科技前沿

器官成形素调控果蝇翅芽细胞形貌的研究进展

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摘 要 果蝇翅芽是研究细胞形貌发生的模式系统。在果蝇翅芽的发育过程中,器官成形素由浓度高的区域(成形素表达细胞)向浓度低的区域(接收细胞)移动,形成动态的浓度梯度。器官成形素信号通路的激活调控翅芽细胞的形貌发生、存活、生长和分化。目前已鉴定的在翅芽细胞表达的器官成形素包括 Hedgehog(Hh),Decapentaplegic(Dpp)和 Wingless(Wg)。结合国际最新研究进展,本文综述了 3 种器官成形素在翅芽细胞形貌发生过程中的重要作用,讨论了细胞形貌发生的分子机制。

关键词 器官成形素,细胞形貌发生,果蝇,翅芽

The research progress of morphogen-regulated cell morphogenesis during *Drosophlia* wing disc development

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Abstract *Drosophila* wing disc is a good model system to study the cell morphogenesis. During the development of the larval wing discs, morphogens secrete from high concentration region to low concentration receiving cells to form a dynamic gradient. Morphogen signaling pathways regulate the cell morphogenesis, survival, proliferation, and differentiation. Up to date, three morphogens have been identified in the wing discs, which are Hedgehog (Hh), Decapentaplegic (Dpp), and Wingless (Wg). In this review, we summarize the functions and discuss the molecular mechanisms of these three morphogens in cell morphogenesis.

Key words morphogen, cell morphogenesis, *Drosophila*, wing disc

19 世纪 60 年代,Lewis Wolpert 在其著名的“法国国旗”模型中提出器官成形素(morphogen)的概念,并描述了器官成形素是如何将器官组织细分为表达不同靶标基因的区域(Wolpert, 1969)。器官成形素是指一类特殊的信号分子,它们由器官发育的组织者细胞合成并分泌出来,运输到接收细胞中,在器官上形成连续的浓度梯度,调控细胞的存活、生长、命运分化和形貌发生。在无脊椎动物和脊椎动物中相继发现了多种器官成形素,它们在不同物种中高度保守,对器官的正常发育和构造形成具有重要的控制作用(Briscoe *et al.*, 2001; Chen and Schier, 2001; Gurdon and Bourillot, 2001;张徐波等,2010)。

1 果蝇翅芽的隔间划分与器官成形素

近年来,随着双翅目黑腹果蝇 *Drosophila melanogaster* 全基因组测序的不断完善,基因功能研究不断深入,果蝇已经成为生命科学研究中的重要模式动物之一(刘素宁和沈杰, 2011)。果蝇成虫的飞行翅是由幼虫体内的翅芽发育而来。翅芽是一个研究细胞命运分化、细胞增殖、细胞形貌发生等基本生物学机理的热点模型(张徐波等, 2010)。果蝇翅芽呈囊状结构,由两层对立的细胞层组成:围肢膜(peripodial epithelium, PE)和翅芽

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盘(disc proper, DP)(Auerbach, 1936; Cohen, 1993),最初仅由 50 个左右细胞组成,到幼虫期结束时,发育到大约 50 000 个左右细胞(Garcia-Bellido and Merriam, 1971; Madhavan and Schneiderman, 1977)。整个发育阶段,翅芽经历了复杂的形貌改变过程。幼虫 1 龄到 2 龄早期,翅芽所有的细胞都是立方体,随后 DP 细胞开始拉长成柱状细胞,PE 中间区域细胞开始变短成鳞片状细胞,边缘地带的细胞仍保持立方体,鳞片状细胞与边缘立方体细胞一起称为围肢膜。从 3 龄早期开始,DP 细胞层特定区域细胞由顶端处缩短、内陷形成沟,将细胞层细分为背板区(notum)、铰链区(hinge)和翅囊区(pouch)。到 3 龄末期,幼虫期的翅芽形貌发生完成(图 1:A ~ C),随后进入蛹期变态发育(Garcia-Bellido, 1975)。

