Identifying the role of lncRNAs in CRPC

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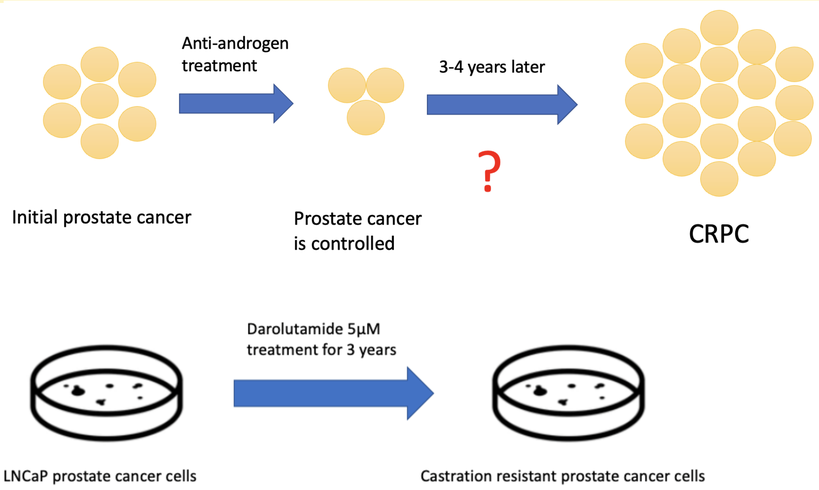


Figure 1: The phenomenon of castration resistant prostate cancer (CRPC) and its production *in situ*.

Different anti-AR treatment groups:

- DMSO vehicle
- R1881 1 nM
- Darolutamide 10 μM
- CRPC

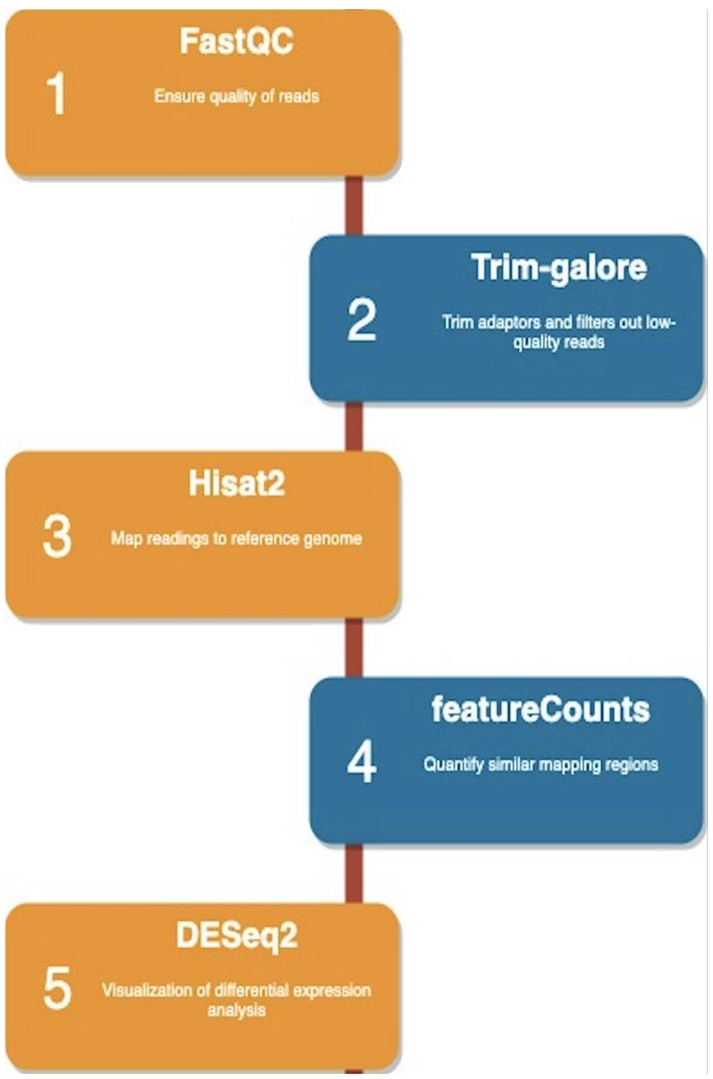


Figure 2: Pipeline for RNASeq of LncRNA library.

