NEXT GENERATION LEARNING

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Update on Testing of Cytology Samples: Beyond the Cell Block

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Molecular testing on cytopathology samples is undergoing a transformation in today’s era of ‘Precision Medicine’. Although the concept is not new – cytopathology specimens have been the specimen of choice for HPV testing since the inception of this molecular methodology, the utilization of molecular testing as applied to cytopathology specimens is undergoing a renaissance, commensurate with the increased utilization of minimally invasive diagnostic techniques.

Many of the gene-based assays utilized in precision medicine testing have been routinely employed on cytology specimens, however until recently, the majority of these efforts have focused on cell block preparations. For example, \textit{EGFR} mutation testing of non-small cell lung cancer (NSCLC) on cytopathology cell blocks has been widely explored in the literature, with specimens deriving from a diverse array of anatomical sites such as lymph nodes (often by EBUS-FNA), pleural space, primary lung lesions and metastases to various organs. Indeed, guidelines on the molecular testing of NSCLC indicated that cytologic samples are suitable for \textit{EGFR} and \textit{ALK} testing, but that cell blocks were the preferred sample preparation.

Recently, additional explorations into utilization of alternate cytopathology specimen types has grown dramatically. This has been driven in part by the need to utilize the often scant material employed for primary diagnosis of NSCLC, and also in part the growing recognition of some technical advantages that come with evaluation of other cytopathology specimen types.

Despite requirements for rigorous validation in order to employ testing on a clinical basis, many laboratories have undertaken these efforts to enable clinical testing on a variety of specimen types, including stained smears, smears, imprint slides, cytospin preparations, and material harvested from fine-needle aspirate and effusion cytology specimens and held in liquid media. There are various advantages and disadvantages to each approach. Notably, all carry a substantial advantage over cell block prepared material, in that the quality of nucleic acid is generally substantially improved compared to cell blocks, owing to the lack of formalin fixation. Such approaches have been employed in a variety of disease settings, such as NSCLC, evaluation of thyroid nodules, and melanoma, among others. These recent developments call into question the superiority of the cell block as the substrate of choice for molecular testing on cytopathology specimens.

Outside of the clinical realm, use of cytopathology specimens for molecular analysis also holds great promise for translational research. Fine needle aspiration procedures can serve as an effective means of procuring samples for research study, and archived diagnostic cytopathology specimens represent a potential use of archival material to enable translational research.
References [1-18]: