Dispatch
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Organelle Motility: Running on Unleadened

The study of fish and amphibian melanocytes has yielded a wealth of information on the regulation of microtubule- and actin-based motor proteins involved in organelle transport. A new zebrafish mutant provides further insight into how the actions of these motors are coordinated *in vivo*.

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The intracellular translocation and positioning of organelles is driven by molecular motor proteins that walk along either microtubules or actin filaments. Understanding how these motor proteins attach to their cognate organelle and how their activities are regulated and coordinated are major goals of current research. Studies using one model cell type, the melanocyte, have contributed a great deal towards realizing these goals (for review, see [1]). These vertebrate pigment cells contain melanosomes, a specialized type of organelle that synthesizes and accumulates the melanin pigments responsible for the coloration of animals. Collectively, studies of fish, frog and mouse melanocytes have implicated the plus-end-directed microtubule motor kinesin II, the minus end-directed microtubule motor dynein, and the barbed-end-directed, actin-based motor myosin V in the intracellular movement and positioning of melanosomes [1–4].

An important milestone in the investigation of myosin V-dependent melanosome motility was the identification in 2002 of the melanosome receptor for myosin Va [5–8]. This work grew out of efforts by several groups to characterize the phenotypes of melanocytes isolated from the mouse coat color mutants *dilute*, *ashen* and *leaden*, which harbor mutations in myosin Va, the Rab GTPase Rab27a, and the Rab27a-effector protein melanophilin, respectively [5–9]. Collectively, these studies demonstrated that Rab27a localizes to the membrane of the melanosome, where it then recruits melanophilin in a GTP-dependent fashion. Finally, melanophilin recruits myosin Va, thereby allowing the organelle to connect with the actin cytoskeleton. This connection, together with long-range, bidirectional, microtubule-dependent melanosome movements along the length of the melanocyte's dendrites, drives the accumulation of melanosomes at dendritic tips, the primary site of melanosome transfer from the melanocyte to surrounding keratinocytes. When the connection between the melanosome and actin is broken as in *dilute*, *ashen* or *leaden* mutant melanocytes, the myosin Va-dependent capture of melanosomes at dendritic tips is abrogated and the organelles accumulate in the central cytoplasm, rather than the periphery, by virtue of their remaining microtubule-dependent motility. This redistribution decreases the amount of pigment transferred to keratinocytes at dendritic tips, and thus results in animals with a lighter or 'diluted' coat color — hence the original name *dilute*. Now, in a recent issue of *Current Biology* [10], an analysis of the phenotype of melanocytes from zebrafish lacking the zebrafish homolog of melanophilin reveals a novel and surprising role for this protein in regulating dynein-dependent melanosome motility.

While the study of mouse melanocytes has benefited enormously from the availability of mouse coat color mutants, fish and amphibian melanocytes, or melanophores, represent a model system with several powerful advantages over mouse melanocytes, the most important of which is that the motility of their melanosomes is subject to rapid and relatively synchronous control by hormones [1]. Specifically, melanophores do not give away their melanosomes to keratinocytes like mammalian melanocytes do. Rather, in response to different hormones that act through cAMP, they rapidly switch the intracellular distribution of their melanosomes between two states: an aggregated state (Figure 1A), where melanosomes congregate at microtubule minus ends, i.e. at the MTOC, and an evenly dispersed state (Figure 1B). In this way, the animal can change its color rapidly from light (aggregated state) to dark (dispersed state), a behavior critical for camouflage and sexual attraction [1]. These changes in melanosome distribution are driven by the coordinated actions of kinesin II, dynein, and myosin V [1–3].

An observation made by Rodionov *et al.* [11] greatly enhanced our basic understanding of melanosome motility in melanophores and is crucial to the interpretation of the zebrafish melanophilin mutant described now: When fish melanophores are triggered to disperse their melanosomes in the presence of latrunculin (i.e. in the absence of filamentous actin), rather than attaining their normal even cytosolic distribution, melanosomes move unimpeded to microtubule plus ends, accumulating dramatically at the margins of the cell (Figure 1C). Therefore, an actomyosin V-dependent component of melanosome motility is clearly required along with microtubule-dependent motility to generate the even dispersion of melanosomes required for darkening of the animal; an animal containing melanophores exhibiting a melanosome distribution like that in Figure 1C would probably be as light as a normal animal triggered to aggregate its melanosomes.

