# EMBRYONIC ECDYSONE-INDUCED GENE EXPRESSION AND PROGRESSION OF ORGAN MORPHOGENESIS

### AKADEMISK AVHANDLING

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin vid Göteborgs Universitet kommer att offentligen försvaras i hörsal Arvid Carlsson, Medicinaregatan 3, **onsdagen den 1 juni 2011 kl 13:00** 

av:

## Tina M. Chavoshi Alizadeh

**Fakultetsopponent:** Professor Ylva Engström Department of Molecular Biology and Functional Genomics, Stockholm University

Avhandlingen baseras på följande delarbeten:

- I Tång E.\*, Byri S.\*, <u>Chavoshi T.M.</u>, Norum M. and Uv A. A gene program that regulates tube length in the *Drosophila* trachea *Manuscript*
- II Zulfaqhar A. S., Bougé A-L\*, <u>Chavoshi T.M.</u>\*, Byri S., Tång E., Bouhin H., Härd I., Uv A.

A luminal mucin-like protein promotes diameter expansion of the *Drosophila* hindgut.

Submitted manuscript. \* Joint second authors

#### III <u>Chavoshi T.M.</u>, Moussian B., Uv A.

Tissue-autonomous EcR functions are required for concurrent organ morphogenesis in the *Drosophila* embryo *Mechanisms of Development 127 (2010) 308-319* 

#### IV Chavoshi T.M. and Uv A.

Embryonic ecdysone is required for progression of tracheal gene programs in *Drosophila Manuscript* 



UNIVERSITY OF GOTHENBURG

# EMBRYONIC ECDYSONE-INDUCED GENE EXPRESSION AND PROGRESSION OF ORGAN MORPHOGENESIS

#### Tina M. Chavoshi Alizadeh

Institute of Biomedicine, Department of Medical and Clinical Genetics, University of Gothenburg, Sweden

#### ABSTRACT

The formation of an epithelial organ requires a set of organ-specific gene programs that instruct parallel and successive developmental events. Still, it is unclear what are the core regulatory programs and how such programs are timely coordinated within the organ. We use mainly the Drosophila trachea (respiratory system) as a model to understand epithelial organ development. The trachea is a network of epithelial tubes, and its morphology is sensitive to mutations in genes whose products participate in consecutive steps of branching morphogenesis and tube size maturation. In paper I, we identified two gene functions required for tracheal tube elongation. We show that tracheal cells, at a specific time in development, acquire an ability to elongate that is mediated by a protein involved in actin organization. A luminal matrix holds back this elongation, and temporal expression of an anion channel appears required to modify the luminal matrix and thereby permit a controlled extent of elongation. In paper II, we show that a mucin-like protein is temporally expressed in the trachea and is required for tube elongation. The protein also drives diameter expansion of the hindgut, where it fills the growing lumen and appears to physically dilate the tube. The work demonstrates that regulated expression of a single protein can model epithelial tube diameter. In papers III and IV, we focused on the temporal regulation of tracheal gene expression, and uncovered an important function for the midembryonic ecdysone hormone pulse in progression of organ development. In paper III, we analysed the mechanism of embryonic ecdysone signalling and found that the hormone causes pan-embryonic activation of Ecdysone Receptor (EcR). EcR acts tissue-autonomously together with Ultraspiracle to promote concurrent progression of organ development. In paper IV, we show that ecdysone, via EcR and a downstream cascade of gene regulators is needed to advance parallel tracheal-specific gene programs. Together, the results reveal novel gene functions during epithelial tube formation, and show that correct temporal unfolding of the tracheal gene network relies on gene-regulatory input from an external cue in form of a hormone pulse.

Key words: Drosophila, trachea, hindgut, tubulogenesis, luminal matrix,ecdysteroid, EcR:USP, dorsal closureISBN: 978-91-628-8279-2Gothenburg 2011