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Homeotic selector genes control the patterning of *seven-up* expressing cells in the *Drosophila* dorsal vessel

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Abstract

The linear cardiac tube of Drosophila, the dorsal vessel, is an important model organ for the study of cardiac specification and patterning in vertebrates. In Drosophila, the Hox segmentation gene *abdominal-A (abd-A)* is required for the specification of a functionally distinct heart region at the posterior of the dorsal vessel, from which blood is pumped anteriorly through a tube termed the aorta. Since we have previously shown that the posterior part of the aorta is specified during embryogenesis to form the adult heart during metamorphosis, we determined if the embryonic aorta is also patterned by the function of Hox segmentation genes. Using gain- and loss-of-function experiments, we demonstrate that the three Hox genes expressed in the posterior aorta and heart are sufficient to confer heart or posterior aorta fate throughout the dorsal vessel. Additionally, we demonstrate that *Ultrabithorax* and *abd-A*, but not *Antennapedia*, function to control cell number in the dorsal vessel. These studies add robustness to the model that homeotic selector genes pattern the Drosophila dorsal vessel, and further extend our understanding of how the cardiac tube is patterned in animal models.

Keywords: Drosophila; Hox genes; Dorsal vessel; Heart; Aorta; *Seven-up*; *Tinman*; AP patterning

1. Introduction

One of the most compelling findings in developmental biology has been the observation that Hox segmentation genes control anteroposterior (AP) identity in the developing embryo, and that the organization, expression and function of these genes is highly conserved across diverse animal Phyla (for review see Carroll et al., 2005). Classical studies in Drosophila have established that the genes of the Bithorax-Complex and the Antennapedia-Complex control AP identity (reviewed in Mann and Morata, 2000), and despite functional redundancy among vertebrate Hox gene clusters, there is strong evidence that the homologous genes in vertebrates have homologous functions.

In addition to patterning the overall body plan of the developing embryo, Hox segmentation genes also contribute autonomously to pattern and cell fate in a number of distinct germ layers, organs, and tissues (reviewed in Castelli-Gair Hombria and Lovegrove, 2003). These diverse examples include the developing vertebrate digits (Johnson and Tabin, 1997) and Drosophila skeletal muscle lineages (Greig and Akam, 1993; Michelson, 1994). Thus, Hox genes function pervasively throughout animal development.

The dorsal vessel is the *Drosophila* linear heart tube, comprising a muscular posterior heart and a more anterior tube termed the aorta. *Drosophila* has a partially open circulatory system, where hemolymph (blood) is drawn in through bilateral openings in the heart, called ostia, in the most posterior region of the dorsal vessel. The heart has a broadened lumen when compared to the aorta, which is the next area the hemolymph enters. The hemolymph is expelled from the anterior opening of the aorta, in the vicinity of the brain and allowed to flow back to the posterior of the animal (Rizki, 1978; Fig. 1A). Similar to the vertebrate heart, the dorsal vessel displays electrical activity or 'heartbeats' (Wessells et al., 2004) and many of the genes expressed in the dorsal vessel have vertebrate

