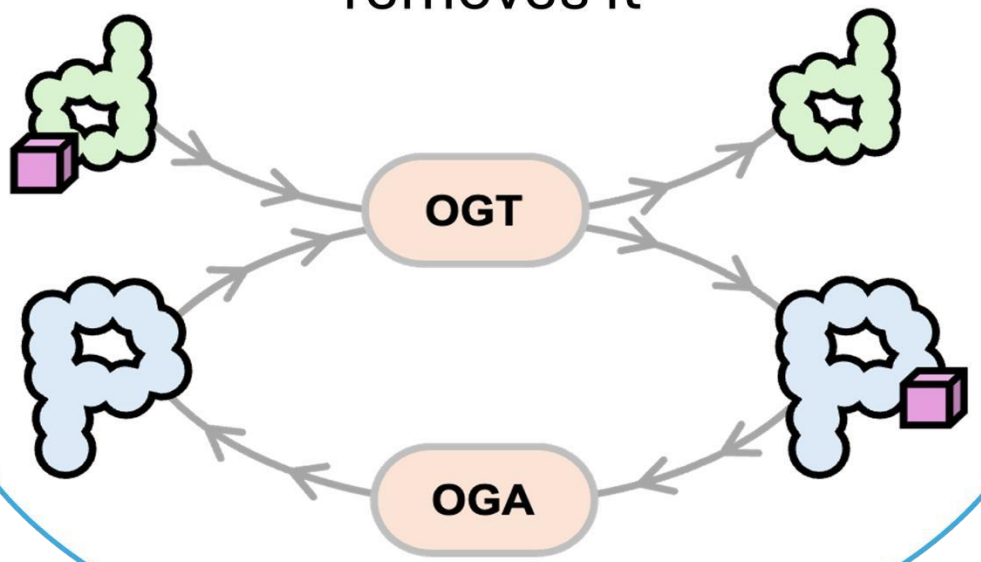

- **Broad influence**
- **Abundant modification**
- **Dynamic cycling**
- **Regulatory simplicity**

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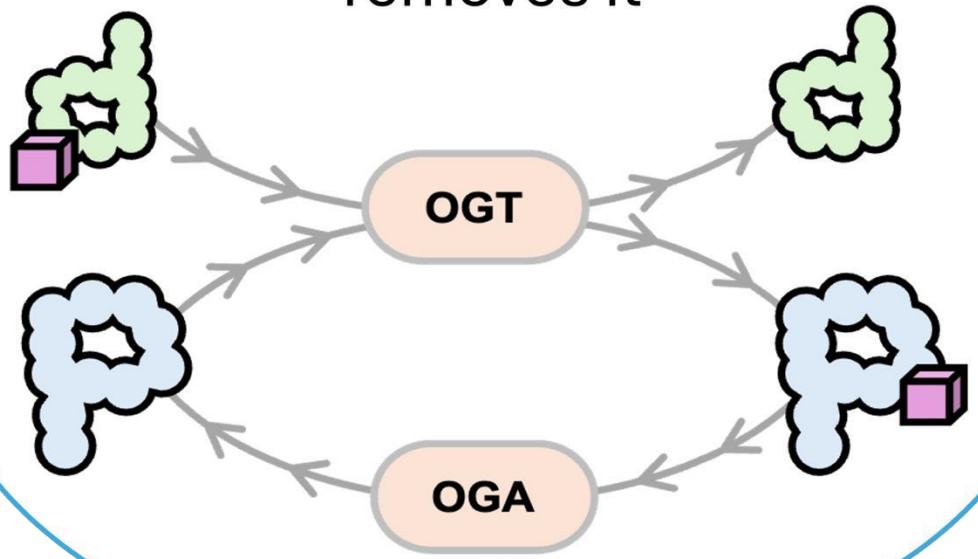
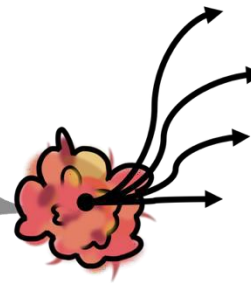


