Universidad de Navarra
Facultad de Ciencias

Propuesta de Trabajo Fin de Máster
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MÁSTER EN CIENCIA DE DATOS PARA CIENCIAS EXPERIMENTALES

Proyecto Nº 27

Título: Identifying novel players in pathogenesis of metabolic dysfunction-associated steatotic liver disease (MASLD) and progression towards liver cancer

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Resumen:
Metabolic dysfunction-associated steatotic liver disease (MASLD) encompasses a spectrum of liver lesions ranging from simple steatosis to steatohepatitis (MASH), a more malignant state that may progress to cirrhosis and liver cancer. Although viral infections and alcohol abuse have been main risk factors for liver cancer up to now, MASLD is now considering the fastest rising risk factor for liver cancer, particularly hepatocellular carcinoma (HCC). However, the mechanisms underlying the progression from MASLD towards HCC remain unresolved. Therefore, there is an urgent need to discover the molecular mechanisms involved in the development and progression of MASLD towards HCC in order to develop novel effective treatments. The aim of this project is to provide an in-depth study of MASLD-associated LC using a multi-omics approach, to be able to identify therapeutic targets that determine its development. In a recent multi-OMICs analysis (bulk miRnomics, transcriptomics, proteomics and metabolomics) of whole-spectrum MASLD, using samples from animal models representative of all disease stages and cancer, we have identified novel miRNAs that are altered during disease progression, identifying their putative protein targets and potential regulation of metabolic pathways. To further study in detail the development of MASLD-associated liver cancer, we will perform parallel analyses of RNA-seq, proteomics, and metabolomics in these same murine models of MASLD and MASLD-associated liver cancer, with different time points corresponding to stages of simple steatosis, early MASLD, established MASLD, MASLD-associated HCC, and MASLD-associated CCA. This analysis will be conducted individually for each omic (using R or Python-derived approaches) and subsequently integrated to identify the proteins responsible to the modulation of metabolic networks during MASLD progression. The identified putative protein targets will be then evaluated in human samples of patients with MASLD, in bulk transcriptomic data as well as in scRNA-seq and spatial transcriptomics data. The results of this project are expected to provide a deeper understanding of the different protein:metabolite circuits crucial for the development novel drugs for the treatment of MASLD and prevention of liver cancer development.

OPTATIVAS RECOMENDADAS
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