Exploiting GALNT7 to improve the diagnosis and treatment of prostate cancer

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Background

- **Prostate cancer** is now the **most commonly diagnosed cancer in the UK** with more than 130 new cases every day.[1,2]
- The widely used **prostate-specific antigen (PSA) test** enables early detection of prostate cancer, but it has **poor accuracy**.[3]
- Prostate cancer can also progress to **become metastatic and castration-resistant**, for which **treatment options are limited**.

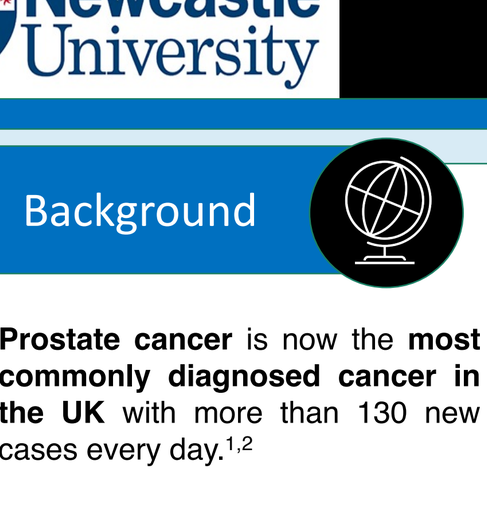


Fig 2. Protein glycosylation. In O-linked glycosylation, glycans attach to the oxygen atom of either serine (S) or threonine (T) residue.

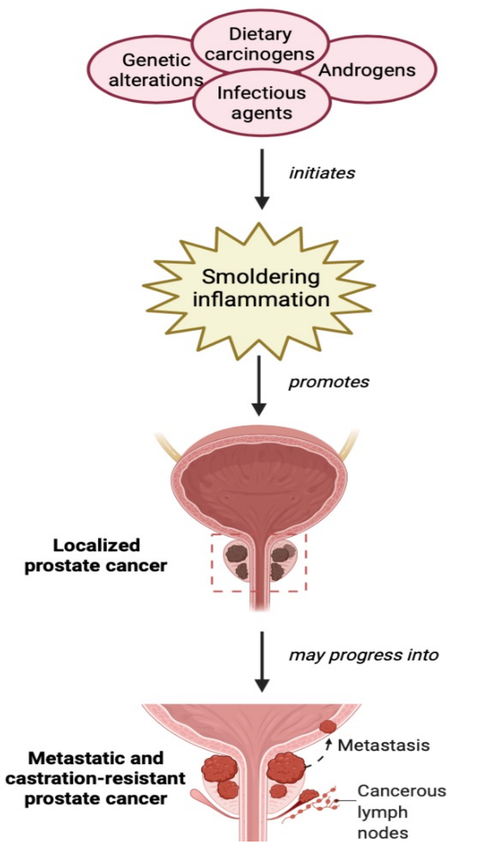


Fig 1. Prostate cancer development

- Glycosylation is the addition of saccharides/glycans to other molecules such as protein. **Altered protein glycosylation** is often seen in **cancer progression**.[4-6]
- The enzyme **GalNAc transferase 7 (GALNT7)** helps initiate O-linked glycosylation. GALNT7, along several other glycosylation enzymes, was found to be **upregulated in prostate cancer**.[7]

Hypothesis & Aims

Hypothesis:
GALNT7 is upregulated in prostate cancer, and its overexpression alters the expression of certain proteins, genes, and signaling pathways implicated in prostate cancer.