Role in Cancer

- cell cycle regulation
- transcription
- metabolism
- apoptosis
- signaling



- tumorigenesis
- metastasis
- proliferation
- drug resistance

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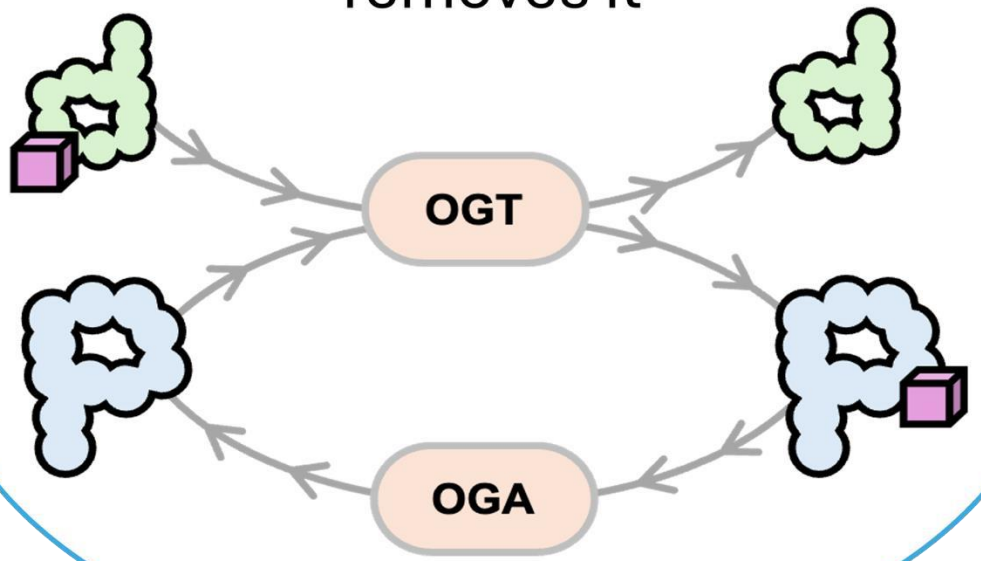

Challenges in O-GlcNAcylation Research

difficult measurement

difficult target

- **Broad influence**
- **Abundant modification**
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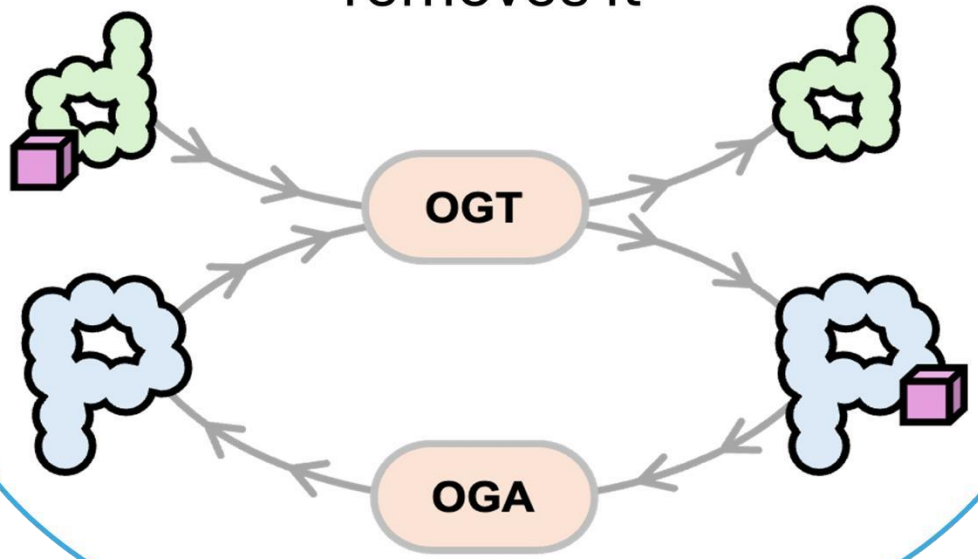

Opportunity for Research

- regulatory simplicity
- large datasets (gene exp.)
- O-GlcNAc modified proteins are cataloged

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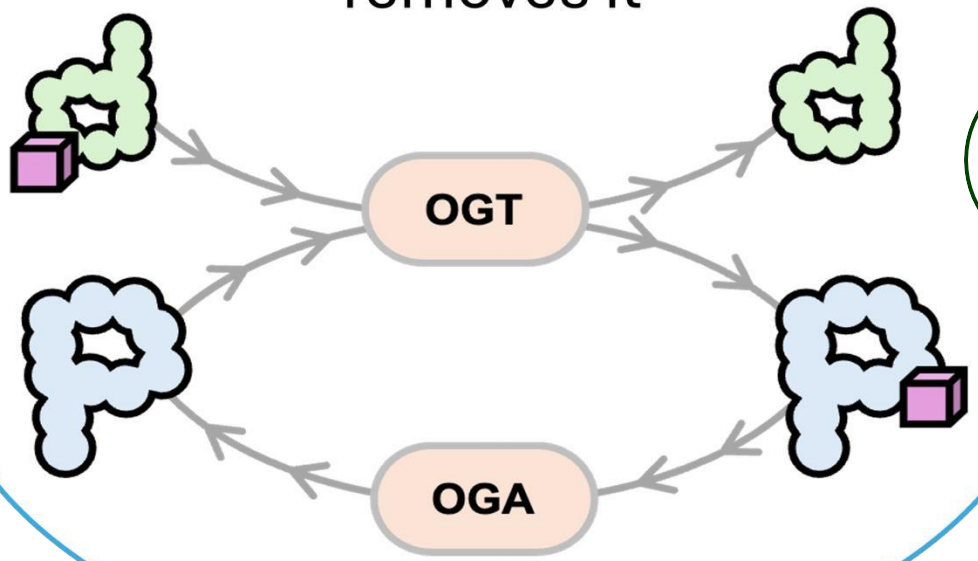

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Central Questions

Can we use + to infer O-GlcNAcylation dysregulation?

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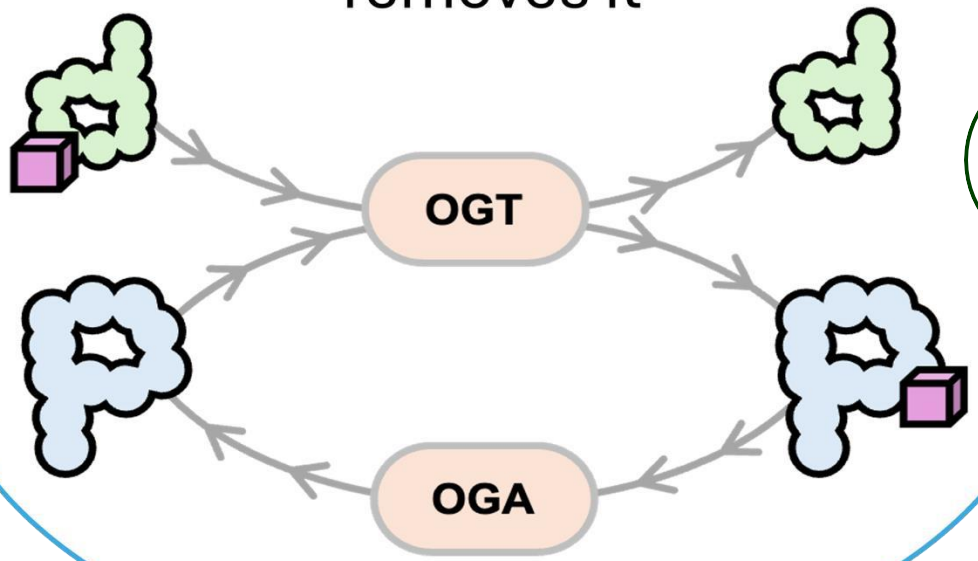

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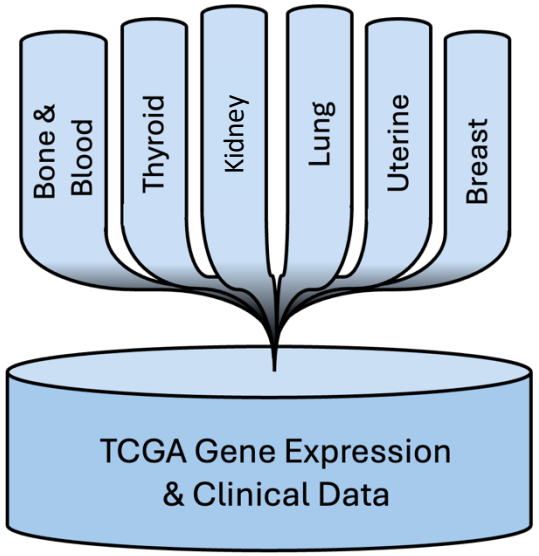

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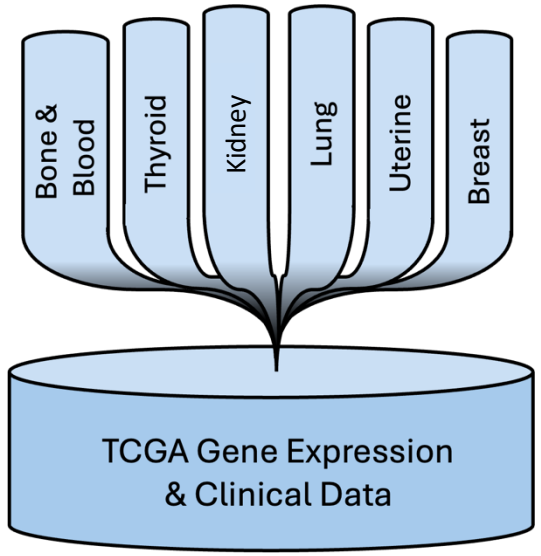

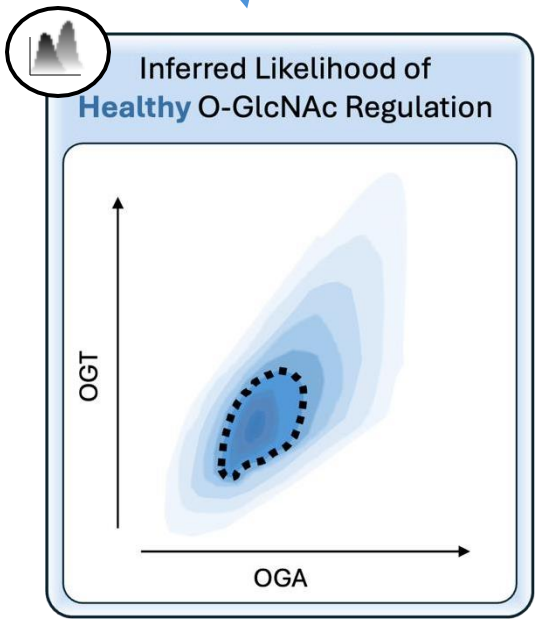

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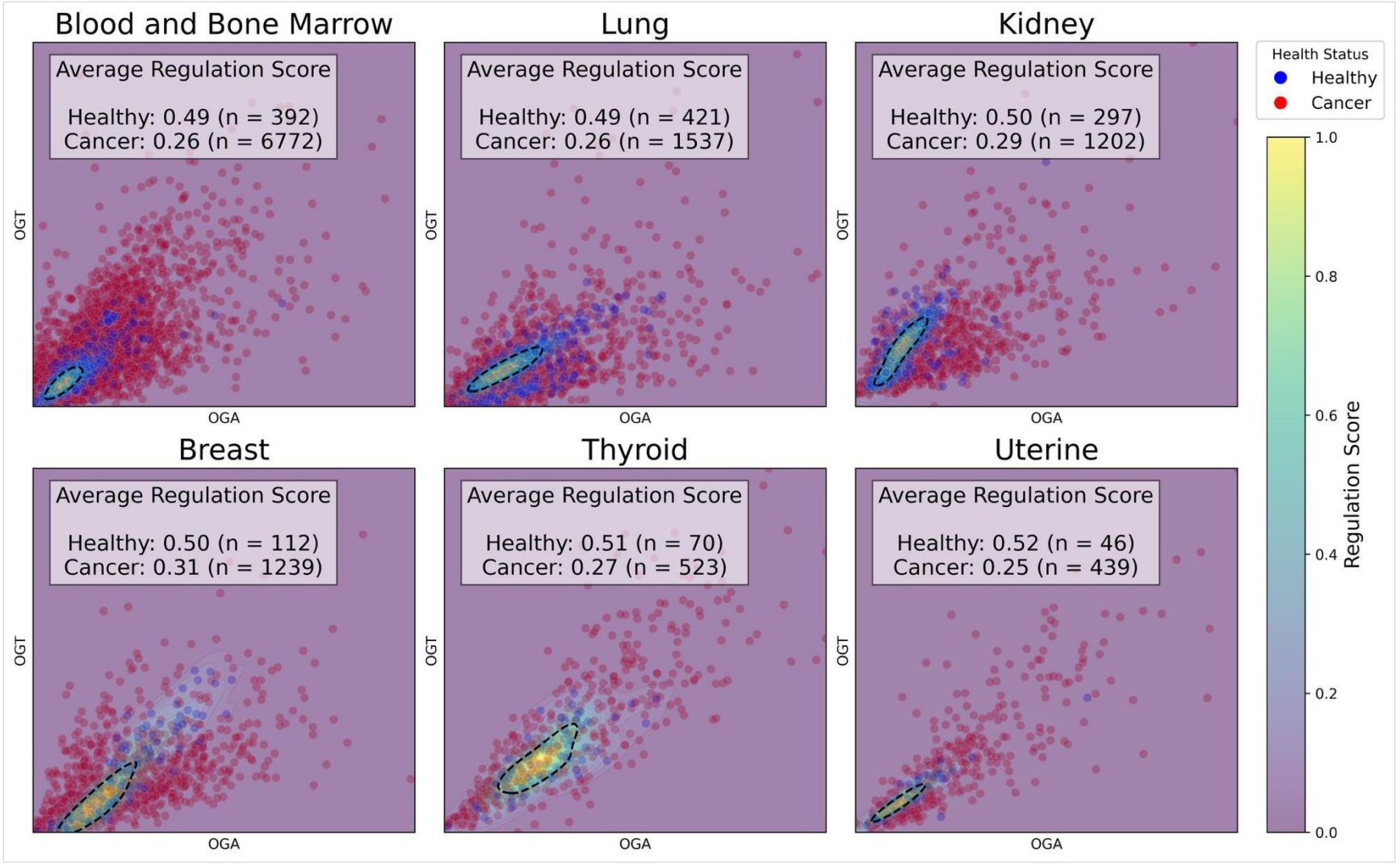