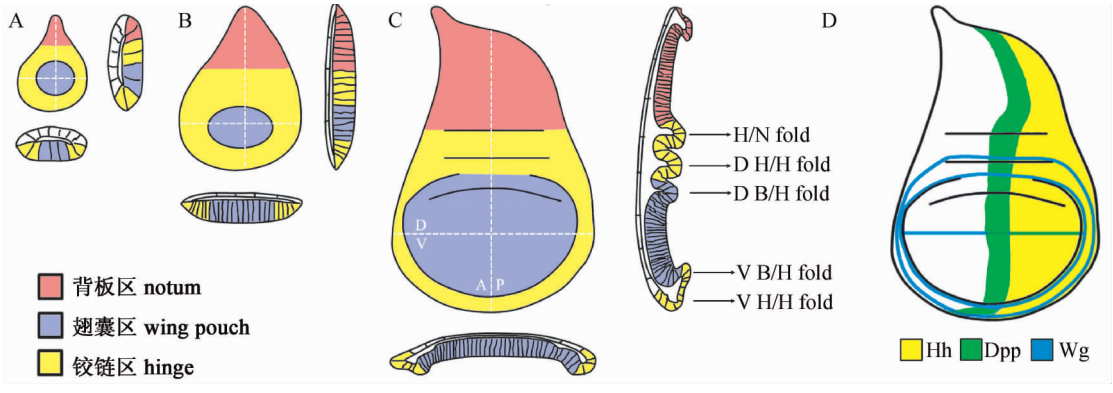

图 1 果蝇翅芽在幼虫期的形貌发生过程及 3 种器官成形素表达模式

Fig. 1 Morphogenesis of the *Drosophila* wing imaginal disc in the larval stage and expression patterns of the morphogens

1 龄(A)、2 龄(B)、和 3 龄(C)幼虫的翅芽形貌示意图。铰链/背板沟 H/N fold;背隔间的铰链内部沟,D H/H fold;背隔间的翅囊/铰链沟,D B/H fold;腹隔间的翅囊/铰链沟,V B/H fold;腹隔间的铰链内部沟 V H/H fold。每个龄期左上图为 x-y 轴平面,右上图为 y-z 轴平面,下图为 x-z 轴平面。D. 3 种器官成形素在 3 龄翅芽的表达模式。

Diagrams of the wing disc morphology in the first (A), second (B), and third (C) instars. H/N fold: hinge/notum fold, D H/H fold: dorsal hinge-internal fold, D B/H fold: dorsal blade/hinge fold, V B/H fold: ventral blade/hinge fold, V H/H fold: ventral hinge-internal fold. In each diagram, top left shows the x-y view, top right shows the y-z view, and below shows the x-z view. D. expression patterns of the morphogens in third larval instar.

进入蛹期后,翅囊区沿前/后隔间边界折叠,随后鳞片状细胞在翅芽与幼虫表皮连接处发生降解,大部分鳞片状细胞被降解,一小部分融于幼虫表皮,翅囊区细胞开始缩短并延展,然后外翻到幼虫表皮外,待蛹壳脱去后,变为成虫的翅(图 2)(Pastor-Pareja *et al.*, 2004; Aldaz *et al.*, 2010)。在这个过程中,先是 *Dorsolcross*(*Doc*)基因通过激活基质金属蛋白酶 2 表达,降解细胞外基质,促进翅囊区沟的发展和翅芽折叠为双层结构(Sui *et al.*, 2012)。然后,Jun N-terminal kinase(JNK)信号途径促进 PE 细胞层的降解和与体表融合,从而促进翅芽由体内向体外的外翻过程(Agnes *et al.*, 1999; Pastor-Pareja *et al.*, 2004)。翅囊区部分细胞会转化为翅脉细胞,Dpp、EGFR、Notch 信号通路综合调节了翅脉细胞命运转化(Sotillos and De Celis, 2005),这些翅脉细胞会有进一步的细胞形貌改变,这一细胞形貌改变过程是 EGFR 信号调节 E-cadherin 表达所调节的(O'Keefe *et al.*, 2007)。