In the recent study, Sheets *et al.* [10] identified a zebrafish line that is homozygous for a functional null allele of *Mlpha*, the zebrafish homolog of mouse melanophilin. The

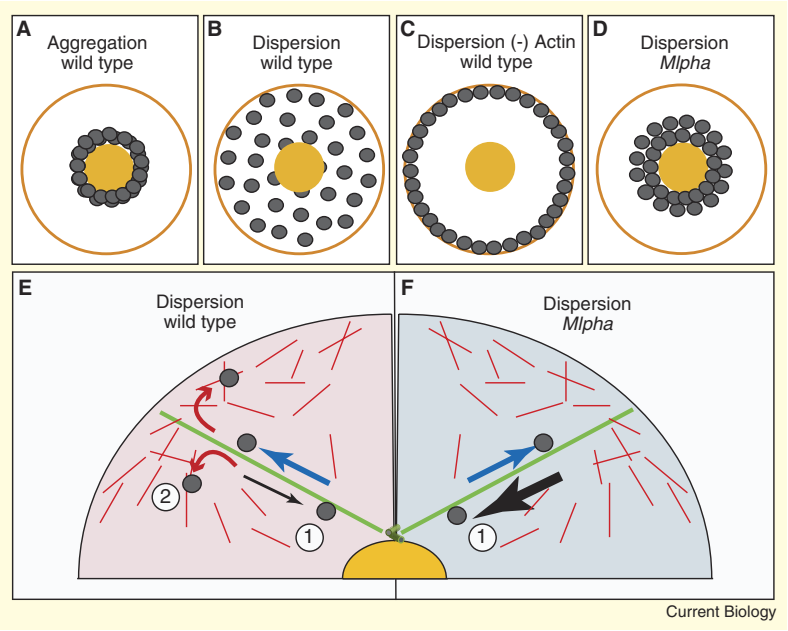

Figure 1. Melanophore biology and Mlpha functions.

(A–D) The distribution of melanosomes in wild-type and *Mlpha* melanophores under the conditions indicated. The MTOC is indicated in orange at the center of the cell. (E,F) Arrows of different sizes represent the relative activities of the plus-end-directed (blue arrows) and minus-end-directed (black arrows) microtubule motors early in dispersion (phase 1) within a wild-type cell (E) and a *Mlpha* mutant cell (F). In mutant cells, the enhancement of minus-end-directed melanosome movements that results from the absence of the Mlpha-dependent suppression of dynein activity results in a dramatic reduction in overall dispersion. Mlpha's putative second function — linking melanosomes to actin by recruiting myosin V to the melanosome surface — comes into play a bit later in dispersion (phase 2) to help drive the even cytosolic distribution of melanosomes (red arrows), and is absent in *Mlpha* cells (blue tracks: microtubules, red tracks: actin filaments, gray balls: melanosomes).

single most defining phenotype of this zebrafish version of mouse *leaden* mutant melanocytes is that when *Mlpha* melanophores are stimulated to disperse their melanosomes, the organelles remain largely aggregated (Figure 1D). Moreover, melanosomes remain largely aggregated in the mutant even when they are triggered to disperse in the presence of latrunculin. If the sole function of Mlpha in these cells was to link melanosomes to actin by simultaneously binding to myosin Va and to Rab27a present on the organelle surface (as in mouse melanocytes), then one would predict, based on the phenotype of wild-type melanophores treated with latrunculin, that melanosomes in *Mlpha* cells triggered to disperse would accumulate dramatically at the cell margin. That the mutant does not phenocopy the hyperdispersion phenotype of latrunculin-treated wild-type melanophores argues strongly that something else is going on. By careful, quantitative analyses of the movements of individual melanosomes in mutant and wild-type cells induced to disperse, the authors show that both the frequency and persistence of minus-end-directed, dynein-dependent melanosome movements are significantly enhanced in the mutant. Based on these observations, the authors propose that Mlpha normally promotes dispersion by suppressing dynein-dependent movements early in the dispersion phase. Importantly, the authors speculate that later in dispersion Mlpha assumes as a second function the recruitment of myosin V on to the melanosome surface, most likely via the same mechanism described for mouse melanophilin (Figure 1E). Together with microtubule-dependent melanosome motility, these two functions of Mlpha would help drive the normal, even distribution of melanosomes. In the case of the mutant cells, the authors conclude that the partial dispersion phenotype results from the loss of Mlpha-dependent suppression of melanosome-associated dynein activity early in dispersion, and the complete absence of Mlpha- and myosin V-dependent interaction of melanosomes with the actin cytoskeleton later in dispersion (Figure 1E).