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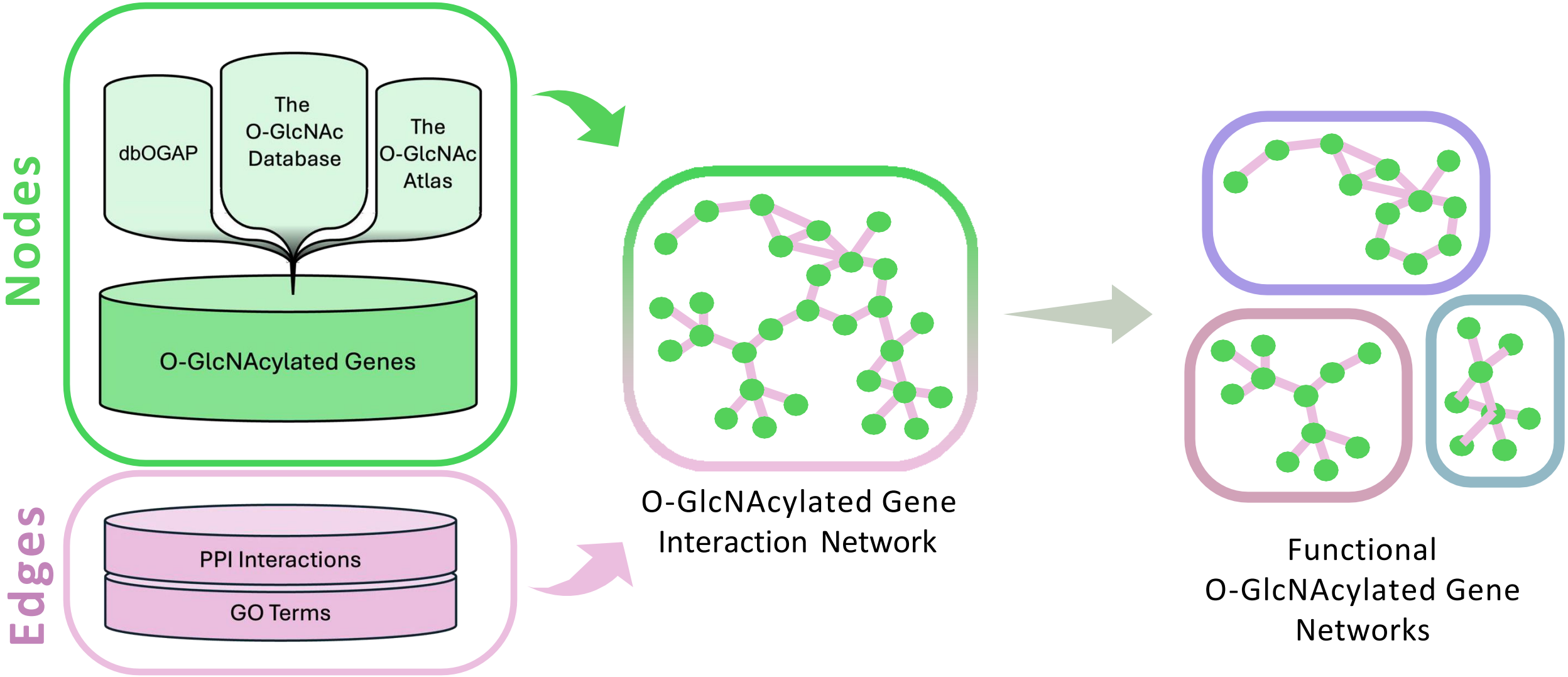

