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Identification of tumor cellular origins by anchored multiplex PCR and next-generation sequencing

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Tumors within the same anatomic locations often show significant heterogeneity, exhibiting diverse mutation and gene expression profiles. Distinct cellular origins or microenvironments of tumor-initiating cells have both been shown to uniquely influence the development of specific driver mutations. For example, lung cancer subtypes that arise from different anatomic locations exhibit distinct mutation profiles. Furthermore, subtypes of Diffuse Large B-Cell Lymphoma (DLBCL) exhibit unique clinical behaviors and can be distinguished based on their cell-of-origin (COO), which can be identified based on the cells' unique gene expression patterns. Therefore, identification of a tumor's COO through gene expression profiling aids in the prediction of tumor behavior. Despite advances in next-generation sequencing (NGS) to detect mutations, these assays often cannot measure gene expression, leaving the COO elusive. Archer® FusionPlex® assays are based on Anchored Multiplex PCR (AMP™), a target enrichment strategy for NGS that uses molecular barcodes that enable the counting of unique molecules to assess differences of expression levels across target genes and between samples. This allows for simultaneous mutation detection and gene expression profiling to identify COOs. We analyzed expression patterns to predict the cellular origins of several 100 lung tumor FFPE samples by performing a principle components analysis on data generated by FusionPlex Comprehensive Thyroid Lung (CTL) NGS assays. Similarly, we identified DLBCL subtypes in a small cohort of samples using the FusionPlex Pan-Heme assay. These results show that AMP-based NGS, which is used to identify multiple mutation types, can also identify the cellular origins of tumors through gene expression profiling.

Biography

Craig Pierson earned his BSc in Zoology from the University of Canterbury, New Zealand. His work started with Ovine Linkage Mapping projects while at AgResearch in Dunedin and continued into genome sequencing while at Baylor College of Medicine in Houston. He has trained and supported customers in Sanger sequencing, qPCR, NGS, and gene expression applications while at Applied Biosystems, Illumina, HTG, VelaDx and ArcherDx. He joined the ArcherDX team as a Field Application Specialist in July, 2015.

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