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Review

Mechanical force-driven cell competition ensures robust morphogen gradient formation

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ABSTRACT

Morphogen gradients provide positional data and maintain tissue patterns by instructing cells to adopt distinct fates. In contrast, morphogen gradient-forming tissues undergo dynamic morphogenetic movements that generate mechanical forces and can disturb morphogen signal transduction. However, the interactions between morphogen gradients and these forces remain largely unknown. In this study, we described how mechanical force-mediated cell competition corrects noisy morphogen gradients to ensure robust tissue patterns. The Wnt/β-catenin morphogen gradient—that patterns the embryonic anterior-posterior axis—generates cadherin-actomyosin interaction-mediated intercellular tension gradients—termed mechano-gradients. Naturally generated unfit cells that produce noisy Wnt/β-catenin gradients induce local deformation of the mechano-gradients. Neighboring fit cells sense this deformation, resulting in the activation of Piezo family mechanosensitive calcium channels and secretion of annexinA1, which specifically kills unfit cells to recover morphogen gradients. Therefore, mechanical force-mediated cell competition between the morphogen-receiver cells supports robust gradient formation. Additionally, we discuss the potential roles of mechanical force-driven cell competition in other contexts, including organogenesis and cancer.

1. Introduction

For tissues and organs to function properly, cells with specific properties should be placed at appropriate locations and numbers during development and regeneration. This precise cellular arrangement is mediated by morphogen gradient. Morphogens are diffusible chemicals that act over long distances to instruct cells to adopt suitable fates for tissue patterning by forming activity gradients [1,2]. The concept of morphogens—introduced between the 1950s and 1970s—has been foundational in developmental biology [3–5]. Biochemical and molecular genetic studies have revealed morphogenetic molecules and their diffusion and signaling mechanisms [6–8]. For example, a morphogen protein, wingless-related integration site (Wnt), is secreted from the posterior tissue of early embryos and generates the Wnt/β-catenin signaling activity gradient to establish the anterior-posterior (AP) axis pattern [9] (Fig. 1**A**). In posterior tissues, Wnt stimulates the nuclear translocation of β-catenin, thereby inducing the expression of genes controlling differentiation into posterior neural tissues, such as the spinal cord. In contrast, in Wnt-unstimulated anterior tissues, genes required for differentiating into anterior neural tissues, such as the forebrain, are upregulated (Fig. 1**A**). In adult tissues undergoing regeneration and cell replacement, such as the liver and intestinal epithelium, cell proliferation and differentiation into functional cells is guided by Wnt morphogen gradients. These gradients ensure the maintenance of tissue homeostasis by facilitating appropriate fates to the specific tissue site [10,11] (Fig. 1**B**).

In contrast, as morphogen gradient-forming tissues undergo dynamic morphogenetic movements, cell adhesion and actomyosin contractile force are dynamically regulated [11,12]. Therefore, morphogens and mechanical forces may interact to maintain tissue homeostasis; however, the details remain unclear. Additionally, during tissue patterning, dynamic morphogenesis, such as rapid cell proliferation and movement occurs in parallel with morphogen gradient formation [13–15]. Rapid cell proliferation may spontaneously generate unfit cells that cannot transduce proper signals, whereas rapid cell movement may disrupt morphogen diffusion and stable formation of morphogen gradients. Therefore, developing tissues should have a system that prevents the generation of erroneous cells to achieve robust patterning through

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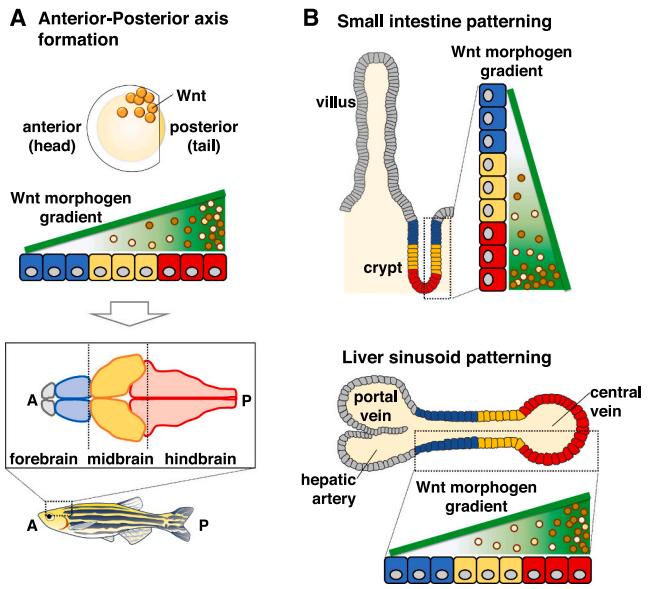

Fig. 1. Wnt morphogen gradients generate tissue patterns. (A) Schematic illustration of the Wnt morphogen gradient-mediated anterior-posterior (AP) pattern formation. In early vertebrate embryos, Wnt proteins are secreted from posterior tissues to generate an activity gradient of Wnt/β-catenin signaling along the AP axis. **(B)** Schematic illustration of the Wnt morphogen gradient-mediated patterning in the small intestine (upper panel) and liver sinusoid (lower panel).

morphogen gradient formation.

