# The Role of PHA-4/FoxA Transcription Factor in Establishing the Cellular Context for in vivo Forced Transdifferentiation

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#### Introduction

- -Transdifferentiation or direct cell reprogramming is defined as a switch of one cell type to another resulting in the loss of one cellular characteristic and gain of the other.
- -We currently do not understand how cellular context influences a cell's susceptibility to be directly reprogrammed.
- -We hypothesize that PHA-4, a transcription factor exclusively expressed in the intestine, pharynx, and uterus, may have a role in establishing the cellular context that results in transdifferentiation into intestine.
- Uncover the process behind transdifferentiating cells into different cell-types from different germ layers without going through the intermediate pluripotent stage of a cell's life

### **Future Methods**

- Deplete PHA-4 starting in early stage larvae (L1) using feeding RNA interference.
- Induce GATA factor expression via heat shocking inducible promoter (30-33°C for 30 minutes)
- Study the morphological effects of induced expression of a specific GATA transcription factors.

#### Past Results

The graphs and pictures below show us the ectopic expression of an intestine-specific GATA transcription factor, ELT-7, resulting in the pharyngeal cells transdifferentiating into intestinal cells. It has also been shown to have similar reprogramming effects in the uterus.

#### **Future Methods using** hs-elt-7; elt-2::lacZ::GFP Expression of *elt-7* via heat shock inducible promoter RNA interference (RNAi) 100 worms with ectopic elt-2::lacZ::GFP 80 Transfer 60 ~100 L1 larvae 40 Control to each RNAi plate 20 (include non heat OPA OPA OPA OPA shock controls) hs-elt-7 ( - ) ( + ) ( + ) ( + ) ( + ) Ectopic EII.7 T(hrs) 48-96 5-96 4 N 46 126 13 13 Key Point: No expression of elt-2 outside of pharynx after 144 hours heat shock heat shock heat shock heat shock Observe after two days after 2 day after 1 day after 3 day after 4 day

## Discussion / Anticipated Results

Our goal is to determine the reprogramming susceptibility of the pharynx and uterus into intestine after knocking down PHA-4 using feeding RNA interference. We anticipate that by knocking down PHA-4, there will either be a decrease or increase in the expression of elt-2 after the GATA (end-1 or end-3) is expressed via a heat shocking inducible promoter. With these observations we can determine how necessary the presence of PHA-4 is in making the pharynx and uterus more or less susceptible to be transdifferentiated.

Misty R. Riddle, Abraham Weintraub, Ken C. Q. Nguyen, David H. Hall, Joel H. Rothman. 2012. In vivo Transdifferentiation and Remodeling of Fully Differentiated Somatic Cells by a Single Transcription Factor.