

Sample 1: Shavenbaby Couples Patterning to Epidermal Cell Shape Control.
Chanut-Delalande H, Fernandes I, Roch F, Payre F, Plaza S (2006) PLoS Biol
4(9): e290

Introduction

A general feature of development is the control of tissue and cell morphogenesis, a process whereby each cell acquires a specific **shape** depending upon its individual identity. Although the mechanisms that permit the patterning of a cellular field are now relatively well understood in different systems, how cell fate becomes translated into **cell-shape control** remains largely unknown.

Genetic analysis of epidermal differentiation in *Drosophila* has made this process a paradigm for our attempts to understand the subsequent steps of morphogenesis in animals. During early embryogenesis, cascades of transcription factors progressively refine the different cellular territories and define their respective identity [1]. Signaling pathways then act to establish boundaries between adjacent cell fields (reviewed in [2,3]) and participate in the regulation of the size of these territories through the control of cell survival [4]. Finally, when the epidermis is composed of a monolayer of post-mitotic cells, signaling pathways specify cell fates, ultimately determining morphological differentiation [1,2,5]. Epidermal cells in a given embryonic segment display a stereotyped pattern of two distinct morphological fates: cells with a smooth apical surface, which generate naked cuticle, and cells producing actin-rich cytoplasmic extensions, which eventually become the mature larval microtrichiae or trichomes, generally called denticles (ventral) and hairs (dorsal).

In the ventral region of the abdomen, each segment possesses six to seven rows of pigmented denticles, which are involved in locomotion. Activation of the Wingless (Wg) pathway determines the naked fate [6], whereas activation of the d-EGF-receptor (DER) pathway promotes denticle formation [7]. In addition, Serrate-Notch signaling also contributes to define the denticle field [8,9] through a fine-tuning of the extent of DER activation [10]. The activities of Wg and DER pathways on epidermal differentiation converge in the transcriptional regulation of **shavenbaby (svb)** [11]. DER activates *svb* transcription in denticle-forming cells, whereas Wg acts as a repressor in the naked territories (Figure 1A), leading to the precise expression of *svb* in denticle cells. In turn, *svb* is required for denticle formation, since *svb* mutants display essentially naked cuticle. In addition, the ectopic expression of *svb* in smooth cells is sufficient to produce cuticular extensions [11], which nevertheless do not display the typical morphology of denticles, likely because those cells lack auxiliary factors involved in the fine shaping of these structures. *svb*, which encodes a zinc finger transcription factor [12–14], is the most-downstream regulator so far known to specify the denticle pattern [11].

Francoise Chanut 9/26/06 10:07 PM

Comment: Statement of the big picture problem: acquisition of cell shape during development. Note how the last sentence contrasts what is known with what is unknown. Note use of power position=end of paragraph, to state the unknown, i.e. hint at the problem the paper addresses.

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Comment: First paragraph of background: initiates the funnel shape by going from genetic analysis of epidermal differentiation to the different kinds of cuticles (naked or hairy) to ventral denticles and dorsal hairs.

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Comment: Topic sentence: suggests that the paragraph will address the genetic control of epidermal differentiation. Note the chronological arrangement of the other sentences in the paragraph.

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Comment: Second paragraph of background: we're moving down the funnel-shaped Introduction, from the ventral denticles to the paper's main player: shavenbaby.

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Comment: Note the link between the paragraphs: one ended with dorsal hairs and ventral denticles, the other starts with ventral denticles. The repetition serves as transition and provides flow.

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Comment: First mention of *svb*, the gene being studied.

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Comment: Last sentence of the paragraph (power position) contains information worth remembering: last gene so far known in this process.

