

Post-doctoral position at the Cancer Research Center of Lyon (CRCL), Lyon, France

Equipe: Epigenomics and Epigenetic of Hepatocellular Carcinomas

A **postdoctoral position** is available at the CRCL - INSERM Unit 1052 in the research team of **Pr Massimo Levrero** to work on the role of HBV proteins and lncRNAs in the molecular pathogenesis of HBV-related hepatocellular carcinomas.

The position is open for **3 years** and it is funded by the National Agency for Research against AIDS and Hepatitis (ANRS) within the frame of the research program "**Role of the HBx - DLEU2 lncRNA functional interaction in the regulation of Ezh2/PRC2 activity and HBV-related liver carcinogenesis**", in collaboration with the Center for Life Nanosciences (CNLS) of the Italian Institute of Technology in Rome, Italy (**Dr. Francesca Guerrieri**)

The project aims to investigate the interplay between the viral protein HBx, the lncRNA DLEU2 and the Enhancer of Zeste Homolog 2 (EZH2) histone-lysine N-methyltransferase in HBV infected cells and their impact on the cellular epigenome. More in detail the project will address the following questions, which are key for the understanding of HBV-related HCCs as well as the discovery of novel strategies for HCC prevention and treatment:

- generate a map of global genomic binding sites for DLEU2-HBx and DLEU2-Ezh2 complexes by coupling ChIRP (Chromatin Isolation by RNA Purification) followed by NGS (ChIRP-Seq) and ChIP-Seq experiments in HBV infected cells;
- identify DLEU2-HBx and DLEU2-Ezh2 regulated genes by cross analysis of: a) DLEU2 ChIRP-Seq; b) HBx and Ezh2 ChIP-Seq and c) RNA-seq data sets in HBV infected cells;
- validate the virus-induced modifications of Ezh2 repressed and Ezh2 activated genes in liver tissues of chronic HBV-infected patients and HBV-related HCCs.
- investigate the mechanism of HBV-induced / DLEU2 mediated modifications using chemical compounds (Ezh2/PRC2 modulators; folded guanine quadruplexes (G4) stabilizing ligands).

The post-doctoral candidates should be proficient in molecular and cellular virology. Experience in chromatin analysis technologies and primary hepatocytes culture would be welcome. Fluent English (spoken and written) is required.

Candidates should submit their application (CV and 2 letters of recommendation) to Massimo Levrero (massimo.levrero@inserm.fr) and Francesca Guerrieri (francesca.guerrieri@iit.it)

Recent publications by the host laboratories:

- Levrero M, Zucman-Rossi J. Mechanisms of HBV-induced hepatocellular carcinoma. *J Hepatol.* 2016;4:S84-S101.
- Fiscaro P, Barili V, Montanini B, Acerbi G, Ferracin M, Guerrieri F, Salerno D, Boni C, Massari M, Cavallo MC, Grossi G, Giuberti T, Lampertico P, Missale G, Levrero M, Ottonello S, Ferrari C. Targeting mitochondrial dysfunction can restore antiviral activity of exhausted HBV-specific CD8 T cells in chronic hepatitis B. *Nat Med.* 2017;23:327-336.
- Guerrieri F, Belloni L, D'Andrea D, Pediconi N, Le Pera L, Testoni B, Scisciani C, Floriot O, Zoulim F, Tramontano A, Levrero M. Genome-wide identification of direct HBx genomic targets. *BMC Genomics.* 2017;18:184-192.
- Plissonnier ML, Lahlali T, Raab M, Michelet M, Romero-López C, Rivoire M, Strebhardt K, Durantel D, Levrero M, Mehlen P, Zoulim F, Parent R. Reciprocal antagonism between the netrin-1 receptor uncoordinated-phenotype-5A (UNC5A) and the hepatitis C virus. *Oncogene.* 2017;66:398-415
- Zhang W, Chen J, Wu M, Zhang X, Zhang M, Yue L, Li Y, Liu J, Li B, Shen F, Wang Y, Bai L, Protzer U, Levrero M, Yuan Z. PRMT5 restricts Hepatitis B Virus replication via epigenetic repression of cccDNA transcription and Interference with pgRNA encapsidation. *Hepatology.* 2017;66:398-415.
- Lebossé F, Testoni B, Fresquet J, Facchetti F, Galmozzi E, Fournier M, Hervieu V, Berthillon P, Berby F, Bordes I, Durantel D, Levrero M, Lampertico P, Zoulim F. Intrahepatic innate immune response pathways are downregulated in untreated chronic hepatitis B patients. *J Hepatol.* 2017;66:897-909.
- Testoni B, Durantel D, Lebossé F, Fresquet J, Helle F, Negro F, Donato MF, Levrero M, Zoulim F. Ribavirin restores IFN α responsiveness in HCV-infected livers by epigenetic remodelling at interferon stimulated genes. *Gut.* 2016;65:672-82.