HONORABLE MENTION

Exploring the Genomic Landscape of Hepatobiliary Cancers to Establish a Novel Molecular Classification
Anthony J. Scholer MD\textsuperscript{1}, Mary Garland-Kledzik MD\textsuperscript{1}, Debopryia Ghosh D PhD\textsuperscript{2}, Adam Khader MD\textsuperscript{1}, Juan Santamaria-Barria MD\textsuperscript{1}, Javier Orozco MD\textsuperscript{1}, Melanie Goldfarb MD\textsuperscript{1}, Diego M. Marzese PhD\textsuperscript{1}. \textsuperscript{1}John Wayne Cancer Institute at Providence St. John’s Health Center, Santa Monica, CA; \textsuperscript{2}Rutgers University, Applied Probability and Data Analytics Lab, Newark, NJ

Abstract

Background:
Hepatobiliary cancers (HBCs) originating from a different tissue may have similar molecular phenotypes. The aim of this study was to evaluate the genomic alterations of HBCs as a first step towards creating a novel molecular subtype classification.

Methods: A multidimensional analysis of next-generation sequencing created a genomic landscape for HBCs using mutational data from the AACR-GENIE database. HBC genomic alterations specific to the tissue of origin (hepatocellular (HCC), cholangiocarcinoma (CCA), and gallbladder carcinoma (GBC)) were identified and associations between the histomolecular characteristics and gene mutations were analyzed.

Results: A total of 1,017 alterations were identified in 329 patients. IDH1 and KRAS mutations were associated with CCA, CTNNB1 and TERT mutations with HCC, while all tumors of HBCs had TP53 and ARID1 mutations (p < 0.001) (Figure 1). Clustering by mutation or copy number variant was not informative for molecular subtype identification, but integrative analysis identified a unique value molecular alteration (99 features, mutations, and copy number variants) in 324 patients with three molecular subtypes identified (HC-1, 2, and 3).

Conclusion: This study identified three unique molecular HBC subtypes that do not resemble the traditional criteria HBCs (anatomic location and histologic subtype (GBC, CCA, HCC)) supporting tumor biology may be influenced by molecular subtype rather than tissue of origin. This novel finding is the first step towards developing a histomolecular classification algorithm that can be used to determine staging and therapeutic stratification. Further exploratory genetic and epigenomic research is needed to complete the histomolecular classification algorithm.
Genomic Alterations by HBC Tissue of Origin

IDH1, KRAS, CDKN2A

N = 115

Genomic Alterations by Tumor Molecular Subtype

TP53 and TERT

N = 34

N = 177

N = 167