戦略セミナーのお知らせ

スウェーデンUppsala大学のAristidis Moustakas先生が学会で来日されるのにあわせて、本学でのセミナーをお願いしました。Moustakas先生はがんにおけるTGF-βシグナルと上皮間葉移行(EMT)の分野において先駆的な研究をされており、最先端の研究成果を紹介して頂けると思います。皆様のご来聴をお願い申し上げます。

日時： 9月26日(金)17時00分ー18時30分

場所： 研3・12階・セミナー室G

講師： **Aristidis Moustakas**, Ph.D
Professor
Ludwig Institute for Cancer Research and
Department of Medical Biochemistry and Microbiology,
Uppsala University, Sweden.

題目： **Regulation of cancer stem cell potential by HMGA2, a chromatin regulator of epithelial-mesenchymal transition and biological aging**

講演要旨：

Epithelial-mesenchymal transition (EMT) contributes to tumor cell invasiveness and the generation of cancer stem cells. Our laboratory aims at deciphering molecular mechanisms that link EMT to the generation and maintenance of cancer stem cells. We study the nuclear protein high mobility group A2 (HMGA2) that is required for the induction of EMT by transforming growth factor β (TGFβ) (Thuault et al. J. Cell Biol. 174:175-83, 2006). HMGA2 regulates a cohort of transcriptional regulators of the EMT process, such as Snail1 and Twist1 (Thuault et al. J. Biol. Chem. 283:33437-46, 2008; Tan et al. J. Biol. Chem. 287:7134-45). HMGA2 is an embryonic chromatin factor that is gradually and steadily downregulated during adult life with the exception of tissue stem cells, where its downregulation is induced by the aging process. Signal transduction by TGFβ and its related polypeptides, bone morphogenetic proteins (BMPs), coordinates physiological responses in diverse cell types. TGFβ promotes EMT, tumor cell invasiveness and metastasis, while BMP promotes mesenchymal-epithelial transition (MET) and suppresses tumorigenicity. The work that we will present focuses on the role of HMGA2 in breast carcinoma cell invasion and stem cell survival. Breast cancer cells that express high or lower levels of HMGA2 present a corresponding degree of self-renewal based on mammosphere assays. When HMGA2 is silenced from aggressive breast cancer cells, the phenotype shifts to an epithelial, indicative of MET, and concomitantly, tumor cells lose their self-renewing capacity. Transcriptomic analysis identified genes that are regulated by HMGA2 and which functionally link to the processing of miRNA biogenesis. Finally, by focusing on non-epithelial cancer stem cells, namely glioblastoma, we demonstrate that the ability of BMP to suppress glioma cancer stem cell self-renewal and tumorigenic potential depends on the transcriptional induction of Snail1, which induces differentiation of glioma cells and promotes a dramatic invasion of these cells within the recipient brain, while depleting the tumorigenicity from the same cells. Our work starts explaining in molecular detail how embryonic nuclear factors like HMGA2 and Snail1, when reactivated in human cancer, provide coordinated control of multiple genes, thus, promoting both the mesenchymal transition and tumor cell

主催： 心血管医科学研究室　渡部 琢也（watanabe@toyaku.ac.jp）
腫瘍医科学研究室　　渡部 徹郎（twatabe@toyaku.ac.jp）

共催： 私立大学戦略的研究基盤形成支援事業
「オルガネラ接触場の形成機構と破綻による疾患」