CDB SEMINAR

Victoria Prince

University of Chicago

Monday, November 10, 2008
16:00~17:00 C1F CDB Auditorium

Using Zebrafish to study pancreas development

Summary

The powerful genetics and accessibility of the zebrafish make it a good model to study vertebrate pancreas development. We have found that Retinoic Acid (RA) plays a conserved role in specifying the pre-pancreatic endoderm. RA synthesized in anterior paraxial mesoderm signals to adjacent endoderm of the zebrafish late gastrula to specify pancreatic cell fates. Proper size and localization of the pancreatic field are thus dependent upon tight control of RA signaling. We find that the Cdx4 transcription factor functions within posterior endoderm to delimit the posterior boundary of the pancreatic field. By contrast, the Cyp26 RA degrading enzymes play a critical role in defining the normal anterior limit of the pancreatic field. Disruption of Cyp26 function using the R115866 pharmacological inhibitor causes a dramatic expansion of pancreatic cell types towards the anterior of the embryo. Our analysis of the *cyp26a1/giraffe* mutant reveals that *cyp26a1* plays the primary role in setting the anterior limit of the pancreas. Consistent with these findings, *cyp26a1* expression co-localizes with the pancreatic primordium at developmental stages when RA is signaling to specify pancreas. Together with our finding that endodermal expression of *cyp26* genes is subject to positive regulation by RA, our data suggest a feedback loop within the endoderm that ensures consistent levels of RA signaling, despite environmental fluctuations in RA concentration. In ongoing experiments we testing the hypothesis that Cyp26a1 functions directly within the endoderm germ layer to regulate pancreas size and position. We are also identifying additional downstream targets of RA signaling that function in pancreas development.

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