Additional evidence supports the hypothesis that, whereas all other upstream regulators act to define epidermal cell fates, *svb* controls epidermal cell shape changes. Although different mechanisms specify morphological fates in the dorsal epidermis [15], *svb* is required for the formation of dorsal hairs as it is for denticles. It has been shown that the modification of *svb*, leading to the restriction of its expression in a subset of dorsal epidermal cells, is the unique cause of the modification of the trichome pattern in a sibling *Drosophila melanogaster* species, *D. sechellia*, in which several rows of dorsal hairs are replaced by naked cuticle [16]. Somewhat surprisingly, given the large number of genes that are theoretically capable of modifying dorsal hair patterning [1], all cases of dorsal hair-pattern evolution examined in dipterans are the consequence of the modification of *svb* expression only [16–18]. Thus, developmental and evolutionary studies show that *svb* is critical for epidermal differentiation and that the presence/absence of *svb* expression ultimately determines the pattern of denticles and dorsal hairs [19].

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Comment: Third paragraph of background: moving farther down the funnel, from *svb*'s involvement in cell differentiation to *svb*'s involvement in cell shape differentiation.

Francoise Chanut 9/26/06 10:14 PM

Comment: Classic topic sentence, plainly announcing the topic of the paragraph. The following sentences substantiate the claim made in the topic sentence (list form).

How does *svb* control the formation of denticles and dorsal hairs during epidermal differentiation? Little is known about the cellular mechanisms underlying trichome formation. Epidermal cells are highly polarized along the apico-basal axis, with actin microfilaments accumulating at the cell cortex where they interact with apical junction complexes [20,21]. The formation of denticles and dorsal hairs is initiated by F-actin accumulation and reorganization, leading to the production of an apical bundle in the posterior region of the cell [14,22,23]. Each bundle then grows perpendicularly to the apical cell surface [22,23] and probably provides the mechanical force for the modification of the apical membrane. At later stages, ecdysteroid hormones induce epidermal cells to synthesize components of the cuticular envelopes, which are modified by the catecholamine biosynthetic pathway to ensure trichome pigmentation and hardening [24]. Despite the large number of genetic screens based upon cuticle observation [25,26], the molecular mechanisms responsible for the different steps of epidermal differentiation still remain to be uncovered.

Francoise Chanut 9/26/06 10:16 PM

Comment: Wrap up sentence: summarizes the evidence listed above.

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Comment: Question: Is all the information given in the background necessary to understand the motivation for this research? Couldn't paragraphs 2-4 be summarized into just one?

Francoise Chanut 9/26/06 10:24 PM

Comment: Statement of the main question the paper addresses: how does *svb* control the formation of denticles and hairs? This question could also be asked further down, for instance at the end of this paragraph or the beginning of the next one.

Francoise Chanut 9/26/06 10:28 PM

Comment: True topic sentence for this paragraph. "Little is known" is a signal that serves as justification for the study.

Francoise Chanut 9/26/06 10:30 PM

Comment: Concluding sentence that points out the shortcoming of former studies—hence justifying the approach of this study

Francoise Chanut 9/26/06 10:34 PM

Comment: Last paragraph, after the statement of the question. We're in the funnel's neck. Statement of the experimental approach and summary of observations.

Francoise Chanut 9/26/06 10:35 PM

Comment: Signal for the experimental approach.

Since *svb* activity acts cell autonomously to promote denticle formation [11,14], we searched for genes whose expression is controlled by *svb* as an alternative approach to identify players responsible for the morphological differentiation of epidermal cells. We identified several cellular factors involved directly in subsequent steps of denticle formation. Although actin remodeling is generally regarded as the outcome of post-translational modifications, we show that denticle formation relies on the *svb*-dependent transcriptional activation of several factors involved in microfilament formation or bundling. We provide evidence that *svb* directly controls the transcription of *miniature* (*m*), which encodes a membrane protein containing a Zona Pellucida (ZP) domain, and we show that *m* is required for the membrane/cuticle interaction in the denticle. We also identified a *svb* target responsible for denticle pigmentation, therefore demonstrating that *svb* coordinates several aspects of denticle differentiation. Finally we show that

svb regulates the same set of genes for the formation of dorsal hairs and suggest that the evolution of the dorsal hairs pattern in *D. sechellia* results from the concerted modification of the expression of cellular effectors regulated by *svb*.