翅芽发育的早期,选择者基因(selector gene)通过赋予细胞不同的亲和性把翅芽组织划分为若干隔间,隔间与隔间相邻的边界称为隔间边界(compartment boundary)。隔间边界细胞作为组织者(organizer)通过分泌信号分子(器官成形素)来

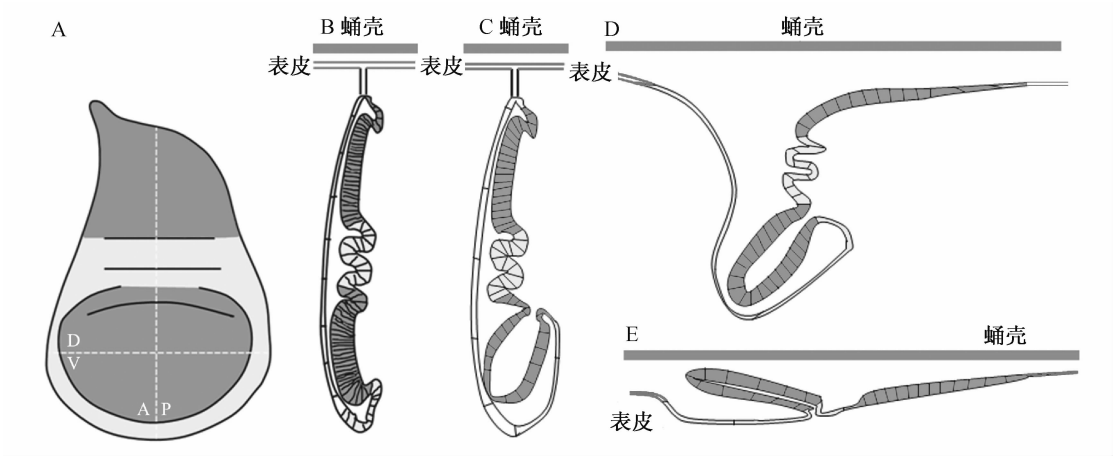

图 2　果蝇蛹期翅芽的变态过程

Fig. 2　Metamorphosis of the *Drosophila* pupal wing imaginal disc

A. 果蝇 3 龄幼虫翅芽平面示意图。横虚线表示背/腹隔间边界,纵虚线表示前/后隔间边界;B. 果蝇 3 龄幼虫翅芽纵切面示意图。C. 进入蛹期后,翅囊区细胞沿背腹隔间边界折叠;D. 鳞片状细胞从翅芽与虫体表皮连接处开始降解,一部分融于虫体表皮;E. 翅囊区彻底外翻出虫体外。

A. diagram of the third instar wing disc in the x-y view. The horizontal and longitudinal dotted lines indicate the D/V and A/P boundaries, respectively; B. diagram of the third instar wing disc in the y-z view; C. in the pupal stage, wing pouch cells fold along the D/V boundary; D. the squamous cells begin to degrade from the stalk and part of the squamous cells fuse with the epidermis. E. wing pouch is everted out of the epidermis.

促进细胞的存活和增殖,控制细胞的分化和命运,以及确保正确的细胞形貌发生。果蝇翅芽发育过程中主要形成两种隔间边界,前/后(anterior/posterior,A/P)隔间边界和背/腹(dorsal/ventral,D/V)隔间边界。前/后隔间边界从翅芽发育开始就一直存在,它的位置由"选择者"基因 *engrailed*(*en*)决定(Morata and Lawrence, 1975; Kornberg *et al.*, 1985)。*en* 只在后隔间细胞中表达,它编码的转录因子指导了器官成形素 Hh 的合成,并抑制后隔间细胞对 Hh 的响应(图 1:D)(Tabata *et al.*, 1992; Zecca *et al.*, 1995)。Hh 是一种短距离信号分子,它可以向前隔间单向传递,形成浓度梯度,只有靠近前后隔间边界的细胞才能接收 Hh 信号分子,从而打开 Hh 信号通路(Tabata and Kornberg, 1994; Torroja *et al.*, 2005)。这些接收 Hh 信号的细胞位于翅芽中心区域,它们会表达 Hh 的靶标基因——另外一种器官成形素 Dpp,使得这些细胞成为翅芽的"组织者"(图 1:D)。Dpp 是一种长距离信号分子,属于 TGF-β 大家族(Padgett *et al.*, 1987)。Dpp 信号分子从组织者细胞向两侧双向运输,在翅芽上形成连续的浓度梯度,指导靶标基因区域化表达,区域化地调控翅芽的生长,促进细胞存活,确保正确的细胞形貌,控制图示形成(Lecuit *et al.*, 1996; Nellen *et al.*, 1996; Shen and Dahmann, 2005; Zhang *et al.*, 2013)。

