

Role of processing-bodies in chronic liver diseases and hepatocellular carcinoma

Summary

Contexte : Tristetraprolin and HuR are key post-transcriptional regulators of gene expression controlling mRNA decay and translation (e.g., TNF α , MYC). TTP-mediated mRNA decay occurs within small cytoplasmic compartments referred as processing Bodies (P-bodies). Although our previous work has highlighted the importance of these proteins in the development of Non-Alcoholic Fatty Liver Disease (NAFLD) and hepatocellular carcinoma (HCC), the role of P-bodies in these diseases remains totally unknown. Our preliminary data indicate that P-bodies assembly importantly contributes to the development of NAFLD and HCC. This Ph.D project (3 years starting in October/November 2023) aims at deciphering the role of P-bodies in these diseases and evaluating the potential of their therapeutic targeting.

This project will be carried out in the INFINITE unit (U1286 Inserm | University of Lille | CHU), which is devoted to the study of inflammation and associated disorders. This project requires several approaches, including cellular/molecular biology (hepatic cell lines, primary cells, confocal microscopy, molecular cloning), bioinformatic and animal experimentations (mouse models).

Requirements

- A Master-2 with strong knowledge in cellular, molecular biology and physiology.
- **Working with rodents (mice) is mandatory.**
- Willingness to learn new skills and techniques.
- Excellent written and verbal communication skills in English.
- Teamwork/enthusiasm.

References

1. Cyril Sobolewski, Daniel Abegg, Flavien Berthou, Dobrochna Dolika, Nicolas Calo, Christine Sempoux, Margot Fournier, Christine Maeder, Anne-Sophie Ay, Pierre-Alain Clavien, Bostjan Humar, Jean-François Dufour, Alexander Adibekian and Michelangelo Foti. S100A11/ANXA2 belongs to a tumor suppressor/oncogene network deregulated early with steatosis and involved in inflammation and hepatocellular carcinoma development. *Gut*. 2020 Jan 9. pii: gutjnl-2019-319019. doi: 10.1136/gutjnl-2019-319019.
2. Dobrochna Dolika, Michelangelo Foti, and **Cyril Sobolewski***. The Emerging Role of Stress Granules in Hepatocellular Carcinoma. *Int J Mol Sci*. 2021 Aug 30;22(17):9428. doi: 10.3390/ijms22179428.
3. Dobrochna Dolika[§], **Cyril Sobolewski[§]**, Monika Gjorgjieva, Marta Correia de Sousa, Flavien Berthou, Claudio De Vito, Didier Colin, Olivia Bejuy, Margot Fournier, Christine Maeder, Perry J Blackshear, Laura Rubbia-Brandt and Michelangelo Foti. Tristetraprolin promotes hepatic inflammation and tumor initiation but restrains cancer progression to malignancy. *Cell Mol Gastroenterol Hepatol*. 2020 Sep 25:S2352-345X(20)30155-7. doi: 10.1016/j.jcmgh.2020.09.012.
4. Dobrochna Dolika, **Cyril Sobolewski**, Marta Correia de Sousa, Monika Gjorgjieva and Michelangelo Foti. mRNA Post-Transcriptional Regulation by AU-Rich Element-Binding Proteins in Liver Inflammation and Cancer. *Int J Mol Sci*. 2020 Sep 11;21(18): E6648. doi: 10.3390/ijms21186648.

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