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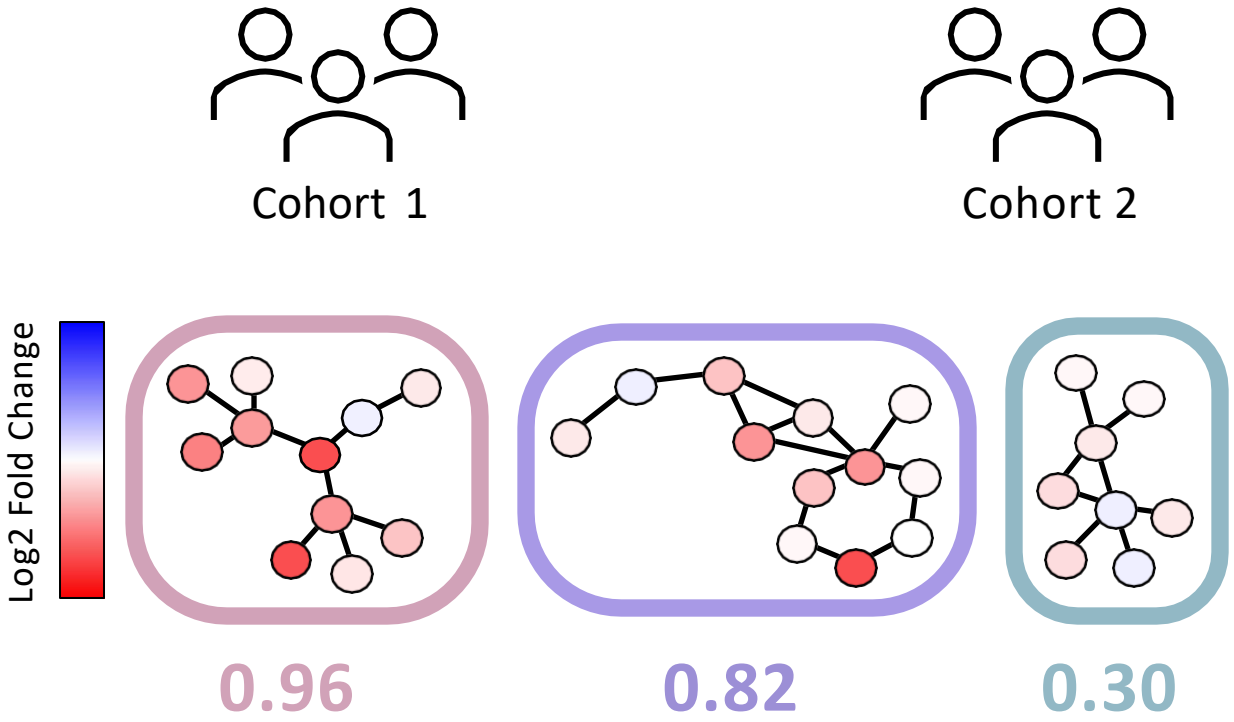

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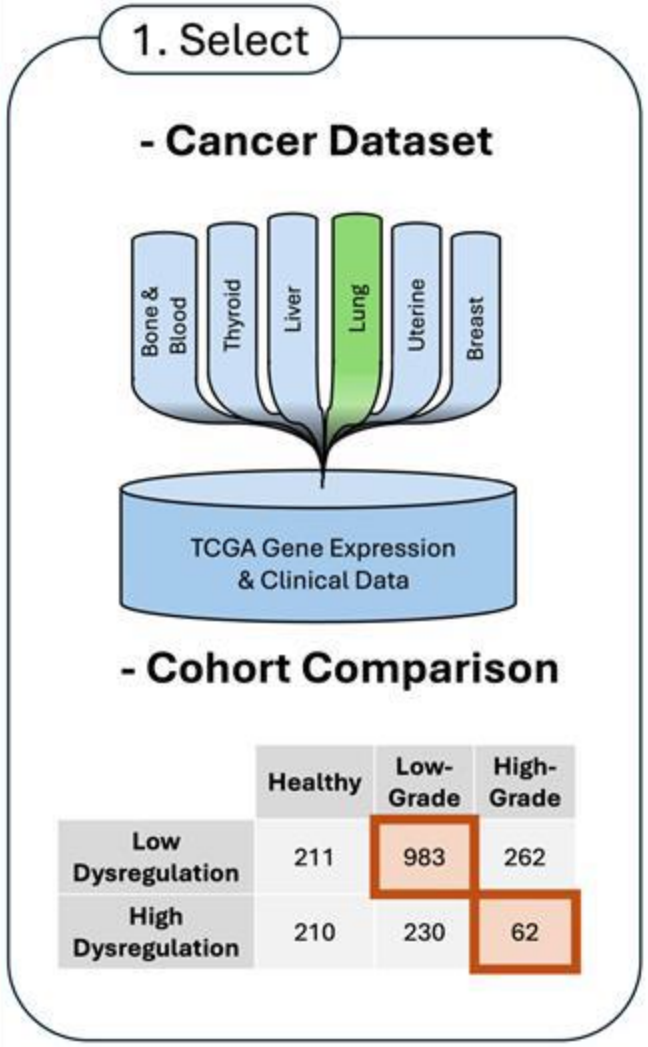
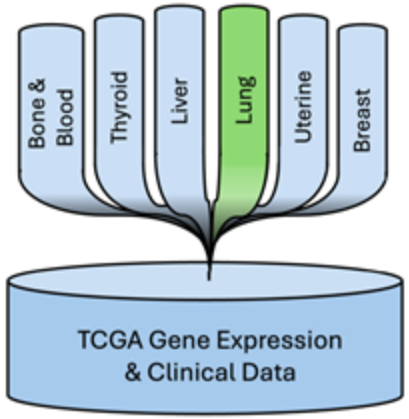


	Healthy	Low-Grade	High-Grade
Low Dysregulation	211	983	262
High Dysregulation	210	230	62

Can we use inferred dysregulation + + to identify cancer relevant downstream pathways?

