

Master Santé Publique

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Parcours M2 B3S : Biostatistique, Biomathématique, Bioinformatique et Santé

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Descriptif du stage

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Titre du stage	Une protéine oncogénique appelée netrine-1 et ses fonctions hépatiques. Exploitation de données cliniques issues des biopsies du laboratoire pour évaluer son potentiel d'implication dans l'hépatocarcinome.
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Sujet détaillé du stage	Netrin-1 is a ligand for dependence receptors that sustains tumorigenesis (for review: Mehlen, Nat Rev Cancer, 2011; Cancer Res 2015), in particular in inflammation-associated tumors. One of its cognate receptor often down-regulated in general carcinogenesis is UNC5A. In a seminal study on dependence receptors ligands and virology in the liver setting, we have shown that Netrin-1 and UNC5A are respectively dramatically up- (+20-fold) and down-regulated (-44-fold) in HCV+ cirrhosis
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	compared to virus negative histologically matched samples, and that Netrin-1 exerts a proviral effect through the EGFR (Plos Biol. 2016, in press). One therefore believes that their profound dysregulation at the cirrhotic level may represent a strong rationale for the evaluation of their implication in HCC as supported by ourselves in another study (CMGH, 2016, in press). The laboratory hosts a liver biopsy repository amongst which 500-600 samples were previously analyzed, mainly, but not exclusively, related to HBV, HCV, and alcoholic liver disease. In this context, the goal of the internship will be to evaluate by biostatistical means the likelihood of implication of netrin-1 and its Unc5a in liver carcinogenesis by testing associations between netrin/unc5a levels and cirrhosis severity, HCC prevalence, life expectancy after HCC onset, various HCC biological and histological markers, recurrence after treatment, and any other relevant correlation. Netrin-1 targeting approaches are currently being implemented in general carcinogenesis in phase 1 clinical trials in Lyon, France. Altogether, if conclusive, these results should ultimately contribute to paving the way for the consideration of Netrin-1-based dual antiviral/anti-HCC prophylactic strategies at the cirrhotic level, in combination with direct acting antivirals in the case of HCV infection.
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Bibliographie de référence sur le sujet (Max 4 réf)	1: Plissonnier ML, Lahlali T, Michelet M, Lebossé F, Cottarel J, Beer M, Neveu G, Durantel D, Bartosch B, Accardi R, Clément S, Paradisi A, Devouassoux-Shisheboran M, Einav S, Mehlen P, Zoulim F, Parent R*. Epidermal Growth Factor Receptor-Dependent Mutual Amplification between Netrin-1 and the Hepatitis C Virus. PLoS Biol. 2016 Mar 31;14(3):e1002421. doi: 10.1371/journal.pbio.1002421. eCollection 2016 Mar. PubMed PMID: 27031829; PubMed Central PMCID: PMC4816328. 2 : Lahlali T, Plissonnier ML, Romero-López C, Michelet M, Ducarouge B, Berzal-Herranz A, Zoulim F, Mehlen P, Parent R*. Netrin-1 Protects Hepatocytes Against Cell Death Through Sustained Translation During the Unfolded Protein Response. Cell. Mol. Gastroenterol. Hepatol. 2016 May;2(3), 281–301.
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