Cell competition is a mechanism that removes unfit cells by enabling higher-fit cells to selectively eliminate lower-fit or unfit cells through intercellular communications in a tissue environment [16–19]. Cell competition was discovered 50 years ago as a phenomenon where artificially induced cells with a ribosomal gene mutation were eliminated through communication with normal neighboring cells in the *Drosophila* epithelium [20]. Subsequently, the mechanism of cell competition was studied in *Drosophila* and mammalian culture cells [21–23]. Additionally, mouse model studies have demonstrated that cell competition can eliminate artificially introduced cells with low myelocytomatosis oncogene (Myc) expression from the heart and rat sarcoma viral oncogene (Ras)-activated oncogenic cells from the intestine and pancreas [24–26]. Therefore, cell competition is considered an unfit cell elimination mechanism for maintaining tissue homeostasis. However, the majority of research has focused on the analysis of artificially introduced unfit cells; therefore, the physiological significance of cell competition remains unclear. Recent studies are revealing that physiological cell competition corrects heterochrony in mouse embryos. For instance, Myc levels are intrinsically heterogeneous in the epiblast of early mouse embryos, and prematurely-differentiated cells with low Myc levels are eliminated from tissues, promoting the expansion of cell populations with high Myc levels [27,28]. The fate specification-delayed cells produced by low Transcriptional Enhanced Associate Domain (TEAD) activity are also eliminated by cell competition with the fate-specified cells during epiblast formation [29]. In this review, we introduce physiological cell competition driven by mechanical forces to ensure robust formation of morphogen gradient and spatial tissue patterning during development and discuss its potential role in adult tissue homeostasis.

2. Cell competition-driven correction of noisy morphogen gradients

2.1. Cadherin-mediated cell competition corrects noisy Wnt morphogen gradients

Recently, using zebrafish live-imaging analysis, we discovered that unfit cells with abnormally high or low Wnt/β-catenin activity appeared spontaneously and disrupted the Wnt/β-catenin activity gradients during embryonic AP axis formation [30]. Notably, these unfit cells were eliminated through apoptosis to repair the Wnt/β-catenin activity gradient. This elimination is driven by converting Wnt/β-catenin signaling activity to E-cadherin levels. In the posterior tissues with strong Wnt/β-catenin signaling activity, stabilized β-catenin proteins translocate to the nucleus and plasma membrane. The plasma membrane-recruited β-catenin facilitates the accumulation of membrane E-cadherin.

In contrast, in the anterior tissues with low Wnt/β-catenin activity, β-catenin is not stabilized at the plasma membrane, resulting in low levels of membrane E-cadherin. Therefore, gradients of membrane E-cadherin levels formed along the Wnt morphogen gradient (Fig. 2**A**) [30]. Because membrane E-cadherin levels increase with Wnt/β-catenin activity, unfit cells with abnormal Wnt/β-catenin activity disrupt this balance. In unfit cells with abnormally high or low Wnt/β-catenin activity, the membrane E-cadherin levels increase or decrease, respectively, generating an imbalance in E-cadherin levels between the unfit and neighboring fit cells. This imbalance activates the transcription factors—suppressor of mothers against decapentaplegic (Smad) and Forkhead box O3 (Foxo3)—to upregulate Foxo3 gene expression, suppress the negative regulator of reactive oxygen species (ROS), such as selenophosphate synthetase 1 (Sephs1), and produce ROS in the unfit cells. Accumulated ROS induce the degradation of apoptosis-suppressor B-cell lymphoma 2 (Bcl2), thereby triggering apoptosis in the unfit cells [30]. Because this morphogen gradient-correcting apoptosis selectively eliminates abnormal cells with unfit signaling activity through cell-cell communication, we consider this as a new type of physiological cell competition.

When the Foxo3-Smad-ROS-Bcl2 signaling pathway was suppressed to prevent the apoptotic elimination of unfit cells, naturally unfit cells accumulated in the embryo—thereby significantly disrupting the morphogen gradient and causing various morphological abnormalities, such as head and tail deformation and tumor-like cell mass formation [30,31]. These observations indicate that the morphogen gradient-noise correction system contributes to the formation of precise morphogen gradients and tissue patterning.

