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LINC01137/miR-186-5p/WWOX: A Novel Axis in Bladder Cancer

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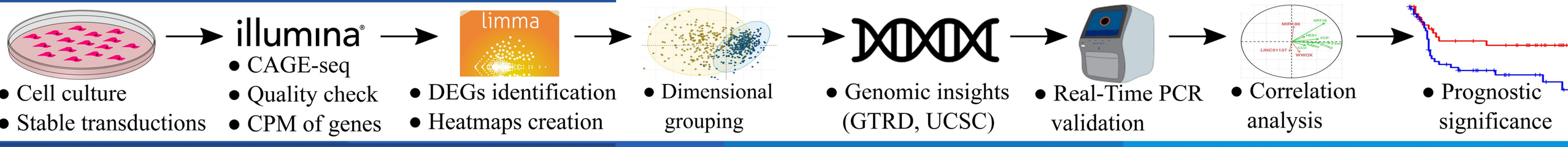
Introduction, aim of study:

Recently, we observed bladder cancer signaling changes that were orchestrated by WWOX, AP-2α, and AP-2γ proteins. However, in that project, we mainly focused on signaling pathways regulated by protein-encoding genes. **Since the literature on WWOX/AP-2 and non-coding (nc)RNA merits attention, this study aimed to initially construct an ncRNA-containing network with WWOX/AP-2 and then investigate the most relevant observations in the context of bladder cancer cell lines and patients**. Our research brings significant value in the field since WWOX has not been investigated for its role in regulating non-coding RNA in bladder cancer, placing our study at the beginning of such literature.

Materials and methods:



- Cell culture
- Stable transductions
- CAGE-seq
- Quality check
- CPM of genes
- DEGs identification
- Heatmaps creation
- Dimensional grouping
- Genomic insights (GTRD, UCSC)
- Real-Time PCR validation
- Correlation analysis
- Prognostic significance

Results and discussion:

