Hepatocellular carcinoma: The role of host immunity in the regulation of proliferative responses

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Hepatocellular carcinoma (HCC) is the most common primary liver malignancy, with over 600,000 cases annually around the world. Less than 20% of cases are not amenable to curative therapy either surgery or transplant, so the overall outcome of patients with HCC is poor. Cirrhosis of the liver is a major driver in the pathogenesis of HCC in addition to direct proliferative stimuli from hepatitis viruses. The nature of the influence of cirrhosis has emerged as an area of intense study, where the long-term effects of chronic inflammatory states might include creating a host environment driven by a perpetual activation of inflammatory responses which may lead in some cases to abnormal cell proliferation or inappropriate persistence of activation of inflammatory states culminating in malignancy. Recently, PDL1 ligand inhibition with novel therapies that up regulate MHC-1 targeted markers on the malignant cells has shown exceptional promise for various malignancies including melanoma, lung cancer, renal cell carcinoma and sub-classes of colon cancer as well as in hepatocellular carcinoma. The mechanisms remain to be clarified in HCC. However, the impact of cirrhosis in creating the framework within which the host's immune system can benefit from these therapies may be critical in determining how effective these therapies can be. Future study in the area of HCC will highlight how survival/proliferative and immune signaling pathways communicate in the background of cirrhosis compared other conditions and what may be the impact on the ability of driving the key pathogen etic events in the development and progression of HCC as well as influence the therapeutic approaches that are being actively studied to achieve control of this disease and thereby improve survival. In our discussion we will: Provide an overview of the major etiologic factors associated with the development of HCC; Review the major biological and molecular pathways that have been shown to be important in the pathogenesis of HCC and review the current therapies that are in use or in study for treatment; Review the data which demonstrates the impact of host inflammation on the pathogenesis of HCC in the absence versus presence of liver cirrhosis; and summarize the widely used systemic therapies in HCC and refractory HCC and highlight the more promising/actively studied therapies that show reasonable promise in improving the outcomes of patients with advanced and or refractory HCC.

Speaker Biography

Natalyn N Hawk obtained her MD and PhD from Brown University in Providence, Rhode Island, earning her doctorate in molecular pathology as a visiting scientist at M.D. Anderson Cancer Center in Houston, Texas where she identified a molecular complex important in the pathogenesis of chronic myeloid leukemia. She completed residency training in internal medicine at Johns Hopkins Bayview Medical Center in Baltimore, MD. She completed fellowship training in hematology and medical oncology at Emory University which included a one year post-graduate fellowship where she studied the efficacy of dual inhibition of mTOR and EGF receptor pathways as a potential therapy in Non small cell lung cancer. She is an Assistant Professor of Hematology and Medical Oncology at Emory University and is a member of the Gastrointestinal Oncology Working Group of Emory Winship Cancer Institute. She is also a member of the Discovery and Developmental Therapeutics Research Program at Winship Cancer Institute of Emory University.

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