2.2. Cell competition corrects noisy Sonic hedgehog (Shh) morphogen gradients during organogenesis

Does cell competition correct noises in other morphogen gradients, too? Shh morphogen signaling forms an activity gradient along the dorsal-ventral (DV) axis and determines the distinct fate of each cell in the developing spinal cord and muscle primordia. In ventral tissues, Shh morphogen binds to its receptor Patched, which then relieves inhibition on Smoothened (Smo), allowing Smo to activate the downstream transcription factors called Gli proteins, leading to the transcription of target genes to induce differentiation into ventral tissues, such as slow muscle and motor neurons. The cells on the dorsal side, where the Shh morphogen signaling activity is low, differentiate into dorsal tissue such as fast muscle and interneurons [32–35]. We recently discovered that the Shh morphogen gradient is also corrected through a mechanism that eliminates unfit cells in the developing muscle and spinal cord [31]. In contrast to Wnt signaling, Shh signaling negatively regulates membrane N-cadherin levels through Smo, creating a dorsal-ventral axis gradient of N-cadherin that inversely associates with Shh morphogen signaling in the developing spinal cord and muscle [31,36]. Regions with high Shh

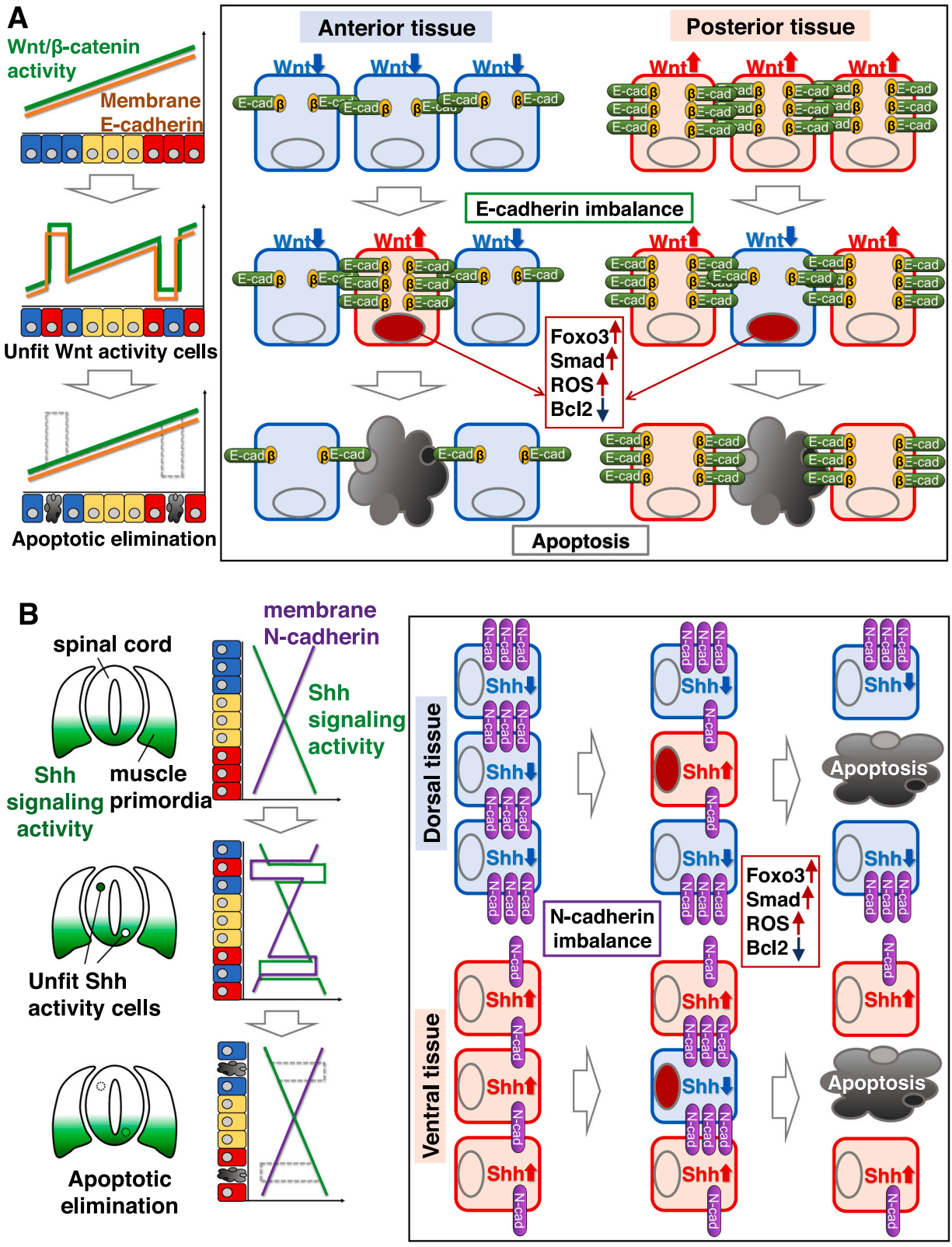

Fig. 2. Cadherin-mediated cell competition corrects noisy morphogen gradients. (A) Schematic illustration of cell competition-mediated noise correction of Wnt morphogen gradients. Unfit cells with abnormally high or low Wnt/β-catenin activity increase or decrease membrane E-cadherin levels, respectively, and generate an E-cadherin imbalance between unfit and neighboring fit cells. Neighboring fit cells sense this E-cadherin imbalance and trigger the activation of Foxo3 and Smad in unfit cells. Foxo3-Smad activation induces ROS production and reduces the anti-apoptotic protein Bcl2 to trigger unfit cell apoptosis. **(B)** Schematic illustration of cell competition-mediated noise correction of Shh morphogen gradients. Shh signaling negatively regulates membrane N-cadherin levels; therefore, unfit cells with abnormal Shh activity generate an N-cadherin imbalance between unfit and neighboring fit cells. Unfit Shh activity-induced cadherin imbalance is sensed by neighboring cells, and unfit cells are eliminated through the activation of the Foxo3-Smad-ROS-Bcl2 pathway in the same manner as the elimination of unfit Wnt/β-catenin cells.

signaling activity have reduced N-cadherin levels in the plasma membrane, whereas regions with low Shh signaling activity have high membrane N-cadherin levels. Shh-unfit cells are sensed by neighboring normal cells through the conversion of Shh signaling activity into N-cadherin levels. In the developing muscle and spinal cord, unfit cells with abnormally high or low Shh signaling activity are naturally generated and alter (decrease or increase) the membrane N-cadherin levels, respectively, causing N-cadherin imbalance between unfit and fit neighboring cells. This imbalance stimulates apoptosis in unfit cells by activating the Foxo3-Smad-ROS-Bcl2 signaling pathway (Fig. 2**B**) [31].