ABSTRACT

Long non-coding RNAs (lncRNAs) play major roles in the development of cancer, as many of them are implicated in cell growth and tumor-suppressing mechanisms. We have recently used RNA-seq to identify several lncRNAs that are significantly expressed at higher levels in CRPC compared to wild-type controls. The function of these lncRNAs in prostate cancer is not well understood, yet we have found that their expression levels are over 10 times higher than in normal cells. We hypothesize that the lncRNA LOC730101 might contribute to the growth of CRPC without hormones. Therefore, the goal of our research is to determine the function of these lncRNAs in CRPC by knocking down their expression in prostate cancer cells and observing changes in gene expression levels. We will do this by designing siRNAs to perform the knockdown, RT-qPCR to verify that knockdown worked, and then perform a luciferase assay or direct cell count in order to track any changes in cell growth and any possible androgen receptor (AR) related gene expression. Not only can these have a function in prostate cancer cells, but many lncRNAs tend to have overlapping functions in different kinds of cancer. Thus, our findings may have greater implications for the scientific community beyond the scope of our lab's prostate cancer research.

Uncovering the function of novel lncRNAs has the potential to bring forth valuable information on new biological pathways. Understanding how they work may help us better understand the mechanisms through which cancer cells proliferate. Knowledge is power, and learning about these mechanisms can equip us with better tools to fight against cancer.

Identify

- Identify differentially expressed lncRNAs in various AR treatments.
- Foretell which lncRNAs may regulate/be regulated by androgen

LncRNA in CRPC

- Study the lncRNAs specific to CRPC cell lines
- Verify differential expression via qPCR

Uncover involvement in alternative pathways

- Explore possible lncRNA involvement in pathways that allow survival post-AR treatment

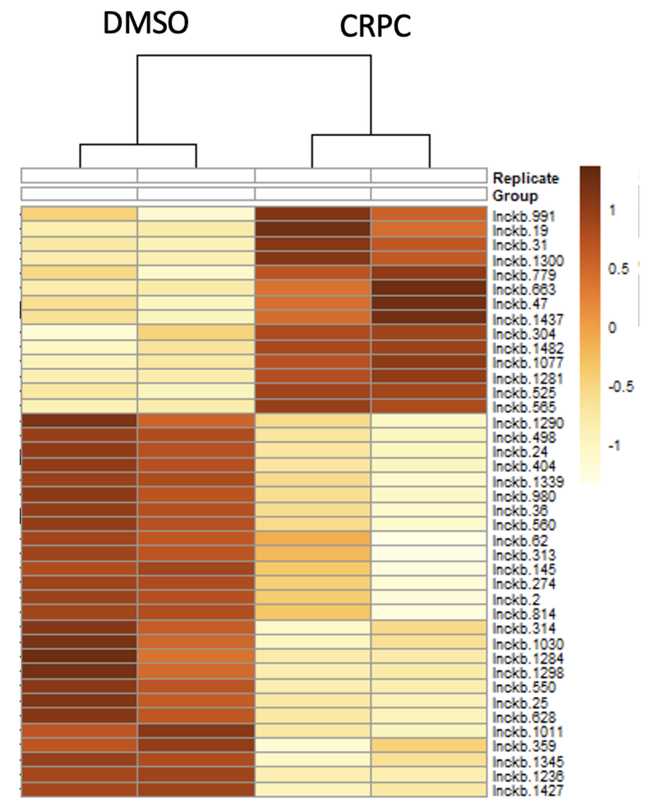
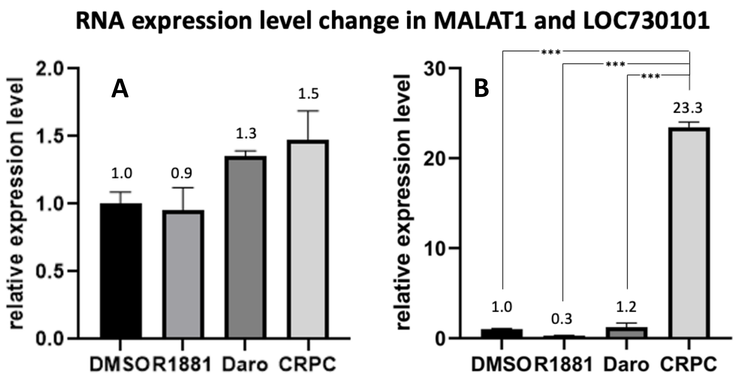
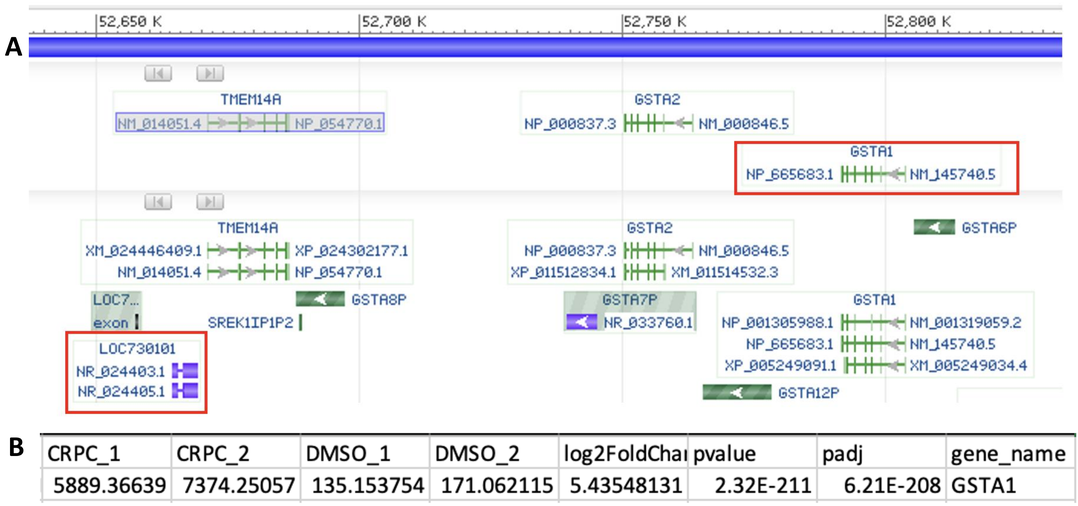


