Institute of Molecular and Cell Biology

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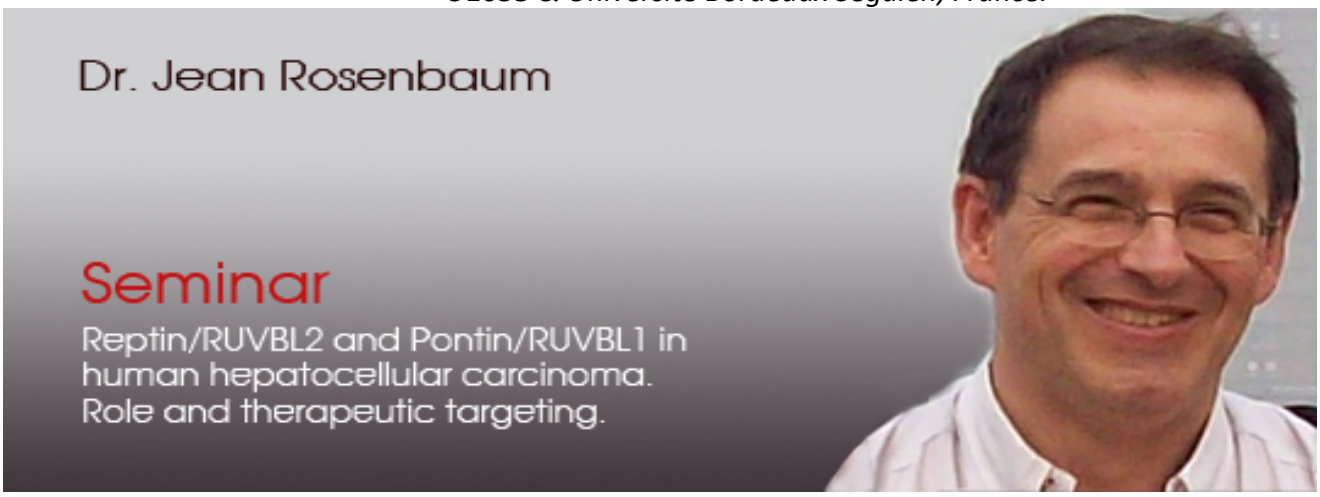
SEMINAR ANNOUNCEMENT

DATE: 1 February 2012, Wednesday

TIME / VENUE: 11:00AM @ IMCB Seminar Room 3-46, Level 3, Proteos, Biopolis

SPEAKER: Dr. Jean Rosenbaum, *Director, INSERM U1053 & Universite Bordeaux Segalen, France.*



Hepatocellular carcinoma (HCC) is the main type of primary human liver cancer and is associated with a poor prognosis. Looking for new targets, we performed a proteomic analysis of human HCC that allowed for the discovery of an over-expression of Reptin in these tumors [1]. Reptin and its homolog protein, Pontin (also overexpressed in HCC), are AAA+ family members and are involved in chromatin remodeling, transcription regulation and DNA repair [2, 3]. They are usually associated within multimeric complexes with a 1:1 stoichiometry. We demonstrated that Reptin [4] and Pontin [5] are required for HCC cell growth and viability. We further showed that Reptin and Pontin are co-regulated at a post-translational level with the consequence that silencing either one with RNAi leads to the simultaneous silencing of the other one [5]. As a proof of concept that Reptin can be a therapeutic target in HCC, we xenografted mice with human HCC cells bearing an inducible Reptin shRNA and showed that Reptin silencing led to tumor regression [6]. Our current work aims at better understanding the functions of Reptin and Pontin in tumor cells using transcriptome analysis, and at designing specific Pontin ATPase antagonists using molecular modeling.

[1] J. Blanc, C. Lalanne, C. Plomion, J. Schmitter, K. Bathany, J. Gion, P. Bioulac-Sage, C. Balabaud, M. Bonneu, J. Rosenbaum, Proteomic analysis of differentially expressed proteins in hepatocellular carcinoma developed in patients with chronic viral hepatitis C, Proteomics 5 (2005) 3778-3789.

[2] A. Grigoletto, P. Lestienne, J. Rosenbaum, The multifaceted proteins Reptin and Pontin as major players in cancer, Biochim Biophys Acta 31 (2011) 91-103.

[3] O. Huber, L. Menard, V. Haurie, A. Nicou, D. Taras, J. Rosenbaum, Pontin and reptin, two related ATPases with multiple roles in cancer, Cancer Res 68 (2008) 6873-6876.

[4] B. Rousseau, L. Menard, V. Haurie, D. Taras, J. Blanc, F. Moreau-Gaudry, P. Metzler, M. Hugues, S. Boyault, S. Lemiere, X. Canron, P. Costet, M. Cole, C. Balabaud, P. Bioulac-Sage, J. Zucman-Rossi, J. Rosenbaum, Overexpression and role of the ATPase and putative DNA helicase RuvB-like 2 in human hepatocellular carcinoma, Hepatology 46 (2007) 1108-1118.

[5] V. Haurie, L. Menard, A. Nicou, C. Touriol, P. Metzler, J. Fernandez, D. Taras, P. Lestienne, C. Balabaud, P. Bioulac-Sage, H. Prats, J. Zucman-Rossi, J. Rosenbaum, Adenosine triphosphatase pontin is overexpressed in hepatocellular carcinoma and coregulated with reptin through a new posttranslational mechanism, Hepatology 50 (2009) 1871-1883.

[6] L. Menard, D. Taras, A. Grigoletto, V. Haurie, A. Nicou, N. Dugot-Senant, P. Costet, B. Rousseau, J. Rosenbaum, In vivo silencing of Reptin blocks the progression of human hepatocellular carcinoma in xenografts and is associated with replicative senescence, J Hepatol 52 (2010) 681-689.

Host: Dr. Frederic Bard