Groups were better discriminated by WWOX than by AP-2α/γ

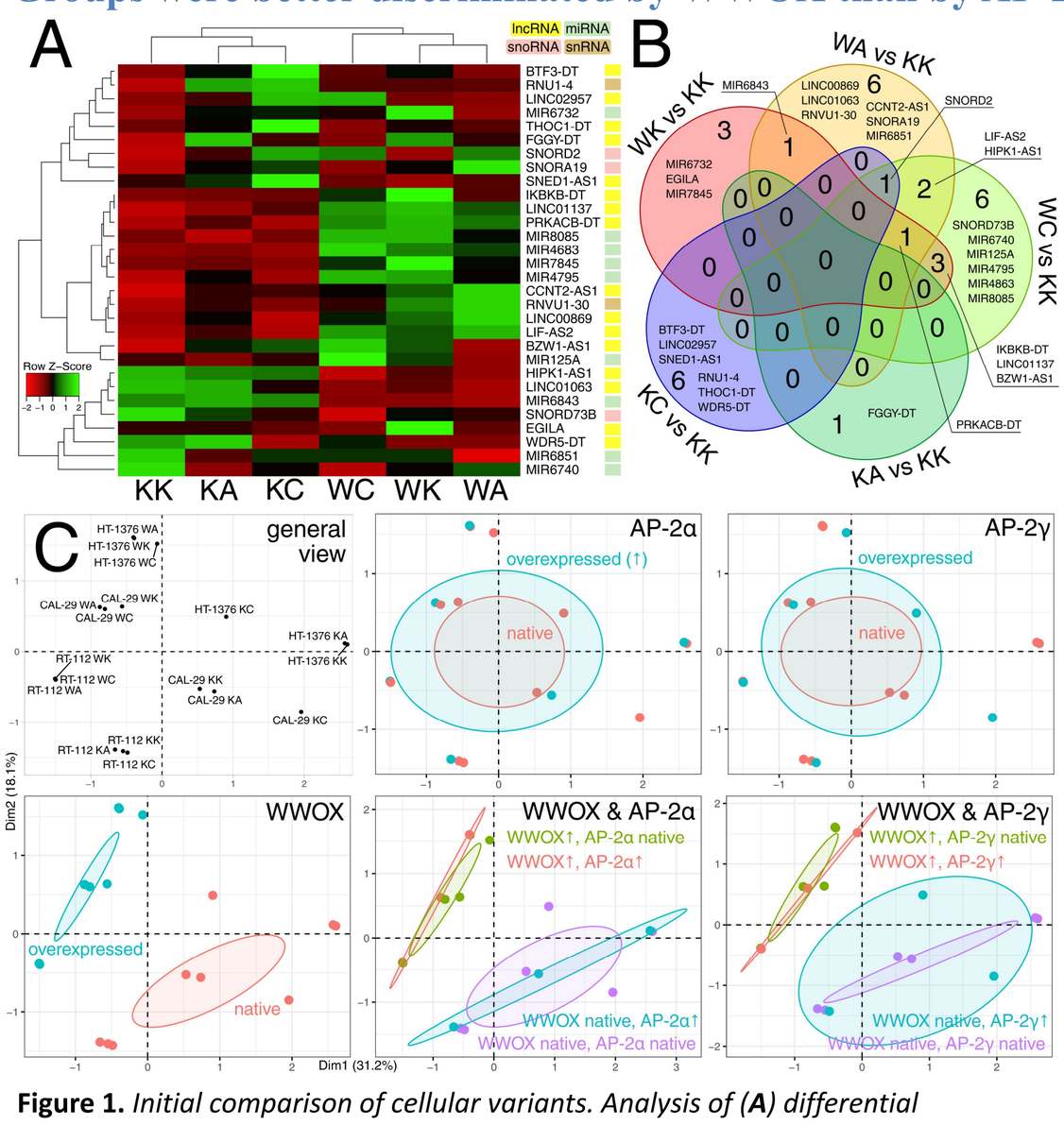


Figure 1. *Initial comparison of cellular variants. Analysis of (**A**) differential expression, (**B**) intersection, and (**C**) data multidimensionality.*

WWOX increases *LINC01137* via UPF1 transcription factor

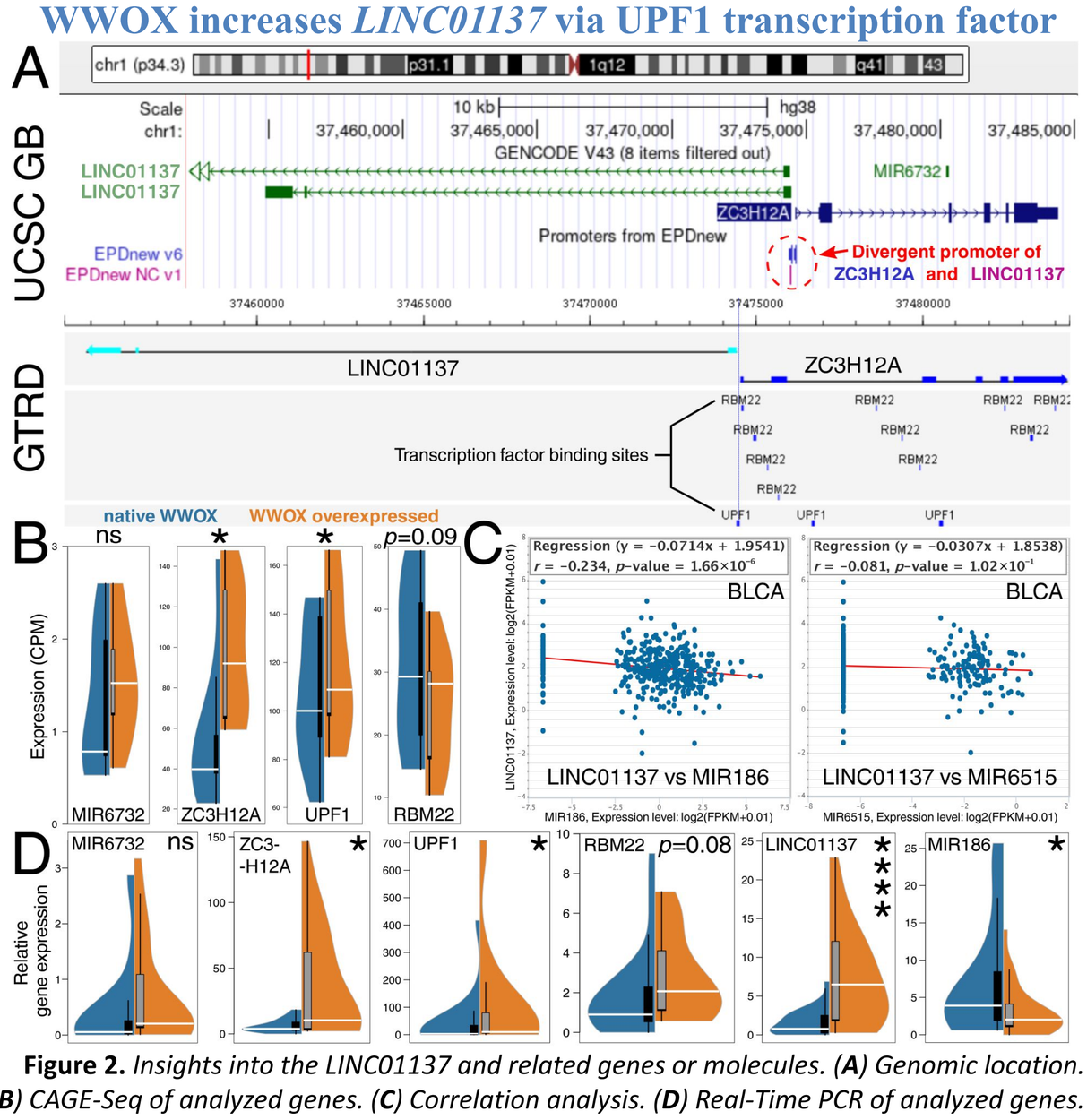


Figure 2. *Insights into the LINC01137 and related genes or molecules. (**A**) Genomic location. (**B**) CAGE-Seq of analyzed genes. (**C**) Correlation analysis. (**D**) Real-Time PCR of analyzed genes.*

