Universität Basel

Research Project

C. elegans Embryogenesis

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The formation and physiology of organs is one of the fundamental mysteries of biology: how are cells specified to be part of an organ? How is the development of organ precursors coordinated in space and time? My lab has a longstanding interest in organogenesis of the foregut, or pharynx, with a particular focus on its transcriptional regulatory processes. We use C. elegans because its simple, transparent anatomy and its rapid genetics, genomics and molecular biology provide a powerful system for analysis. In this application we explore how the foregut develops in response to changing environmental conditions. The central regulator of the C. elegans pharynx is pha-4, which encodes a FoxA transcription factor (Horner et al. 1998; Kalb et al. 1998). FoxA factors are critical regulators of digestive tract development in all animals studied to date. They function as selector genes that specify foregut fate during early embryogenesis, and they drive gut differentiation and morphogenesis at later stages (Mango 2009; Lalmansingh et al. 2012; Zaret and Mango 2016). To accomplish these diverse tasks, FoxA factors like PHA-4 control a broad spectrum of target genes expressed at different times or in different cells within the foregut (Gaudet and Mango 2002; Gaudet et al. 2004; Zhong et al. 2010; Zaret and Mango 2016; Von Stetina et al. 2017b). While studies in multiple organisms have identified conserved components required to establish the foregut (Mango 2009; Grapin-Botton 2008), it is less clear what mechanisms modulate these components to allow the digestive tract to respond to varying environmental conditions. C. elegans worms are acutely aware of their surroundings and can sense a wide array of chemicals through 32 chemosensory neurons. These chemicals elicit both short-term responses (feeding or movement) and longer-term effects that alter longevity or development (Bargmann 2006; Hsieh et al. 2017). My lab has found a surprising link between mutations that alter chemosensation in the mother and pha-4 silencing in progeny. We will test the hypothesis that mothers detect chemicals in the environment and impart this information to their progeny. In Aim 1 we will examine the genetic requirements for this cross-generational interaction. This will help elucidate the mechanism. In Aim 2 we will explore the anatomical site of action of factors involved in this process, to delineate how signaling in neurons communicates to embryos. In Aim 3, we will sequence RNAs inherited in very early embryos to identify candidate regulatory molecules. We will test these candidates for modulatory behavior.

Keywords pha-4; C. elegans; intergenerational signaling; embryogenesis
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