Aims:
- To investigate the potential role of GALNT7 as biomarker to improve prostate cancer diagnosis and treatment
- To explore the role of GALNT7 in prostate cancer progression

Methods

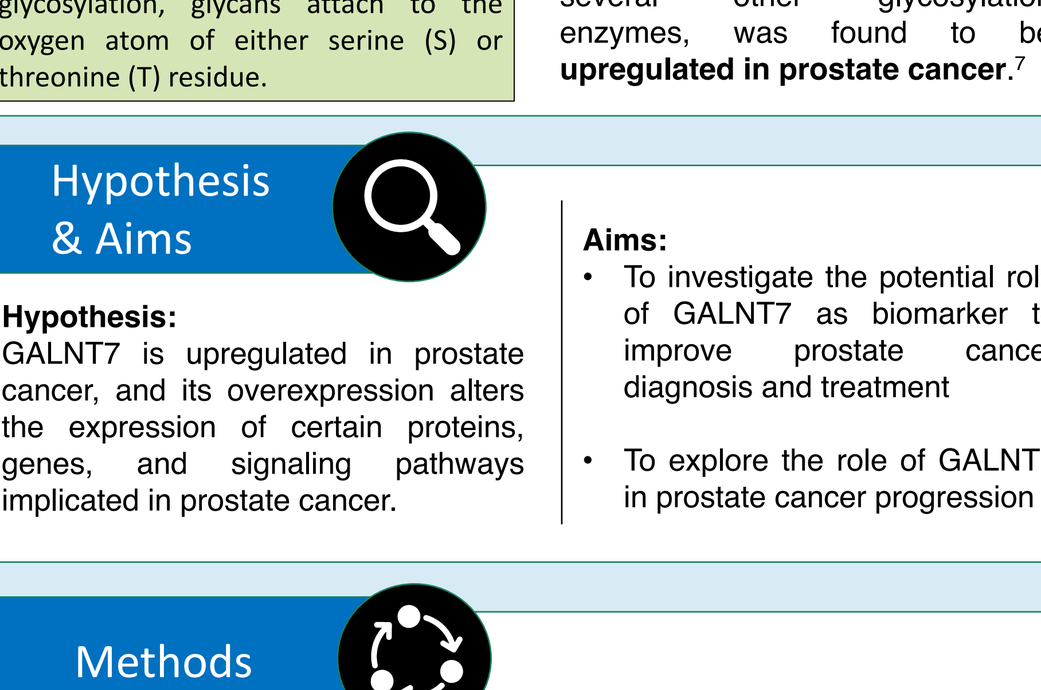
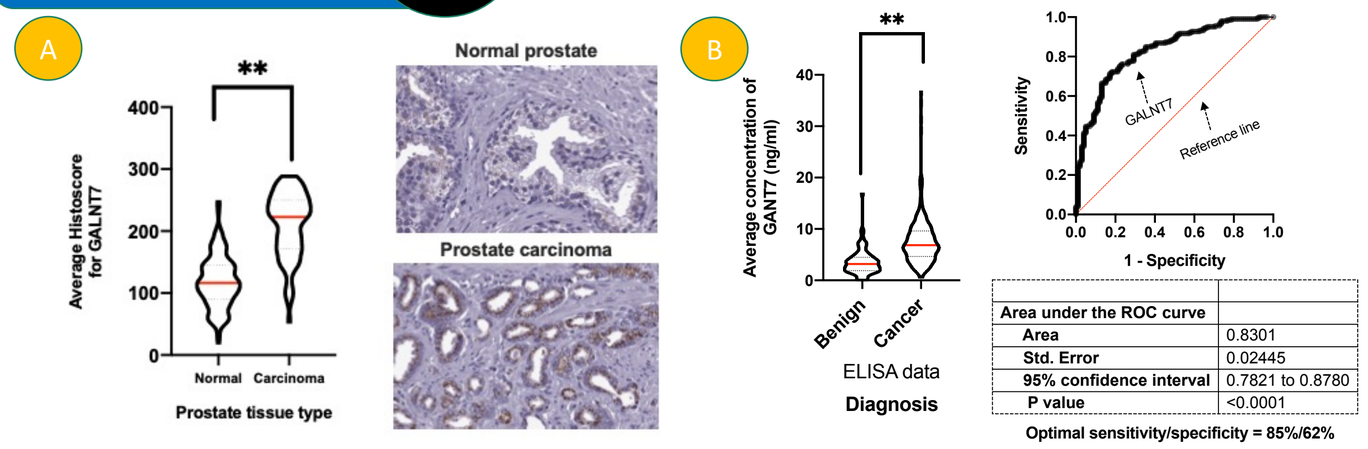


Fig 3. Flow of methodology. OE refers to overexpression, while KD refers to knockdown.