Figure 3: Heat map depicting relative expression levels of various lncRNAs between DMSO and CRPC.



MALAT1 (left) levels compared to LOC730101 (right)

Figure 4: LOC730101 is highly overexpressed in CRPC. A) MALAT1 lncRNA expression levels across the 4 treatment groups. B) LOC730101 expression in 23.3-fold higher in CRPC than DMSO control.



B

CRPC_1	CRPC_2	DMSO_1	DMSO_2	log2FoldChai	pvalue	padj	gene_name
5889.36639	7374.25057	135.153754	171.062115	5.43548131	2.32E-211	6.21E-208	GSTA1

Figure 5: Genome map depicting LOC730101's neighboring region as well as raw expression data of GSTA1. A) Genome map shows the locations of LOC730101 and a nearby gene, GSTA1. B) Raw expression data reveals that GSTA is highly expressed in CRPC cells.

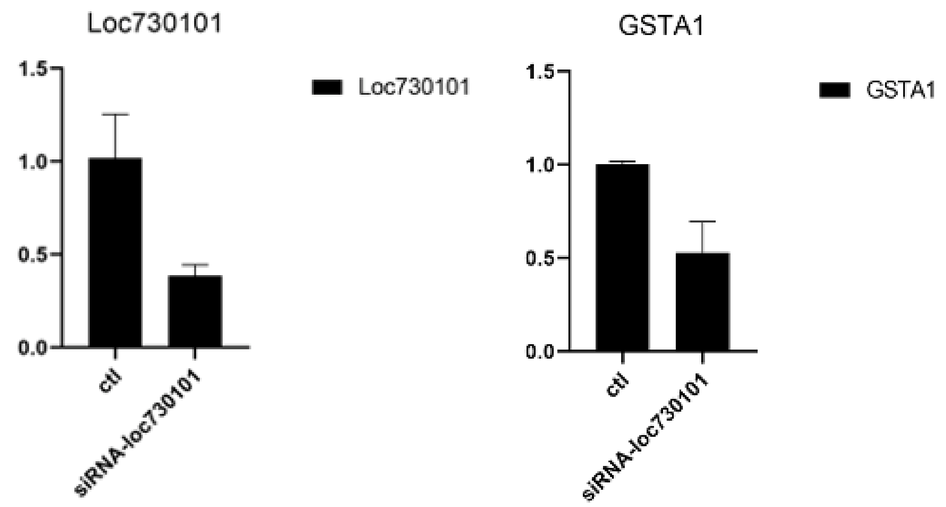


Figure 6: siRNA knockdown reveals positive correlation between LOC730101 and GSTA1 expression. A) qPCR confirms si-LOC730101 knockdown in Darolutamide treated cells. B) si-LOC730101 cells experienced a similar decrease in expression level between GSTA1 and LOC730101.

References

1. Liu, H., Yang, Z., Zang, L., Wang, G., Zhou, S., Jin, G., Yang, Z., & Pan, X. (2018). Downregulation of Glutathione S-transferase A1 suppressed tumor growth and induced cell apoptosis in A549 cell line. *Oncology letters*, *16*(1), 467–474. https://doi.org/10.3892/ol.2018.8608
2. Liu, L., Zhang, Y., & Cao, W. (2017). Highly expressed lncRNA LOC730101 promotes lung cancer cell growth through Wnt canonical pathway. *Biochemical and Biophysical Research Communications*, *493*(2), 992–997. https://doi.org/10.1016/j.bbrc.2017.09.104