1. Select

- Cancer Dataset



- Cohort Comparison

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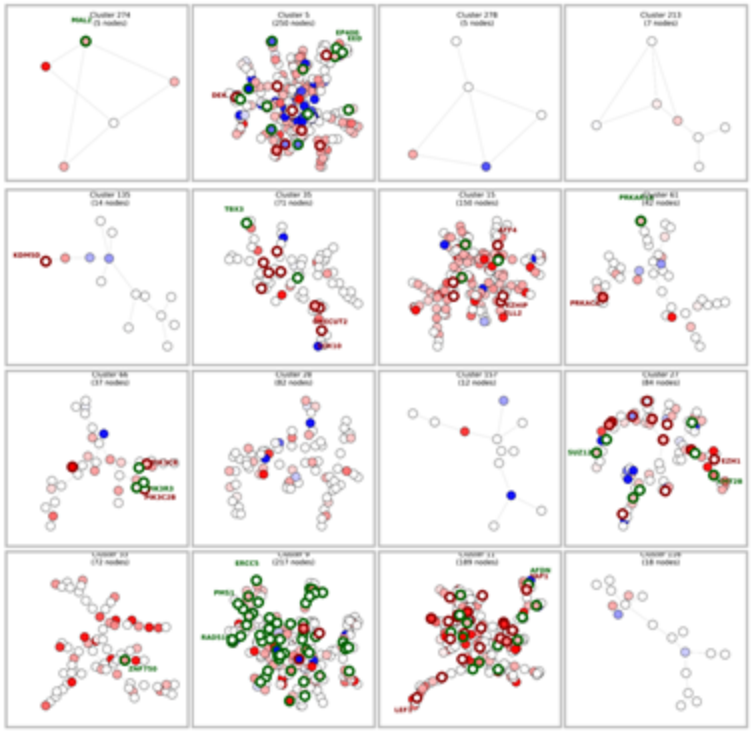
2. Derive

Highly Differentiated Networks



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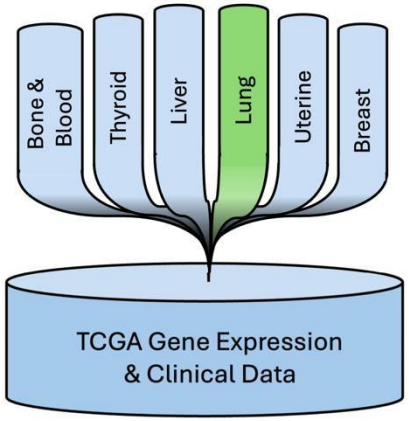

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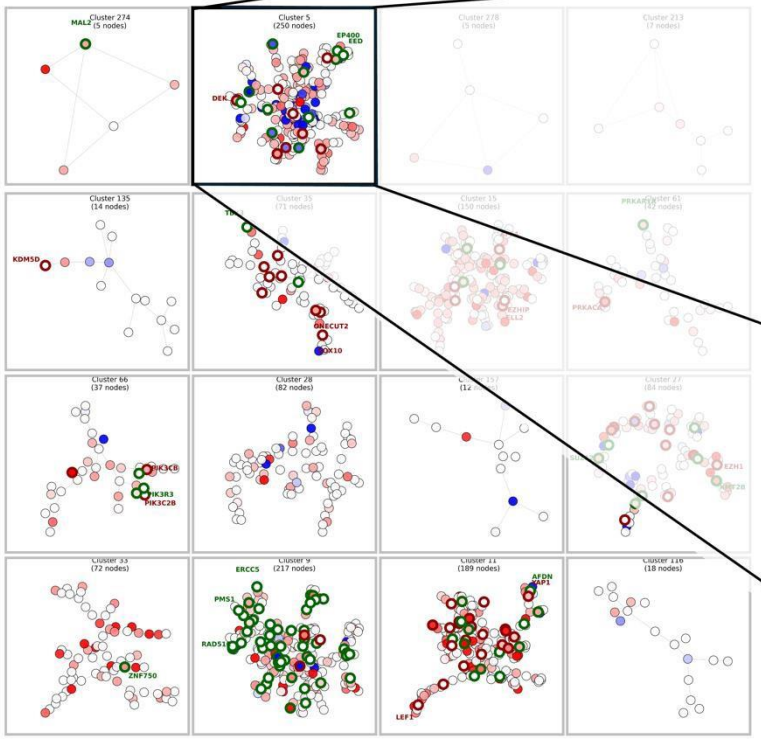
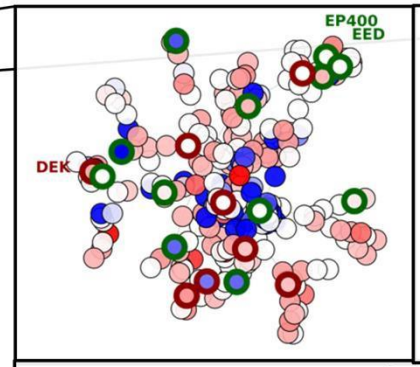
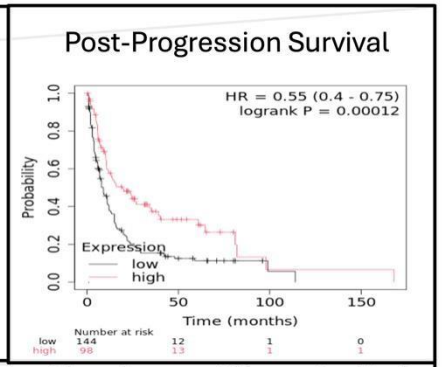