Results



Area under the ROC curve	
Area	0.8301
Std. Error	0.02445
95% confidence interval	0.7821 to 0.8780
P value	<0.0001

Optimal sensitivity/specificity = 85%/62%

Fig 4. GALNT7 is upregulated in prostate cancer and is a potential non-invasive biomarker. (A) Tissue microarray (TMA) confirms significant upregulation of GALNT7 in prostate cancer tissue (**p<0.001). **(B)** Sandwich ELISA confirms significant upregulation of GALNT7 in prostate cancer patients' blood (**p<0.001). Receiver operating characteristic (ROC) curve gives an area under curve of 0.83 and p<0.0001, indicating that GALNT7 is a reliable biomarker to discriminate between prostate cancer and benign lesions.

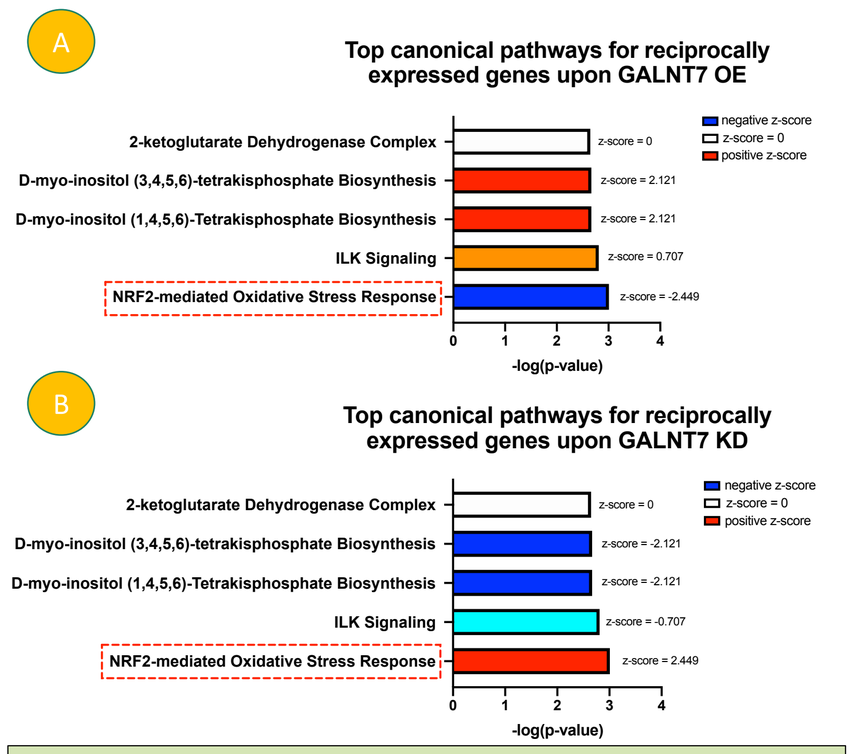


Fig 5. GALNT7 regulates the NRF2-mediated oxidative stress response in prostate cancer cells. Ingenuity Pathway Analysis (IPA) shows the NRF2-mediated oxidative stress response is inhibited **(A)** upon GALNT7 overexpression (OE) and activated **(B)** upon GALNT7 knockdown (KD).

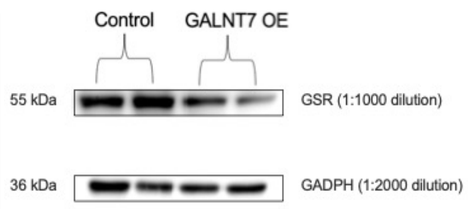


Fig 6. GALNT7 overexpression decreases GSR expression in prostate cancer. Western blot shows reduced band intensity for GSR in GALNT7 OE compared to control.

