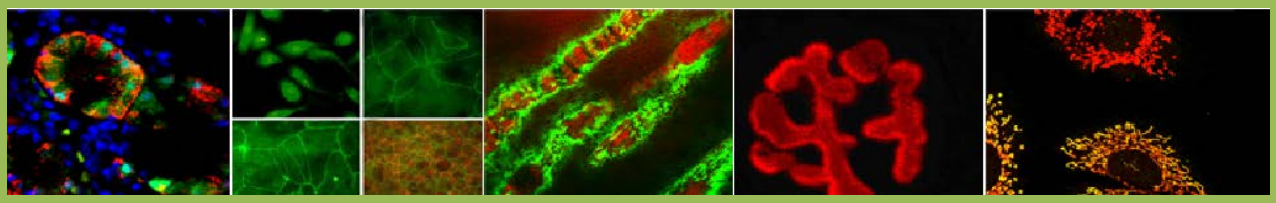

Department of Cell Biology Research Forum

Michael Sheets, PhD

Professor
Department of Biomolecular Chemistry
University of Wisconsin

"How Translational Control of Cell Fates is Controlled"

"Our work in Xenopus embryos demonstrates that the Bicaudal-C (Bicc1) translational repressor protein operates as the central node of a dynamic protein-mRNA network that controls early vertebrate development. The Bicc1 network functions with both temporal and spatial specificity to fine tune the synthesis of proteins that in turn regulate critical temporal and spatially constrained developmental events. We are investigating this network on two fronts. First, we have examined the mechanisms by which Bicc1 recognizes its mRNA target sites. Bicc1 contains multiple KH-domains, known RNA binding modules. Using in vivo and in vitro assays we have defined a single KH domain that is critical for both RNA recognition and translational repression. Second, we have focused on defining the maternal Bicc1-network from initial Bicc1 localization in the vegetal hemisphere of eggs to the expansion of this network through Bicc1-medited translational repression of maternally provided target mRNAs. We have shown that the target mRNAs of Bicc1 encode critical cell fate regulators that, like Bicc1, must function with both temporal and spatial specificity. Indeed, overexpression of several of these cell fate regulators has been shown to cause specific developmental defects, i.e. excess accumulation of anterior structures. When we generated maternal knock-out Bicc1 embryos, we observed the same phenotype- accumulation of anterior structures- providing evidence that loss pf Bicc1 caused the proteins encoded by Bicc1 target mRNAs to be overexpressed. Finally, we have also shown that several Bicc1 mRNA targets encode RNA binding proteins and translational regulators, such as the Nsun2 RNA methylase, suggesting that the Bicc1 network that was established maternally continues to expand into later stages of development. We are currently analyzing Bicc1- regulation of these downstream mRNA targets."

Tuesday, September 26th, 2017
12:00p-1:00p
Rosenstiel Medical Science Building
4th Floor Auditorium

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