Mechanistic insights into translational sciences

Abstract: Translational sciences keep up the big picture beyond the deep-dive in diverse disease areas. Heterogeneity in dynamic cell populations and tissue morphogenesis in evolving organism, here represented by the evolving pancreas in the model of *mus musculus*, are ideal candidates for investigating precursor versus mature cells for the variants in the biologic dogma content, respective RNA versus DNA versus Protein. The gene *Synaptotagmin 13* (*Syt13*) represents a candidate for translational sciences, as the gene itself suggests to be involved in pancreatic organogenesis and cancerogenesis. Preliminary results are pointing to phenotype in type 2 diabetes (T2D) in *mus musculus* along with a phenotype in the establishment of pancreatic duodenal adenocarcinoma (PDAC) in *mus musculus.*

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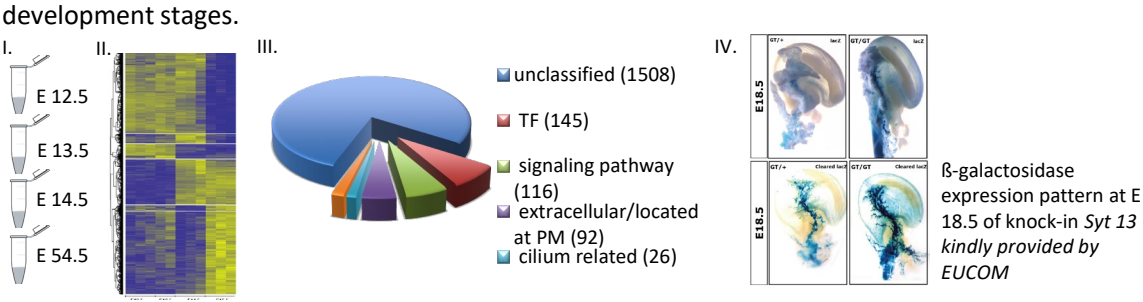
Introduction: Detailed studies are required to determine the interplay of interconnected compartments, f.e, rigorously. The pancreas is a heterogeneous gland, consisting of the compartments with acinar, ductal, and endocrine cells. Thus, an RNA profile of the pancreatic gland during organogenesis suggests revealing lineage determining factors of the adult pancreas' different compartments. Furthermore, the conserved mechanism might be relevant for the fine-tuned lineage segregation in the pancreas and other organ development stages.



ß-galactosidase expression pattern at E 18.5 of knock-in *Syt 13 kindly provided by EUCOM*

Material and Methods: Pancreatic epithelium of consecutive embryonic stages (E) was dissected, single-cell suspension (Collagenase treatment) achieved, and by using the QIAGEN© RNeasy Mini Kit, triplicates of the RNA samples generated, each sample in the different embryonic stage was referenced against each other (I.). Global transcriptional profiling was accomplished by Affymetrix® GeneChip® Gene 1.0 ST Array Card and statistical analyses through the Affymetrix® Expression console (II. and III.). Knock-in mouse of the gene *Synaptotagmin 13 (Syt 13)* was kindly provided by EUCOMM (www.genoway.com). Handling the mice was accomplished using the manual "Manipulating the mouse embryo: a laboratory manual" by Nagy & Behringer (IV).

Figure 1

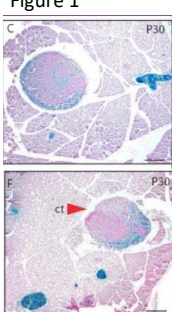


Figure 2

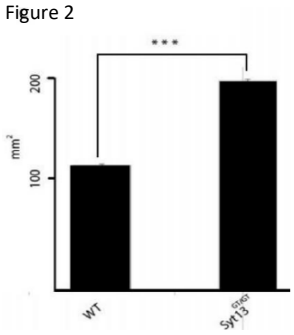
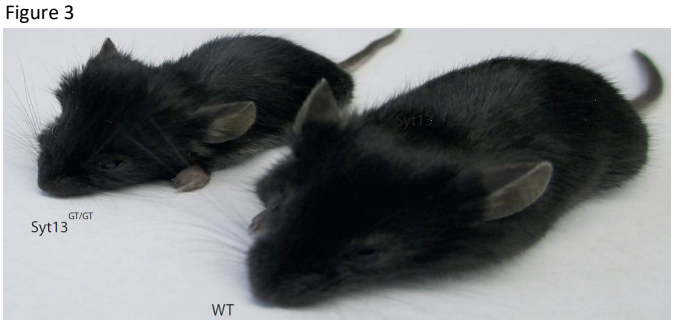


Figure 3



Results & Conclusion: Figure 1 illustrates cyst formation in the pancreatic region of the knock-in mouse model of *Syt 13*. Next to cyst formation, represented here in figure 2, the Islet of Langerhans is enlarged, suggesting a failure in proper organ formation. Furthermore, *Syt 13* knock-in represents a low percentage of hydrocephalus' phenotype, pointing to the relationship between mid-hindbrain boundary and axon guidance for endocrine progenitors (figure 3). Thus, preliminary results point to EMT's mechanism, in which *Syt13* mutants suggests to be a critical player (figure 5). Figure 4 is a model of endocrine lineage segregation versus ductal lesions resulting in pancreatic intraepithelial neoplasia (PanIN), and pancreatic ductal adenocarcinoma (PDAC) is introduced. Different experimental approaches are needed to test this hypothesis (figure 4). Different experimental approaches are needed to test the hypothesis of the mechanism of EMT in endocrine genesis, as well as in cancerogenesis, which represents in state of the art either endocrine and/or mesenchymal cellular properties and polarity cues within a particular cell (figure 5).

Figure 4

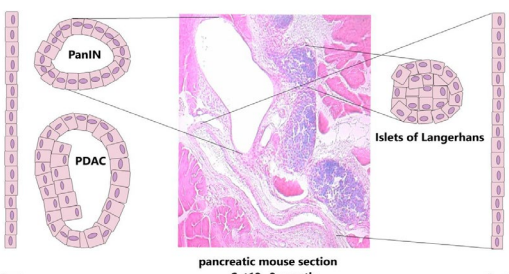
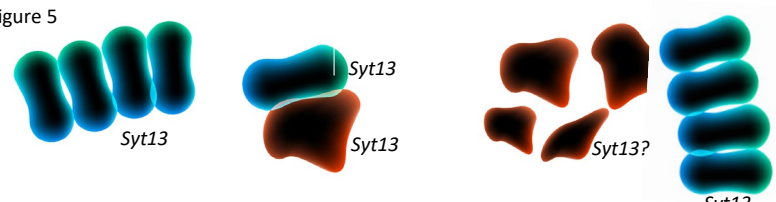


Figure 5



endocrine commited phenotype

Intermediate state > Endocrine and mesenchymal commited

Endocrine commited and/or mesenchymal commited

Partial epithelial-to-mesenchymal-transition

References:

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