Functional Genomics and Metabolism

Distinguished Seminar

Wednesday, May 22 from 14.00-14.45
in BMB Seminar room

"circRNA – elucidating new function in human development and disease"

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Abstract

More complex organism, such as mammals, have developed very sophisticated post-transcriptional systems to diversify the output of each gene. The RNA transcripts from most genes are cleaved and reassembled along alternative routes and form a variety of mRNAs, which sometimes outnumber our total number of genes. Usually, this alternative splicing process occurs forward in a linear fashion, but recently it has become evident that a substantial number of genes are "back spliced", yielding circular RNA (circRNA). As for the linear splicing, back splicing appears to be tightly controlled and differentially expressed in many systems. Most significantly in the development of the brain where thousands of circRNA are temporally and spatially expressed. We are currently elucidating the functional implications of circRNA by targeting them with RNA interference and CRISPR/Cas technology or gain-of-function by designing circRNA expression vectors. Accumulating evidence places circRNA as a prominent new group of non-coding RNAs, which impacts gene regulation during development of tissue, cell homeostasis and development of disease.

Deregulated circRNAs expression is also commonly seen in diseases including cancer and inflammation where some circRNAs appear to work as sponges for miRNA and proteins. In some instances, circRNA expression is regulated by epigenetic events and evidence suggests that this may play a role in the development of drug resistance.
We are also elucidating how the cell balances and regulates the ratio of forward and backward splicing. Here it turns out that an intricate cross talk between intronic RNA elements, RNA binding factors and splicing signals are of key importance.
Apart from being an interesting new player in cell biology, circRNAs prove to be robust biomarkers to predict development and consequence of human diseases. Furthermore, we are able to exploit the increased stability of circRNA therapeutically by letting them bind and thereby block the function of disease related proteins and other non-coding RNAs, including microRNAs.

Host: Prof. Susanne Mandrup, Functional Genomics & Metabolism Research Unit, Dept. Biochemistry and Molecular Biology, SDU