背/腹隔间边界形成于 2 龄期,使翅芽进一步划分(Garcia-Bellido *et al.*, 1973)。选择者基因 *apterous*(*ap*)在背隔间表达,决定背隔间细胞的命运,并为背/腹隔间边界提供位置信息,而腹隔间则不表达 Ap(Diaz-Benjumea and Cohen, 1993; Williams *et al.*, 1993; Blair *et al.*, 1994)。背/腹隔间边界细胞通过两种 Notch(N)配基复杂的交互反应(Diaz-Benjumea and Cohen, 1995; Kim *et al.*, 1995; de Celis *et al.*, 1996; Doherty *et al.*, 1996),激活 N 信号,从而激活第 3 种器官成形素 Wg 在背/腹隔间边界细胞内表达。在幼虫 2 龄中期,Wg 最先在前隔间与腹隔间重叠的呈楔形的一小团细胞中表达(Wu and Cohen, 2002)。随后在 2 龄末期,背腹隔间边界细胞被 N 信号激活而表达 Wg(Williams *et al.*, 1993)。在 3 龄早期,第 1 个 Wg 表达环在远端铰链区(distal hinge)形成,称为 Wg 内环(图 1:D)。在 3 龄晚期,Wg 第 2 个表达环在近端铰链区(proximal hinge)形成,称为 Wg

外环(图 1:D)(Baker, 1988)。背/腹隔间边界细胞表达并向外分泌 Wg,长距离传递,形成连续的 Wg 浓度梯度,控制靶标基因的表达(Zecca *et al.*, 1996)。

2 3 种器官成形素相关的信号通路

器官成形素作用于细胞后,通过信号通路激活其下游不同的靶标基因,从而调节翅芽细胞的生命活动。下面分别介绍 Hh、Dpp 和 Wg 这 3 种器官成形素引起的信号通路。

Hh 信号通路:后隔间细胞合成并分泌 Hh 蛋白,随后 Hh 向前隔间运输。靠近前/后隔间边界的细胞上含有 Hh 受体 Patched(Ptc)(Chen and Struhl, 1996)。Hh 与其受体的结合阻止了 Ptc 对 Smoothened(Smo)的抑制作用(Alcedo *et al.*, 1996),从而激活 Smo。被激活的 Smo 能阻止下游由 Costal-2、Fused、Suppressor of Fused 等组成的多蛋白复合体降解转录因子 Cubitus interruptus(Ci),使 Ci 保持转录激活态,从而进入细胞核促进下游靶标基因的转录(Preat *et al.*, 1990; Preat, 1992; Schwartz *et al.*, 1995; Sisson *et al.*, 1997)。无法接收到 Hh 信号分子的细胞,多蛋白复合体则促进 Ci 由 155 ku 的转录激活态降解为约 75 ku 的 Ci75 转录抑制态,从而抑制下游基因的转录(Aza-Blanc *et al.*, 1997)(图 3:A)。

