Background

Fibrolamellar Hepatocellular Carcinoma (FL-HCC) is a rare primary liver cancer affecting 0.02 per 100,000 in the USA (Lalazar & Simon, 2018). This cancer differs from the most common liver cancer, hepatocellular carcinoma (HCC), due to not being associated with any chronic liver diseases, such as cirrhosis or hepatitis (Lalazar et al., 2018) and occurs predominantly in adolescents and young adults. Through genomic screening, it’s been found that FL-HCC patients have a heterogeneous skeleton of approximately 40-60% on chromosome 19, creating a DNAJB1-PRKACA chimera (Honeyman et al., 2014) as shown in Figure 1. In FL-HCC, there are thick fibrous bands in hepatocytes that pathologists use for diagnosis. The only treatment for this aggressive cancer is liver resection, with any chronic liver diseases, such as cirrhosis or hepatitis (Lim et al., 2014) and occurring commonly in adolescents and young adults. The LMW-E isoform has a weight ranging from 45 to 33 kDa

Proline involvement in FL-HCC: Our collaborator, Dr. Roland P. Graham, at the Mayo Clinic, has recently conducted proteomic screening (mass spectrometry based analysis) on FL-HCC tumor samples and have identified differential expression in different enzymes, involving the proline pathway. Figure 2 depicts the enzymes that are dysregulated in the proline biosynthetic pathway. Figure 3A shows the various proline enzymes using western blotting to test Mayo’s findings of the proteomic screening of the proline pathway. This was done by past research students who were on this project.

How might the upregulation of proline play a role in the molecular cause of FL-HCC? A study done by Oka et al. on rat hepatocytes (normal rat liver cells) found that addition of proline to cultured hepatocytes upregulates cyclin E (via the mTOR pathway) (Kim et al., 2015). Cyclin E is required for the transition from G1/S phase of the cell cycle as shown in Figure 4A and it determines the proliferation of DNA-duplication. When Oka et al. added rapamycin (an mTOR inhibitor) to the hepatocyte that contains proline, upregulation of cyclin E was downregulated as shown in Figure 4B. The mTOR pathway is a regulatory protein synthesis pathway that is controlled by various regulators, such as insulin and growth factors, and is involved in cellular proliferation, cell survival, and cell death.

Results

Liver samples blotted with cyclin E antibody (HE172)

Liver samples blotted with beta actin antibody

Conclusion and Future Research

Future Research

References

Acknowledgments

References


