

Role of the transcription factor *Isl1* in the pancreas development in *Danio rerio*.



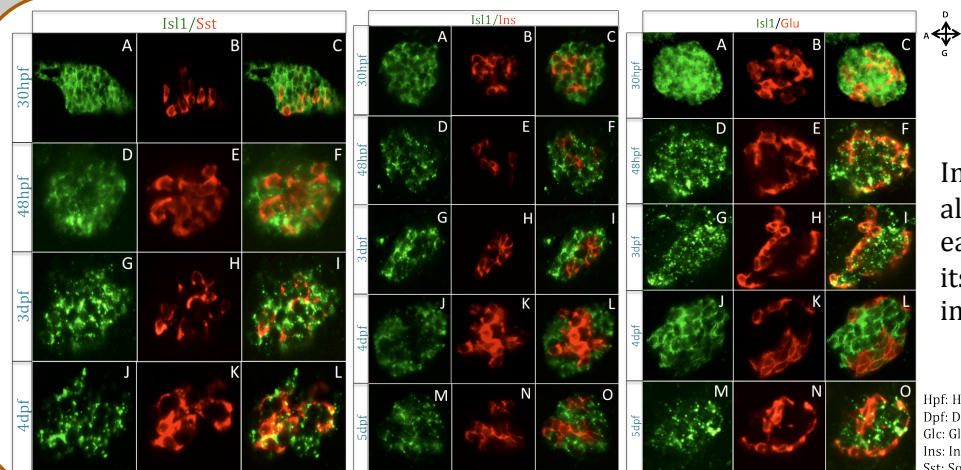
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Introduction

Maturity-onset diabetes of the young 7 results from the insulin-releasing disability caused by a mutation of the *Isl1* gene (Zhang and al., 2009). Moreover nonsense mutations of the *Isl1* gene were found in a Japanese type 2 diabetic patient family (Shimomura and al., 2000). The LIM homeodomain gene *Islet-1* (*Isl1*) is required for the formation of all endocrine cells (Ahlgren and al., 1997) but its targets and its position in the endocrine differentiation pathway are not well defined. Studying its role in zebrafish endocrine pancreatic development could answer these questions.

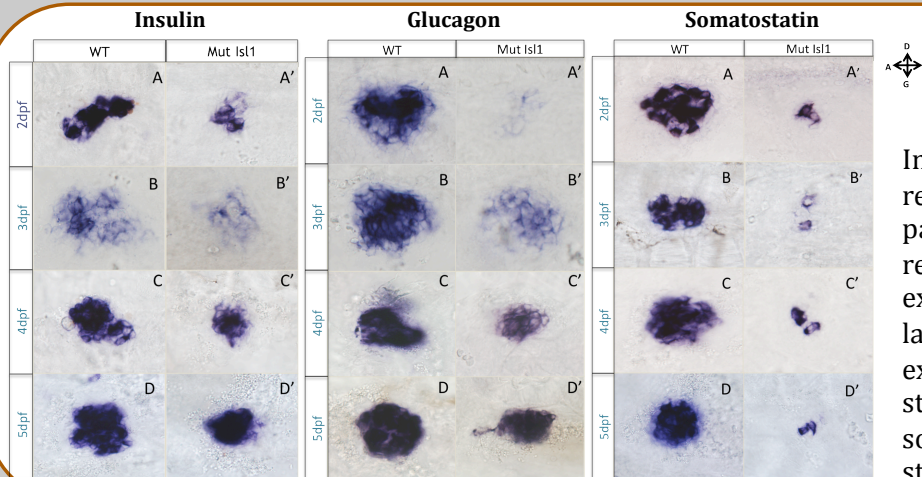
Results and discussion



Expression of *Isl1* in the endocrine pancreas by double hybridization *in situ*

In zebrafish, *Isl1* is expressed in all endocrine pancreatic cells at early stages while at later stages, its expression is only maintained in the somatostatin cells.

hpf: Hours post fertilization
Dpf: Days post fertilization
Glc: Glucagon
Ins: Insulin
Sst: Somatostatin



Function of *Isl1* in the pancreas by hybridization *in situ*

In the mutant *Isl1*, we show a severe reduction of all hormones in the pancreas at early stages. However, the reduction of glucagon and insulin expression seems transient. Indeed, at later stages, the glucagon and insulin expression is reduced but not as strongly as at early stages while for somatostatin, the strong reduction is still observed at later stages.

Conclusions

	Mutant <i>Isl1</i>		
	Glucagon	Insulin	Somatostatin
24hpf	↓↓↓	↓↓↓	↓↓↓
48hpf	↓↓↓	↓↓↓	↓↓↓
72hpf	↓↓↓	↓↓↓	↓↓↓
96hpf	↓	↓	↓↓↓
120hpf	↓	↓	↓↓↓

Colocalization *Isl1*/Hormones



***Isl1* is required for the differentiation of all endocrine hormones at early stages while at later stages, *Isl1* is only important for the formation of somatostatin cells.**

Reference:

Ahlgren, U, Pfaff, S.L., Jessell, T.M., Edlund, T., Edlund, H. 1997. Independent requirement for *ISL1* in formation of pancreatic mesenchyme and islet cells.
Shimomura, H., Sanke, T., Hanabusa, T., Tsunoda, K. 2000. Nonsense mutation of *islet-1* gene (Q310X) found in a type 2 diabetic patient.
Zhang, Wang, Guo, Yang, Ma, Chen, Zhou. 2009. The LIM-homeodomain Protein *Isl1* activates Insulin Gene promoter directly through synergy with *BETA2*.