Dpp 信号通路:*dpp* 是 Hh 信号通路的靶标基因之一,在一个条带状的前隔间边界细胞中表达。Dpp 蛋白与受体 Tkv 和 Punt 结合后磷酸化 Tkv(Ruberte *et al.*, 1995),磷酸化的 Tkv 又将 Mothers against dpp(Mad)磷酸化为激活态的 pMad,接着 pMad 和 Medea 形成复合体进入细胞核中(Gao *et al.*, 2005),从而沉默转录抑制因子 *brinker*(*brk*)(Winter and Campbell, 2004),引起 Dpp 靶标基因如 *optomotor blind*(*omb*)、*spalt*(*sal*)等的脱抑制,而在相应的区域表达(del Alamo Rodriguez *et al.*, 2004; de Celis and Barrio, 2009)。当 Dpp 信号分子不存在时,转录抑制因子 Brk 则抑制靶标基因的表达(Minami *et al.*, 1999)。*daughters against dpp*(*dad*)作为 Dpp 的靶标基因之一,同时也是 Mad 的抑制因子,负反馈调控 Dpp 信号活力(Tsuneizumi *et al.*, 1997)(图 3:B)。

Wg 信号通路:当 Wg 不存在时,细胞内由 Zw3(Siegfried *et al.*, 1992)、Axin(Willert *et al.*, 1999)和 APC(Ahmed *et al.*, 2002)组成的蛋白复合体促进 Arm(Aberle *et al.*, 1997)的降解,无法激活 Wg 信号通路(Cadigan and Nusse, 1997)。当 Wg 存在时,Wg 与由 Fz2 和 Arrow 组成的受体复合体结合,从而激活 Dishevelled。激活态的 Dishevelled 会下调 Zw3 的活力,从而抑制 Zw3/Axin/APC 蛋白复合体的活力,使 Arm 脱离其限制,并在细胞质聚集,最后,Arm 进入细胞核,与 dTCF 形成复合体,参与 Wg 靶标基因的转录激活(Brunner *et al.*, 1997; van de Wetering *et al.*, 1997)(图 3:C)。

3 器官成形素的信号传导调控翅芽细胞的形貌发生

3.1 Hh 对翅芽细胞形貌发生的影响

果蝇幼虫翅芽是一个由两层细胞(DP 和 PE 细胞层)组成的囊状结构。DP 细胞最终拉长形成柱状细胞,PE 细胞中间区域变短成鳞片状。最新研究显示,Hh 通路参与了 PE 细胞层的细胞形貌发生。*hh* 基因发生突变,应该发育成鳞片状细胞的立方体细胞将不能转换成鳞片状细胞;有趣的是,*hh* 功能的丧失,并不影响柱状细胞的形貌发生(McClure and Schubiger, 2005)。*hh* 功能丧失的同时过量表达其下游靶标 Dpp,可以挽救鳞片状细胞不能形成的缺陷。因此,Hh 信号的激活促进了幼虫翅芽鳞片状细胞层的形貌发生(McClure and Schubiger, 2005)。也有研究报道 *hh* 基因在果蝇胚胎上调节细胞形貌的发生(Larsen *et al.*, 2003, 2008; Mulinari and Hacker, 2009),表明 Hh 信号通路参与多种组织器官的细胞形貌发生。

3.2 Dpp 对翅芽细胞形貌发生的影响

Dpp 信号通路也参与调节围肢膜 PE 细胞层的转化。研究发现,在 PE 细胞层通过 Ubx-Gal4 驱动过量表达抑制因子 Dad 来抑制 Dpp 信号传导,PE 细胞保持立方体,不再转变为鳞片状细胞,前/后隔间边界也不再向前隔间移动,这说明 Dpp 信号传导对鳞片状细胞的形貌发生和前/后边界的移动非常重要(McClure and Schubiger, 2005)。同时还发现,过量表达 Dad 柱状细胞层出现异常折叠,表明 PE 层和 DP 细胞层不是两个完全独立的发育系统,它们之间有着一定程度的联系,都受到 Dpp 信号的调控(McClure and Schubiger,

