An emerging body of evidence points towards the significance of long noncoding RNA (lncRNA) in cancer development. These oncogenic molecules therefore lend themselves as predictors of disease outcome, but without the option of antibody-based detection, utilizing non-protein coding molecules as biomarkers can be challenging. Speaking with ACD, Clinical Assistant Professor of Pathology at Michigan Center for Translational Pathology (MCTP), Rohit Mehra, M.D., explains how the potential of the lncRNA SChLAP1 as a biomarker for prostate cancer outcome is being realized through RNA in situ hybridization with RNAscope® technology.

Can you provide a brief summary of your research focus?
Our research focus is on the critical pathogenic events underlying the development of genitourinary cancers, especially prostate cancer. Studying lncRNAs is a core part of this focus. The biology of lncRNAs is a relatively new field of study, however, and we do not yet have a full understanding of their roles in normal and disease states.

Advancing knowledge in this area, our center (MCTP) has discovered several lncRNAs that play an important role in prostate cancer, some of which may have clinical utility as prognostic or diagnostic biomarkers. For this, accessible methods for routine lncRNA detection are vital.

How did you discover that SChLAP1 was a biomarker for prostate cancer progression?
This involved two main stages: biomarker discovery, utilizing next-gen sequencing of the transcriptome, and the validation of SChLAP1, where we used ACD’s RNAscope® technology.

- Discovery
Next generation sequencing has been instrumental for identifying novel, disease-associated lncRNAs. Our lab used RNA-seq to comprehensively profile the transcriptome of >100 prostate cancer tissues and cell lines, and found that ~20% of RNA transcripts in prostate cancer represent novel, uncharacterized IncRNA genes. The novel IncRNAs were distributed throughout the genome, occurring in both intergenic and intronic, and in sense and antisense orientations. We assessed lncRNA expression across all samples and nominated 121 candidate lncRNAs that were overexpressed in prostate cancer. These were termed PCATs (Prostate Cancer Associated Transcripts).

- Validation
One of these PCATs was validated and re-named as Second Chromosome Locus Associated with Prostate-1 (SChLAP1) because it represented a large ~500kb region of high transcription in prostate cancer.

Importantly, we determined that SChLAP1 was a promising biomarker. We used a Mayo Clinic cohort of 235 high-risk prostate cancer specimens obtained from radical prostatectomy of localized prostate cancer patients. High risk disease entailed either advanced Gleason score (>=8), high serum PSA (>20), seminal vesicle invasion or extra-prostatic extension upon surgical resection. In this cohort, SChLAP1 expression measured...
“We found RNAscope technology fast and easy to use, this technology also allows us to directly visualize gene expression in the target tissue of interest. Also, only one 4 micron FFPE section is sufficient to give us all this information.”

1 - Transcriptome sequencing across a prostate cancer cohort identifies PCAT-1, an unannotated lncRNA implicated in disease progression.


2 - The long noncoding RNA SChLAP1 promotes aggressive prostate cancer and antagonizes the SWI/SNF complex.


3 - A novel RNA In Situ Hybridization Assay for the Long Noncoding RNA SChLAP1 predicts poor clinical outcome after radical prostatectomy in clinically localized prostate cancer.

Mehra R. et al. (2014), Neoplasia. 16(12):1121-1127

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