BDR SEMINAR in Kobe

Daniel B. Constam

Associate Professor of Life Sciences, EPFL

Tuesday, May 14, 2019

14:00-15:00, 7F Seminar Room, DB Building A

Regulation and dynamics of Bicaudal-C1 self-interactions and their role in concentrating target mRNAs

Summary

Loss-of-function mutations in the RNA-binding protein Bicaudal-C1 (BICC1) randomize left-right patterning and provoke renal cysts and pancreatic and bile duct dilatations reminiscent of polycystic kidney diseases. Candidate target RNAs include components of TGFβ and cAMP/PKA signaling pathways, but their contributions to phenotypic abnormalities of Bicc1 mutants and the precise mechanisms how such targets are regulated remain unclear. Using fluorescent miRNA mimics in EMSA assays, we found that BICC1 can act as a chaperone of adenylate cyclase 6 mRNA. However, deletion of the major catalytic subunit of PKA did not inhibit cyst formation, suggesting that pathways other than cAMP synthesis and PKA signaling are important. A protein interactome screen revealed new links of Bicc1 to energy metabolism and cytoskeletal organization. Furthermore, binding to the ciliopathy-related factors ANKS3 and ANKS6 modulated the size and shape of cytoplasmic Bicc1 granules assembled by a self-polymerizing sterile alpha motif (SAM). Analysis of the dynamics and phase-separation of such polymers points to a role as gel-like scaffolds for RNA binding and possibly folding.

Host: Hiroshi Hamada
Laboratory for Organismal Patterning, BDR
hiroshi.hamada@riken.jp
Tel:078-306-3002 (ext:3325)