第 1239 回生物科学セミナー

日時:　10 月 19 日（金）　16：50　～　18：30
※講師 2 名を招いて開催いたします。

演者：　Professor Utz Fischer
（Universität Würzburg）

演題:　RNA biology and its implication for human diseases

The generation of messenger RNAs (mRNAs) and their translation into proteins depends on the elaborate interplay of a numerous trans-acting factors. These factors are often organized in macromolecular machines, which enable all steps in mRNA metabolism and timely coordinate their progression. Our group studies the functional dynamics of key macromolecular machines acting on RNA using a combination of biochemical, structural and systems biology approaches. RNA-related pathways have been linked to a broad spectrum of human diseases. By combining basic RNA research with biomedical approaches we investigate how these pathways and networks are changed in different disease settings. Our research hence contributes to detailed insight into disease etiologies and the identification of novel drug targets for therapy.

演者：　Professor Gunter Meister
（Universität Regensburg）

演題：　Gene regulation by non-coding RNA and RNA modification pathways

Gene expression is not only regulated at the level of transcription, but also at many post-transcriptional steps. Various classes of non-coding RNAs have been identified that affect gene expression including microRNAs and lncRNAs. Very recently, circular RNAs that are generated by alternative splicing have been identified. Some of these circular RNAs can function as sponges for miRNAs or RNA-binding proteins. The function of most of these RNAs, however, remains unknown. In addition, mRNAs can be modified a specific bases. M^6A-modification, for example, affects mRNA stability, translation efficiency or localization. We have generated a number of different monoclonal antibodies against modified nucleotides (e.g. m^6A, $m^{26}A$, m^5C, m^3C). We have developed several assays for antibody validation, which is critical for mRNA profiling studies. In addition, we have functionally characterized ncRNAs in metastasis and therapy escape. Using an intrasplenic tumor model for colorectal cancer, we identified several lncRNAs and circular RNAs differently expressed in primary tumors and metastases suggesting a role in tumor progression. One of the circRNA candidates is circZNF609, which is up-regulated in primary tumors as well as liver metastases. Using biochemical approaches, we analyzed the coding potential of circZNF609 and do not find evidence for efficient and specific translation in vivo. We developed a method for knock down and overexpression of circZNF609 and established inducible stable cell lines for in vivo analyses. In xenograft mouse models, overexpression of circZNF609 promotes colorectal cancer development. Vice versa, knock down of circZNF609 inhibits tumor formation. Our data demonstrates that circZNF609 contributes to cancer progression in colorectal cancer and suggests that circRNAs might be a class of RNAs with fundamental functions in disease.
Since circular RNAs are not accessible for exoribonucleases, which turn over most of the endogenous RNAs, we asked how circRNAs are degraded. We used biochemical fractionation experiments and characterize distinct decay pathways in human cells.

場所:　**理学部　1 号館　東棟　287 号室**

担当:　東京大学大学院理学系研究科・生物科学専攻　塩見研究室