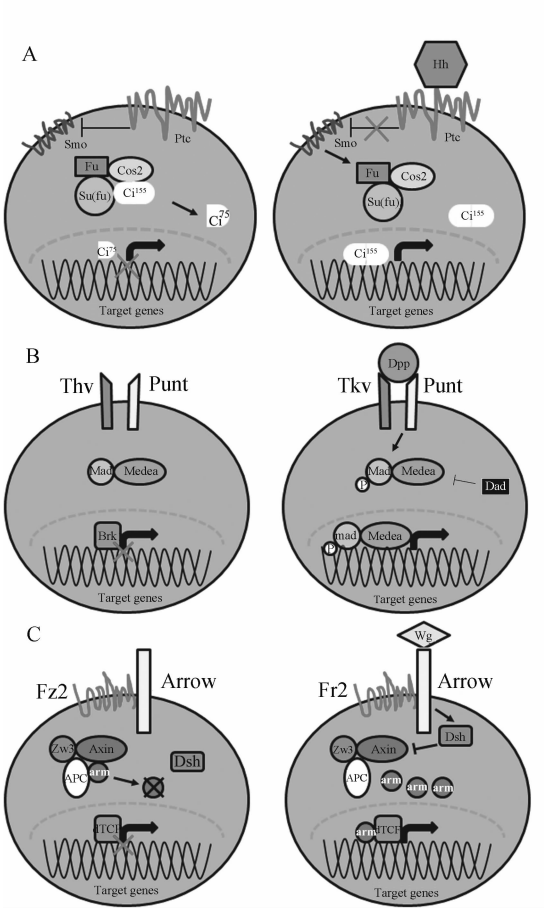

图 3　3 种器官成形素相关的信号通路

Fig. 3　Signaling pathways of Hh, Dpp and Wg

A. Hh 信号通路;B. Dpp 信号通路;C. Wg 信号通路。左图为信号通路未打开时的信号传递过程,右图为信号通路被激活时的信号传递过程。

A. Hh signaling pathway; B. Dpp signaling pathway; C. Wg signaling pathway. In each panel, the left is the unactivated signaling pathway and the right is the activated signaling pathway.

2005)。

Dpp 信号通过调节细胞骨架影响柱状细胞形貌。研究表明,丧失 Dpp 信号的细胞会发生细胞凋亡,而制造 Dpp 受体 *tkv* 和凋亡促进因子 *basket* (*bsk*,编码 C-Junn-terminal Kinase 蛋白)的双突变克隆,能够在丧失 Dpp 信号的同时抑制细胞凋亡,这些克隆细胞会进行细胞骨架的重新排列,双突变克隆细胞由顶端处缩短内陷,最终被排挤出翅囊区(图 4)(Gibson and Perrimon, 2005; Shen and Dahmann, 2005)。在柱状细胞层,由立方体向柱状转换的过程中,如果 Dpp 信号通路活性得到增强,细胞的顶端到底端的高度会增加,细胞会通过增强细胞顶端 Rho1 和 Myosin II 的活力使这种转换提前。而 Dpp 信号通路活性的降低或丧失将造成细胞高度变短,说明 Dpp 信号通路可以通过调节 Rho1-Myosin II 途径来调节细胞的高度(Widmann and Dahmann, 2009a)。

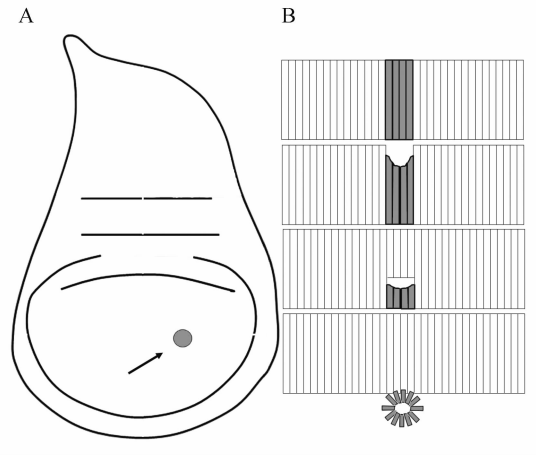

图 4　克隆细胞丧失 Dpp 信号活力后被挤出细胞层

Fig. 4　Extrusion of clonal cells lack of Dpp signaling from the wing disc epithelia

A. 果蝇翅芽平面示意图,箭头所指为 Dpp 信号活力突变克隆细胞群;B. 翅芽横切面示意图。克隆细胞丧失 Dpp 信号活力后,先细胞变短,最后被挤出细胞层。

A. diagram of the *Drosophila* wing disc in third instar in the x-y view. The arrow indicates a clone loss of Dpp signaling; B. clonal cells loss of Dpp signaling are shortened and eventually extruded from the wing disc epithelia.

