HTG Molecular Diagnostics, Inc. Featured Investigator

HTG EdgeSeq Oncology Biomarker Panel for Integrated Molecular Profiling of Genitourinary Tumors: Application for Personalized Radio Therapy

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Dr. Mian's clinical specialty is genitourinary tract cancers (bladder, prostate, kidney). His laboratory investigates mechanisms of epigenetic dysregulation in prostate and bladder cancer. He is developing novel biomarkers using integrated genomics to elucidate epigenetic changes that lead to cell proliferation, transformation, and therapeutic resistance. In a recent Nature webcast, Dr. Mian presented his work using HTG EdgeSeq technology. He also reviewed recent advances, strategies, and challenges in improving patient outcomes in the era of personalized oncology.

Dr. Mian utilized the HTG EdgeSeq Oncology Biomarker Panel to interrogate core needle punches derived from clinically annotated, archival small cell bladder cancer (SCBC) formalin-fixed paraffin-embedded (FFPE) blocks with the goal of developing a prognostic signature to determine the risk of tumor progression and therapy resistance. SCBC is a rare and aggressive cancer type with a poor prognosis and has a histology similar to small cell lung carcinoma. Before Dr. Mian's study, due to the rare nature of the tumor type, there were no prior reports of extensive molecular profiling to determine potential targetable pathways.

After the webinar, Dr. Mian shared the factors he considered when choosing the HTG EdgeSeq Oncology Biomarker Panel over other technology and assay options.

HTG: Could you please tell us why you chose to use the HTG EdgeSeq Oncology Biomarker Panel (OBP) versus a more comprehensive RNAseq analysis?
Dr. Mian: A couple of reasons. The ability to use a very small amount of input material so that we can take the small cell bladder cancer component of an FFPE tissue and profile it specifically. The OBP assay [has gene content that] is useful for subcategorization of tumor specimens. The other reason is you get this tradeoff; you may get more comprehensive expression profiling data from RNASeq or Microarray. However, the HTG OBP assay that has approximately 2600 genes enabled us to analyze very small, and in this case, very old FFPE specimens. Reliable expression profiling can sometimes be a challenge when working with older specimens, ten years and greater. We found our [RNA] integrity was really poor when we used extraction methods. HTG's [quantitative nuclease protection assay] approach gets around the issue of [RNA] extraction, so we were able to take our 46-small cell bladder cancer specimens and get reliable data for nearly all of them. For us, getting reliable gene expression data for the majority of our limited sample set seemed more important than cataloguing every single gene, especially since we were interested in a core group of tumor suppressors and oncogenes.

HTG: What is the typical format and amount of material you get from a prostate / bladder cancer patient?
Dr. Mian: It varies quite a bit and really does depend on the method of acquisition of that tissue. For instance, in the case of a prostate biopsy, it is a core needle biopsy that is obtained by our urology colleagues. These tend to be FFPE. In the case of prostatectomy or in the case of bladder cancer, where you can do a surgery to remove the bladder, you have tumor in situ that produces some other complications in terms of the amount of material and the relationship of tumor to normal tissue within the specimen. For instance, prostate tumors can be very multi-focal, they can exist in a small part of the prostate, or they can infiltrate throughout the prostate. There can be low or high-grade tumor in different parts of the whole mount specimen. So, to be able to macrodissect the tumor from the normal tissue is important. We do have to contend with this quite a bit in archived specimens, dissecting away signal from normal [tissue] versus tumor and to what degree the [tumor micro-] environment is contributing as well. It raises a lot of issues in terms of how we handle complex specimens. It isn't always straight forward.

HTG: Does the age of the FFPE specimens impact the results?
Dr. Mian: In our hands ten years seems to be a meaningful cut-off in terms of high versus low quality RNA extracted from fixed tissues. It probably varies with tumor site, storage, and fixation technique, but this a real issue. We have a tremendous resource of archived tissues here at our hospital and around the country, sometimes associated with robust clinical annotation as happens with correlative studies in cooperative group trials. It would be appropriate to analyze the tissues as we start to think about molecular profiling and genomic classifiers. The appropriate way to analyze these tissues I think is a bit up in the air. The homogeneity that allows us to get reproducible, reliable, genomic information from samples can be variable depending on how they were stored, fixed and extracted. In our hands, the [HTG EdgeSeq Oncology Biomarker Panel] assay seemed to be a very nice way to get consistent data across multiple different age samples.

If you are interested in viewing the full presentation, the webinar recording can be streamed here.

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