3. Confirm



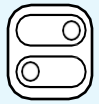


Name	P-value	Adjusted p-value	Odds Ratio	Combined score
EGFR Mutation-Positive Lung Adenocarcinoma	0.07270	0.5440	15.86	41.57
Non-small Cell Lung Cancer	0.07429	0.5478	4.68	12.16
Lung Adenocarcinoma	0.04606	0.5440	3.92	12.07
Lung Function (FEV1)	0.1238	0.5489	1.95	4.06
Lung Cancer In Ever Smokers	0.2088	0.5489	2.41	3.77
Squamous Cell Lung Carcinoma	0.2226	0.5535	2.30	3.46
Lung Cancer	0.2320	0.5672	1.83	2.68
Lung Function (FEV1/FVC)	0.3173	0.6250	1.23	1.42
Lung Function (FVC)	0.6955	0.7983	0.85	0.31
Lung Function (Forced Vital Capacity)	0.8862	0.9197	0.46	0.06

Networks – Biological Validation

Can we use inferred dysregulation +  +  to identify cancer relevant downstream pathways?

	B.B. N=7164	Lung N=1958	Kidney N=1499	Breast N=1351	Thyroid N=593	Uterine N=485
Survival As sociated		94%	88%	88%	63%	50%
Disease Associated		56%	50%	69%	69%	44%

Can we use  +  to infer O-GlcNAcylation dysregulation?

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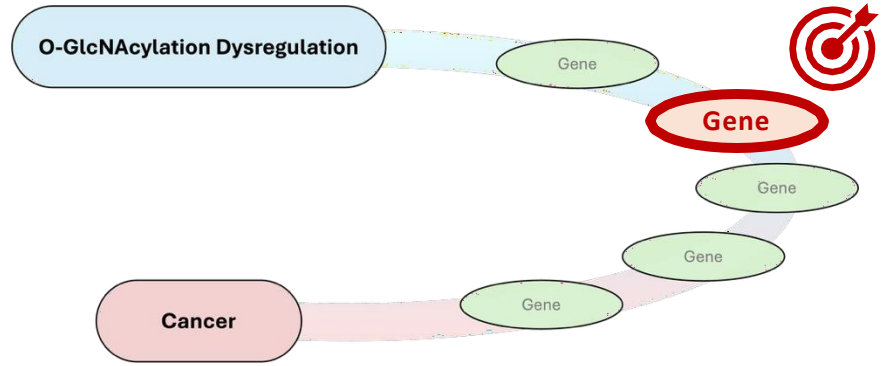
Significance of Research

- Safer therapeutic targets
- Cancer insights relating to O-GlcNAc
- Risk vs protective pathways
- Shared vs cancer specific pathways
- Biomarker discovery
- Applicability beyond cancer
- Generalizable workflow

Knowledge Gap

- O-GlcNAcylation is linked to tumor progression, but its systems-level role remains unclear.

- No established framework exists to study its dysregulation or its downstream protein effects across cancers.



How We Addressed It

- Developed a scalable framework to infer O-GlcNAcylation dysregulation

- Mapped key functional networks to assess its role in cancer progression and patient outcomes.

- Identified risk and protective pathways, guiding targeted hypotheses on tumor growth and therapy resistance.

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Thank You!

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