细胞形貌改变时,如果细胞高度缩短但不被排出细胞层,就会形成细胞凹陷。Dpp 的靶基因 *optomotor-blind* (*omb*)丧失功能后,在翅囊区前/后隔间边界细胞会缩短内陷,从而形成一条明显的深沟(Shen *et al.*, 2008)。Omb 以一种对称的浓度梯度形式分布在前/后隔间边界的两侧,其浓度梯度的破坏将导致上皮细胞细胞骨架的重新组织,细胞收缩至基底膜。Omb 在翅芽上的梯度分布可以确保正确的细胞形貌发生,被认为是通过调控细胞表面发布的一种细胞亲和性分子而实现的(Shen *et al.*, 2010)。Dpp 的另一靶标基因 *sal*

被抑制或过量表达均会引起额外沟的形成(Grieder *et al.*, 2009; Organista and De Celis, 2013)。这些研究说明 Dpp 的靶标基因介导了 Dpp 信号传导对细胞形貌发生的控制作用。

3.3 Wg 对翅芽细胞形貌发生的影响

Wg 信号通路在胚胎中对细胞形貌的作用已有研究(Larsen *et al.*, 2003,2008),随后人们开始探索它在翅芽中的作用。Wg 信号通路的转录因子 Arm 具有双重作用,一种是作为转录因子,当 Wg 信号激活时,Arm 进入细胞核与 TCF 相互反应激活靶标基因;另外一种是在黏着联接处(adherens junction,AJ)起到联接上皮钙粘蛋白(E-cadherin)与肌动蛋白(actin)细胞骨架的桥梁作用(Nelson and Nusse, 2004)。E-cadherin 由 *shotgun*(*shg*)基因编码,是一种同嗜性粘着蛋白,促进上皮细胞的完整性(Gumbiner, 2005)。E-cadherin 表达量的变化有助于细胞分选(Dahmann and Basler, 2000; Foty and Steinberg, 2005)。同时 E-cadherin 也是细胞形貌发生所必需的,*shg* 变异会造成柱状细胞正常形貌的丢失(Tepass *et al.*, 1996)。