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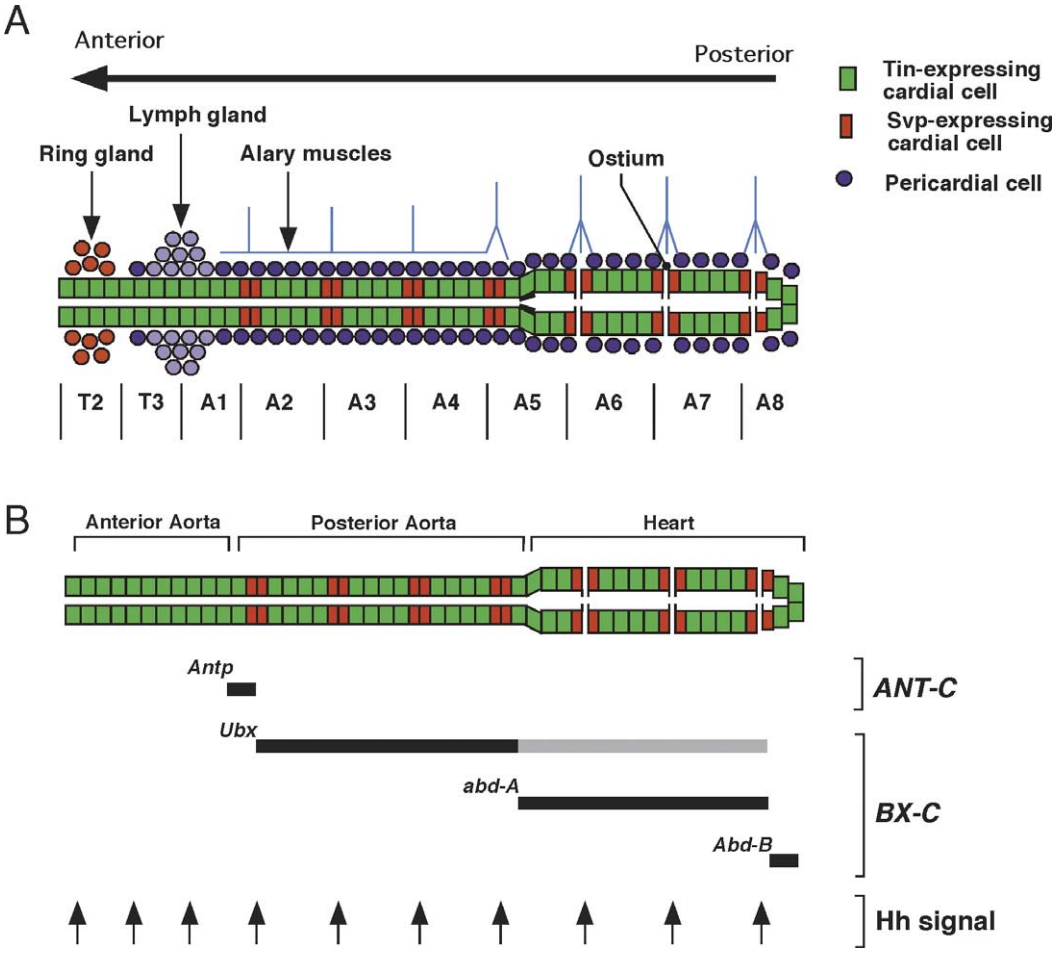

Fig. 1. Structure and cell fate in the Drosophila dorsal vessel. (A) Cartoon of embryonic dorsal vessel structure. The dorsal vessel is a muscular tube comprising Tin-expressing (green) and Svp-expressing (red) muscular cells, and associated pericardial cells (purple). Alary muscles (blue) support the dorsal vessel. At the posterior of the dorsal vessel the lumen is larger and termed the heart region proper. In the embryo and larva, blood enters the heart through ostia, which arise from pairs of Svp cells. Blood is then pumped anteriorly through the posterior aorta and anterior aorta. Although Svp cells are present in the posterior aorta, ostia do not form from these cells at the embryonic nor larval stages. At the anterior of the dorsal vessel specialized structures such as lymph glands and ring glands are apparent. (B) Correlation of regulatory gene expression patterns in the embryo with dorsal vessel regionalization. For clarity, only the muscular cells are shown. No homeotic genes are expressed in the anterior aorta. *Antp* and *Ubx* are expressed in the posterior aorta, *abd-A* is expressed in the heart, and *Abd-B* is expressed at the posterior terminus of the heart. Hedgehog (Hh) signals from the overlying ectoderm correspond to the locations at which Svp cells arise in the developing cardiac tube. Note that there are no Hox genes expressed in the anterior aorta of the embryo; and that there are no Svp cells in the anterior aorta despite the presence of Hh signals in this region. In all panels anterior is to the left.

homologs. This parallel relationship makes the study of the simpler *Drosophila* system useful as a baseline from which the much more complex vertebrate research can stem (reviewed in Cripps and Olson, 2002; Brand, 2003).

Functional studies have served to subdivide the embryonic dorsal vessel into three AP regions (Rizki, 1978; Molina and Cripps, 2001; summarized in Fig. 1B). The most posterior region is the heart which contains the ostia. The heart functions as the inflow tract for the cardiac tube throughout larval development, and is histolyzed during metamorphosis. The adjacent posterior aorta (PA) functions as a simple tube during larval life, but is modified into the adult heart during pupal development. The most anterior cells of the dorsal vessel form the anterior aorta (AA), which functions throughout the life of the animal as a simple tube to convey hemolymph to the head.

AP patterning of the dorsal vessel is also apparent in cell number and lineage decisions. Alvarez et al. (2003) recently showed that cell numbers differ between the AA and the rest of the dorsal vessel, such that the AA comprises only four muscular cells per hemisegment, as opposed to six muscle cells per hemisegment in the PA and most of the heart. Furthermore, the cells of the AA arise from asymmetric divisions, each division giving rise to a cardial and a pericardial cell; by contrast many cardial cells of the PA and heart arise from symmetric division (Alvarez et al., 2003; Han and Bodmer, 2003). *Abd-B* is expressed in the four posteriormost cells of the heart (Lovato et al., 2002; Lo et al., 2002; Ponzielli et al., 2002), and the lineage decisions in this terminal region are a modified form of those of the PA and heart (Han and Bodmer, 2003).