- **GSR** is one of the **antioxidant** proteins in the **NRF2-mediated oxidative stress response pathway**.
- This pathway is crucial for cellular defense against oxidative stress, so its **suppressed activity** may lead to persistent **oxidative stress**.[8]
- **Oxidative stress** is a well-established driver of **prostate cancer progression**.[9]

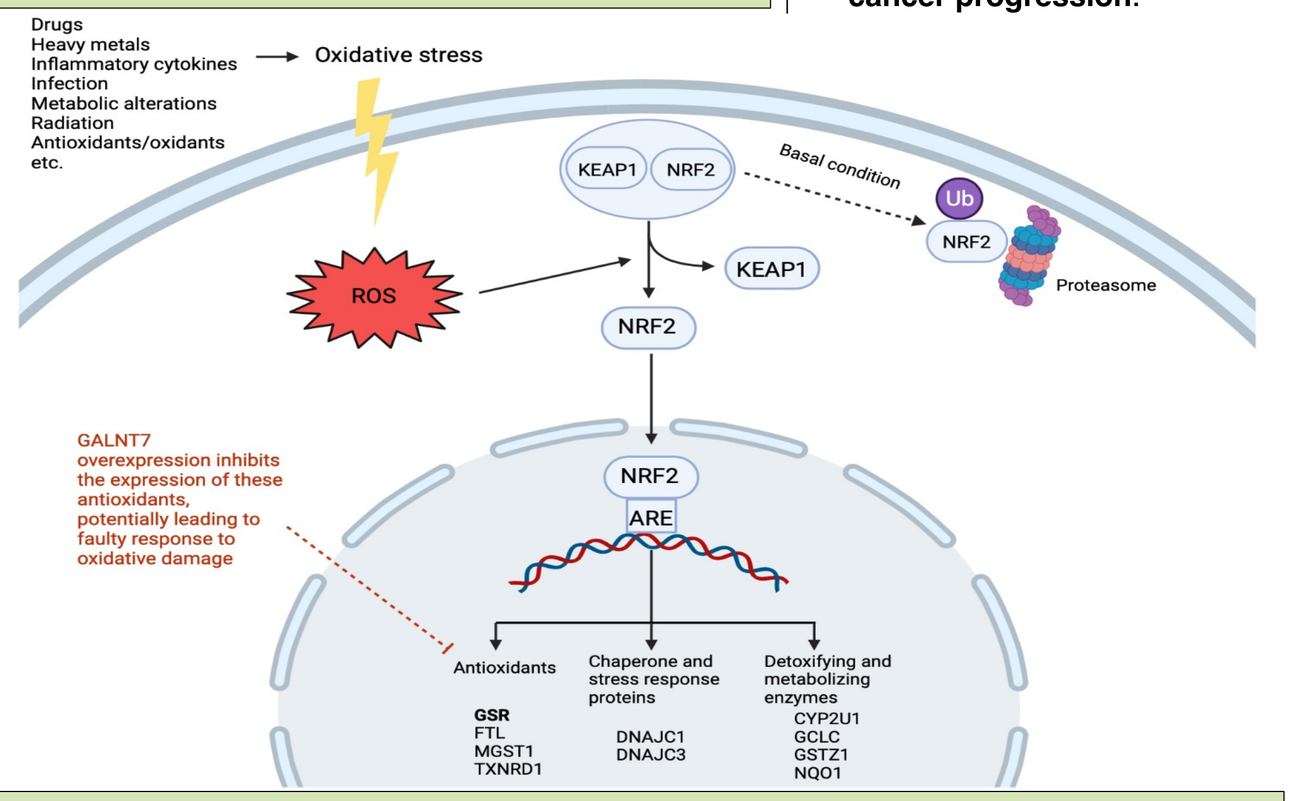


Fig 7. Self-illustrated model showing **how GALNT7 overexpression disrupts the NRF2-mediated oxidative stress response** in prostate cancer, for example by inhibiting the expression of antioxidants like GSR.

Conclusion & Future Work

Future work:
Validation of the findings using assays and *in vivo* models

Conclusion:
- GALNT7 is significantly upregulated in prostate cancer. **GALNT7 could be targeted as diagnostic and therapeutic biomarker**.
- **GALNT7 overexpression is associated with prostate cancer progression**, potentially due to its disruption of the NRF2-mediated oxidative stress response pathway.

References