Anele Jones

Professor Rinehart- Kim

BIO294

23 February 2024

Writing Assignment #4: Summary of Primary Genetics Article

The article "Necroptosis microenvironment directs lineage commitment in liver cancer" delves into the intricate differences between hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma (ICC), highlighting their distinct characteristics and responses to therapy. The study suggests that the hepatic microenvironment plays an important role in determining whether transformed hepatic cells commit to HCC or ICC lineages.

Utilizing in vivo electroporation to induce tumor formation in mice, researchers conducted experiments to pinpoint the cells of origin. Remarkably, they found that differentiated hepatocytes could give rise to both HCC and ICC, laying the groundwork for further investigation into the underlying mechanisms.

Central to their findings is the exploration of microenvironmental factors influencing lineage commitment, particularly focusing on cell death pathways such as necroptosis and apoptosis. The research uncovered that a necroptosis-enriched liver microenvironment fosters the development of ICC from oncogenically transformed hepatocytes. Through epigenome and transcriptome analysis, key regulators of this process, namely Tbx3 and Prdm5, were identified.

Crucially, the study extends beyond murine models, confirming its relevance in human liver cancer cases. By shedding light on the molecular intricacies of liver tumorigenesis, the research provides valuable insights into why specific liver-damaging risk factors may lead to the development of either HCC or ICC. Ultimately, this work contributes to a deeper understanding

of liver cancer pathogenesis and holds promise for the development of targeted therapeutic interventions tailored to each subtype.

Works Cited

Seehawer, Marco. et al. "Necroptosis Microenvironment Directs Lineage Commitment in Liver Cancer." *Nature*; DOI:10.1038/s41586-018-0519-y. **562 (7725)** (2018).