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Order of figures

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There is scarcity of patients with desired expression profile

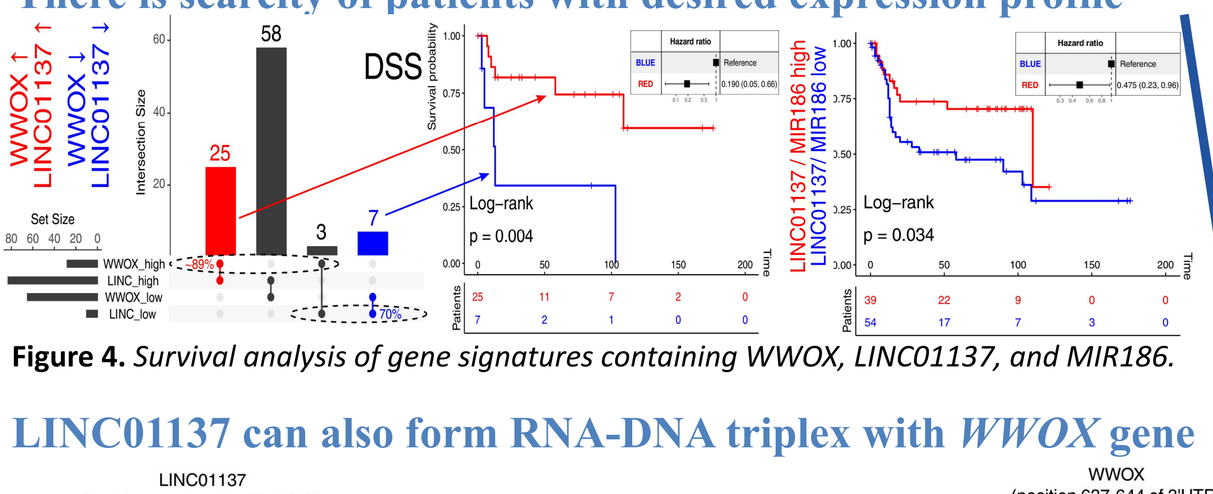

Figure 4. *Survival analysis of gene signatures containing WWOX, LINC01137, and MIR186.*

