Project title: Unravelling the degradome associated with tissue remodelling during liver cancer (**JAEINT20_EX_0475**)

Project leader: Dr Ana Moles Fernández
https://www.linkedin.com/in/annamoles
Placement place: Mitochondrial Regulation of Cell Death. CEK. Barcelona.
http://www.idibaps.org/recerca/408/regulacio-mitocondrial-de-la-mort-cellular-i-esteatohepatitis
https://www.iibb.csic.es/ca/research/59

Associated call: JAE Intro 2020 (competitive call)
Link: https://sede.csic.gob.es/intro2020
Applicants requirements: The equivalent average grade required (in decimal scale) is **>8.00**.

- Students who will finish their degree in the 2019-2020 academic year
- Students who will be students of official Master's Degree in the 2020-2021 academic year, having applied for admission, or enrolment to an official University Master's for the 2020-2021 academic year
- Students who are enrolled in an official University Master's course in the 2019-2020 academic year
- Completed the studies: 1st January 2017, in the case of EHEA degree studies of 240 credits

Length of the project: 5 months (+4 months competitive extension).
Starting: 1st September or 1st October.
Award: 3000 euros
Deadline: 9/03/20-10/06/20

Contact: ana.moles@iibb.csic.es
Applications through: https://sede.csic.gob.es/intro2020

Liver cancer is the 2nd most common cause of cancer-related deaths worldwide and one of the few cancers whose incidence and mortality keeps steadily increasing. Hepatocellular carcinoma (HCC) accounts for 70-90% of liver cancers and has very poor prognosis (5-year survival of 11%). HCC is very resistant to chemotherapy and only 30% of patients are eligible for curative therapies. Despite its enormous clinical relevance, knowledge around the molecular pathogenesis of HCC lags behind other types of cancer. Around 80% of HCC patients present a similar disease progression involving chronic inflammation, recurrent injury, regeneration and fibrosis, which will eventually lead to liver cancer.

The degradome is the complete set of proteases present in an organism. Their main function is to hydrolyse the peptide bond in proteins resulting in irreversible post-translational functional modifications, process also called proteolysis. Proteases build interconnecting webs or networks of multiple proteases, which operate in linear pathways, amplification cascades and regulatory circuits contributing to disease progression. Proteolytic activity in tumours is regulated in a complex manner, as both genetically unstable cells and stromal cells are involved. Proteases, specifically lysosomal cathepsins, are overexpressed in several different cancers and contribute to carcinogenesis, invasiveness potential and metastasis. Thus, they are considered promising targets for anti-cancer therapy. The role of cathepsins in the development of liver disease, fibrosis and NASH, has been studied by our laboratory and others (Hepatology. 2009 Apr; 49 (4): 1297-307; Am J Pathol. 2010 Sep; 177 (3): 1214-24; J Biol Chem. 2012 Jan 6; 287 (2): 1178-88). However, and despite the proven importance of cathepsins in liver diseases and in many types of cancer, the role of cathepsins in the progression of liver cancer is currently unknown. Thus, the aim of this project is to analyse cathepsin D cell-specific role in tissue remodelling during liver cancer progression. In this project the candidate will use both *in vivo* preclinical murine models of liver cancer and *in vitro* cellular models of increasing complexity to mimic the biophysical conditions of the tumour. The candidate will analyse the *in vitro* and *in vivo* models using histological (IHP, IF…), molecular (WB, RT-PCR…) and microscopy (confocal, time-lapse…) techniques and omic technology. This proposal can reveal important biological information about the proteolytic networks controlling tissue remodelling during liver cancer.