3 龄晚期幼虫翅囊区 Wg 信号与柱状细胞顶端到底端的高度有关。翅囊细胞从 2 龄末期开始由立方体向柱状细胞转变。在整个背隔间过量表达 Wg 蛋白或者表达 Arm^{S10} 增强 Wg 信号传导,到 3 龄早期时,背隔间细胞比腹隔间野生型细胞高,说明 Wg 信号的增强在幼虫早期发育中能够有效的促进细胞的拉高(Widmann and Dahmann, 2009b)。Arrow 是 Wg 的受体之一,制造 *arrow* 突变体同时表达抑制细胞凋亡的 P35 蛋白的克隆细胞,发现这些丧失 Wg 信号传导的克隆细胞顶端处发生凹陷,部分细胞会从柱状细胞层排除出去,其他的则定位到柱状细胞层底端。在 *arrow* 突变细胞中表达稳定态的 Arm^{S10} 使 Wg 活力持续激活,突变细胞恢复正常高度,这表明幼虫 3 龄晚期时 Wg 信号在保持翅囊区细胞高度拉高的作用是必需的(Widmann and Dahmann, 2009b)。而在铰链区和鳞片状细胞上的 Arm^{S10} 克隆细胞同样会发生顶端凹陷,说明在 Wg 信号传导弱的区域增强信号传导也会造成细胞的凹陷。而且在翅囊区,这些突变细胞具有细胞自主性,它们不会影响周围野生型细胞的形貌(Widmann and Dahmann, 2009b)。与 *arrow* 突变克隆细胞类似,Wg 途径中其它组分的突变也会使细胞层发生凹陷。Wg 通路指导 *shg* 基因在翅芽上的表达,*shg* 基因的突变或过量表达均会造成细胞顶端凹陷,有一些突变细胞会从底端挤出(Tepass *et al.*, 1996; Jaiswal *et al.*, 2006)。在背隔间区域或整个翅囊区下调 E-cadherin 的表达,这些区域的细胞从顶端到底端的高度比对照细胞短,说明 E-cadherin 起到了保持细胞高度的作用(Widmann and Dahmann, 2009b)。*Vestigial*(*vg*)作为 Wg 信号通路的靶基因,是翅囊区特化和生长所必需的(Couso *et al.*, 1995),许多研究显示 *vg* 介导了由 Wg 信号通路引起的细胞形貌发生,它可以引起 *capping protein* α (*cpa*)的表达,从而调节肌动蛋白的富集来调节细胞形貌(Janody and Treisman, 2006)。其突变克隆细胞会在翅囊区造成细胞的顶端凹陷,过量表达 Vg 的克隆细胞在翅囊区并无明显变化,而在铰链区发生顶端凹陷,这些结果说明 Vg 在 Vg 表达区域的抑制或在非 Vg 表达区域的激活均会造成细胞形貌的改变(Baena-Lopez and Garcia-Bellido, 2006; Widmann and Dahmann, 2009b)。同样在背隔间下调 Vg 的量,背隔间细胞比对照细胞短;相反,在早期发育中过量表达 Vg 可以有效的促进细胞的拉长,说明 Vg 是保持细胞正常长度所必需的(Widmann and Dahmann, 2009b)。抑制 Wg 信号所造成的细胞形貌的变化可以通过表达 Vg 部分恢复,说明 Vg 是 Wg 信号调节细胞形貌发生的一个重要的调节者(Widmann and Dahmann, 2009b)。

Wg 信号通路也可以通过调节细胞骨架来调控细胞形貌发生。*Adenomatous polyposis coli*(*APC*)是 Wg 信号通路下游中一个复合物的组分之一。在果蝇中有两种 *APC* 基因:*APC1* 和 *APC2*。在没有 Wg 信号的情况下同时突变这两种基因,将会完全激活 Wg 信号通路。*APC* 基因同时突变的克隆细胞绝大部分具有光滑的边界,细胞顶端压缩和凹陷,并伴有 Arm 的聚集(Roberts *et al.*, 2012)。在 *APC* 基因都突变的同时表达抑制态的 TCF^{DN} 来抑制 Wg 信号通路,可以阻止细胞顶端凹陷,说明 Wg 信号对细胞的形貌改变具有重要的作用。*APC* 基因突变所引起的细胞压缩和凹陷可以通过丧失 Myosin II 或 Rho1 的活性来挽救,说明 Wg 信号通路可以通过调节 Rho1-Myosin II 途径来

调节细胞形貌(Zimmerman *et al.*, 2010)。

4 展望

在果蝇翅芽发育过程中,器官成形素不仅调控着细胞形貌发生,还调控了翅芽细胞的分化、增殖、生长等生物学过程。Hh、Dpp 和 Wg 3 种器官成形素及其所调控的信号通路在这些过程中既相互独立,又有着千丝万缕的联系。例如 Dpp 信号通路是 Hh 信号通路的下游;Wg 信号通路与 Dpp 信号通路有一些共同的组分(Theisen *et al.*, 2007; Yang *et al.*, 2013),如 *vg* 是 Wg 和 Dpp 的共同靶基因,其缺失或异位表达均会造成细胞形貌的改变(Widmann and Dahmann, 2009b)。总之,这 3 条信号通路控制着翅芽上大量基因的表达,这些靶基因对细胞形貌的改变具有重要的作用,但是许多机理至今还不清楚。3 条信号通路所调控的细胞形貌发生过程以及三者之间的关系,将成为未来研究器官成形素如何调控细胞形貌发生的热点之一。这些信号通路及其靶标基因通过哪些介导因子控制细胞骨架形貌的?后续问题和机理有待于在组学水平上去深入研究。

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