Data from patients and cell lines confirm the relationship

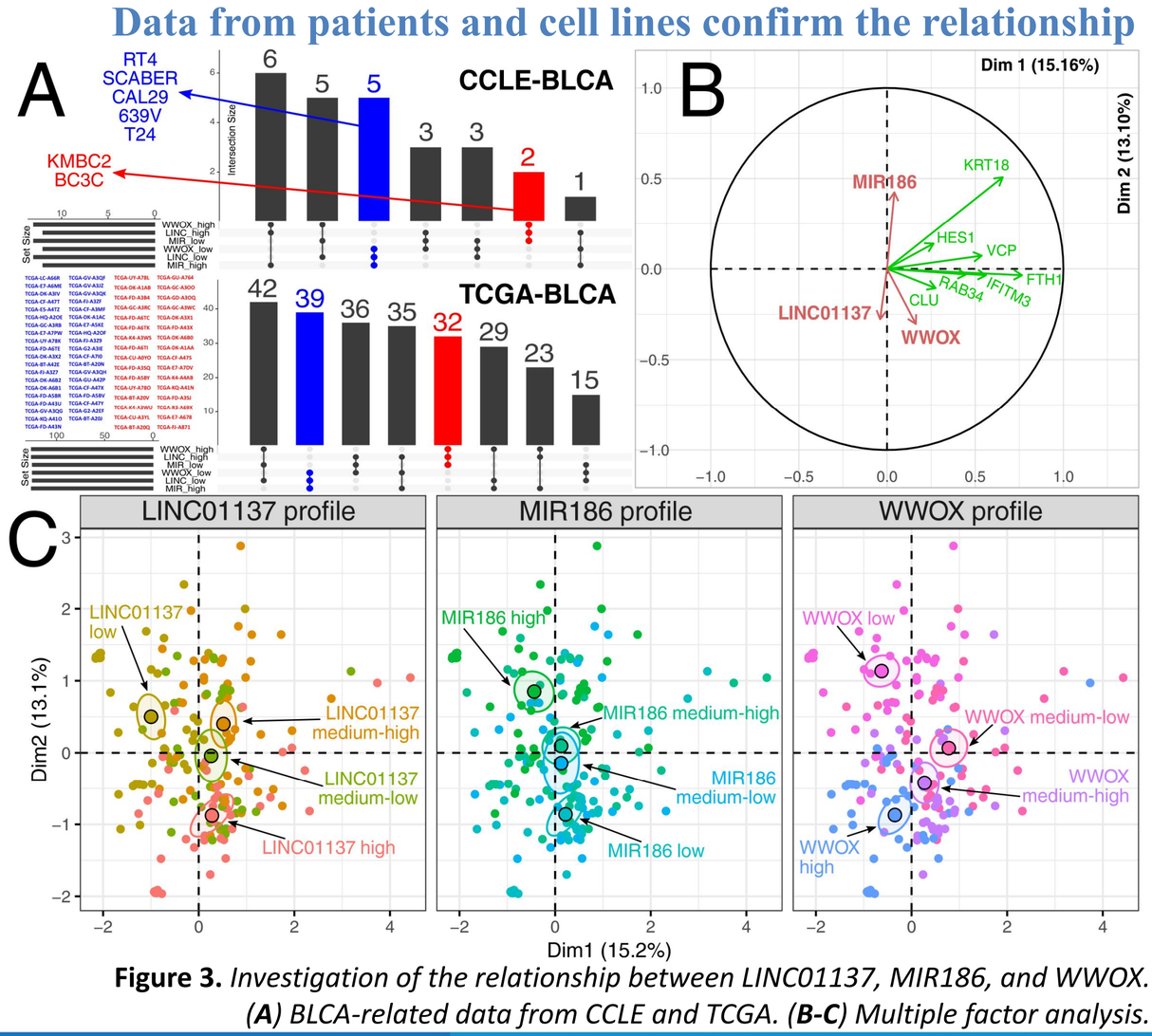

Figure 3. *Investigation of the relationship between LINC01137, MIR186, and WWOX. (**A**) BLCA-related data from CCLE and TCGA. (**B-C**) Multiple factor analysis.*

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LINC01137 can also form RNA-DNA triplex with *WWOX* gene

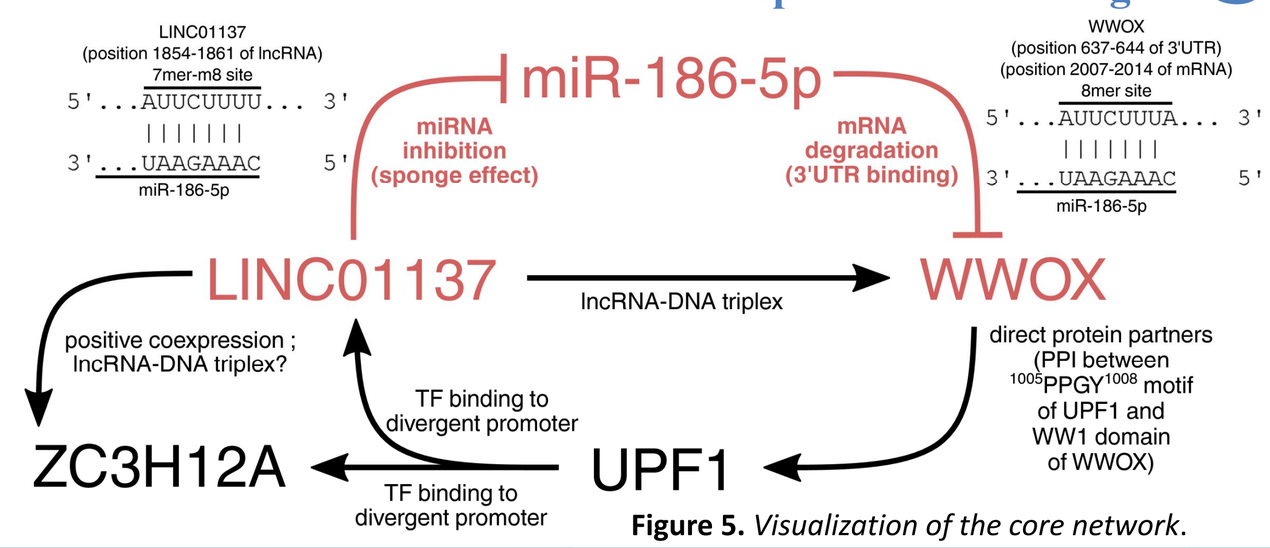

Figure 5. *Visualization of the core network.*

Conclusions:

Ultimately, WWOX was found to be implicated in the positive feedback loop with LINC01137, i.e., the lncRNA that sponges WWOX-targeting miR-186-5p. It is advisable to perform subsequent research to depict the relationships in a broader context, which may confer benefits to the clinic.