The authors' two-phase model for Mlpha function appears to fit fairly well with the two-phase model for melanosome dispersion proposed by Rodionov *et al.* [12] from studies of black tetra fish melanophores. The putative function of Mlpha during the second phase, connecting the melanosome to actin through myosin V, does seem likely, given that Mlpha contains all of the critical interaction domains present in mouse melanophilin (e.g. interaction with Rab27a and with myosin V), and that GFP-tagged Mlpha targets to melanosomes. The ability to complement *Mlpha* cells with mutated versions of Mlpha should greatly facilitate the resolution of this question. More mysterious is the molecular mechanism of Mlpha's novel, actin-independent suppression of dynein's activity. Does Mlpha reduce the recruitment of dynein, or does it reduce dynein's processivity in some way? A key tool to answering these questions will be the identification of a mutant version of Mlpha that does everything correctly except suppress dynein activity. What is certain, however, is that the zebrafish model is a powerful system to explore this and other aspects of melanophilin's role in regulating organelle motility.

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Sensory Ecology: See Me, Hear Me

The animal world is replete with vibrant colours: these are often used as display signals and selection has solved a fundamental problem in information transfer by enhancing the detectability of these signals against the backgrounds on which they are perceived by the particular sensory systems of their receivers.

Michael J. Ryan

In his landmark publication that launched Information Theory, Claude Shannon [1] stated that "the fundamental problem of communication is that of reproducing at one point either exactly or approximately a message selected at another point". Although in its simplest version communication is a dyadic interaction between a signaler and a receiver, there is always the intervening transmission channel, and this channel is often noisy and it causes information to be lost. The fundamental problem in signal evolution is to enhance efficacy in a noisy world.

Noisy channels can vary with habitat, location, and time. Studies of various adaptations of animals to increase the efficacy of signal transmission have long been somewhat of a cottage industry in acoustic communication [2–4]. Sounds do not always transmit the same in all habitats. High frequency sounds usually attenuate (lose energy) more with distance than do low frequencies, and rapidly pulsed sounds usually degrade (lose quality) more than tones. The situation is often more severe in forest than in field. Many animals have evolved calls or songs that enhance signal transmission in their particular environment. Furthmore, the background sounds from wind, waves and other species can mask signals. Another adaptive strategy is to produce signals that are less likely to be masked by other sounds in the environment. Recently, for example, it was shown that great tits in urban environments use higher frequencies to avoid the industrial din of cities [5].

Our understanding of parallel issues in visual communication have lagged behind. There were earlier and insightful studies [6–9], but the visual ecology of communication got a jump start from two sources, one conceptual and one technical. In Endler's [10] presentation of sensory drive, he described the myriad constraints

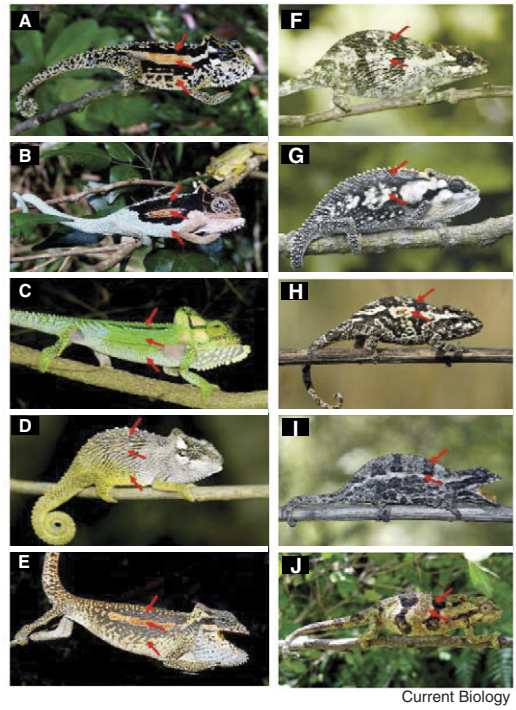

Figure 1. Display coloration in male and female African dwarf chameleons.

On the left are shown examples of male display coloration, with each individual in the display posture (laterally compressed, casque raised, gular pouch expanded). Red arrows show where reflectance spectra were taken. (A) *B. transvaalense*, Woodbush; (B) *B.* sp. Ngome; (C) *B. damaranum*; (D) *B. caffrum*; (E) *B. setaroi.* On the right are shown examples of female display coloration, with each individual showing display coloration. Red arrows show where reflectance spectra were taken. (F) *B. caffrum*; (G) *B. ventrale*; (H) *B. transvaalense*, Graskop; (I) *B. taeniabronchum*; (J) *B. transvaalense*. (Photos reproduced with permission from [12].)

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