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FLESHING OUT THE REGULATORY NETWORKS CONTROLLING HUMAN PANCREAS DEVELOPMENT

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SUMMARY

The transcription factor gene *Pancreatic and Duodenal Homeobox 1* (*PDX1*) encodes an evolutionarily conserved transcription factor that is expressed during the earliest stages of human pancreatic development. The loss of *PDX1* results in complete pancreatic agenesis, a dramatic phenotype that emphasizes the critical role PDX1 plays in coordinating the morphogenesis of this indispensable metabolic organ. My laboratory routinely models human pancreatic development *in vitro* by differentiating human pluripotent stem cells into early pancreatic progenitors (ePP). Using a protocol that tightly adheres to developmental logic, abundant PDX1+ ePP cells emerge after two weeks of *in vitro* culture. These ePP cells display a molecular signature that significantly overlaps with the developing human pancreatic primordium. In my talk, I will describe how we have used a variety of "omics" and bioinformatic approaches to unveil the gene regulatory network operating directly downstream of PDX1. Interestingly, several PDX1 target genes currently under investigation in the lab are not only essential for pancreatic development but are also redeployed in insulin-secreting beta cells that ensure glucose homeostasis and whose dysfunction leads to diabetes.