3. Mechanical force drives morphogen gradient-noise correction

As described above, unfit cells with abnormally high or low Wnt/Shh signaling activity undergo apoptosis through the Cadherin-Foxo3-Smad-ROS-Bcl2 pathway. However, it is challenging to interpret how neighboring normal cells sense the opposite signaling activity and activate the same signaling pathway. Recently, we successfully addressed this issue from the perspective of mechanical forces.

3.1. Morphogen gradients generate mechano-gradient

β-catenin functions both as a transcription factor downstream of Wnt morphogen signaling and as an adherens junction component that regulates cadherin localization, and it can connect morphogen signals and mechanical cell-cell interaction [37]. In adherens junctions, E-cadherin and N-cadherin are associated with actomyosin through catenin proteins, with the contractile force driven by myosin activation by the small GTPase RhoA [38–43]. This alteration in mechanical force can be transmitted to neighboring cells through cadherin, generating intercellular tension (Fig. 3) [44].

We observed that a gradient of intercellular tension was formed in correlation with the Wnt/β-catenin signaling gradient along the zebrafish embryonic AP axis [45]. The activity of myosin and RhoA that regulate actomyosin contraction forms a gradient along the AP axis. Therefore, intercellular tension also forms a gradient associated with the Wnt morphogen signaling gradient (Fig. 4). Additionally, laser ablation assays demonstrated that a tension gradient is formed downstream of Wnt/β-catenin signaling and membrane E-cadherin levels. We termed this mechanical force gradient of actomyosin contractile force the "mechano-gradient" [45].

Notably, blocking the mechano-gradient formation by treatment with the myosin inhibitor blebbistatin induced the accumulation of unfit cells with ectopic activation and abnormal reduction of the Wnt/β-catenin activity [45], indicating that the mechano-gradient may be involved in the elimination of morphogen-signaling-unfit cells.

3.2. Noisy morphogen gradients cause local mechanical stress

In Wnt/β-catenin-unfit cells, the actomyosin contractile force is abnormally increased or decreased, resulting in local tension alterations. These alterations contribute to the "sensing" process of unfit cells [45]. Wnt-hyper-activated unfit cells abnormally increase actomyosin contractile force, altering intercellular tension through cadherin, thereby applying a directional pulling force on neighboring cells (Fig. 4). In contrast, Wnt-inhibited unfit cells reduced intercellular tension to stimulate neighboring cells to move away from the unfit cells (Fig. 4). These mechanical stresses deform neighboring cells to activate the Piezo family of mechanosensitive calcium ion channels in neighboring cells. Piezo channels form a three-bladed propeller-shaped homotrimer that responds to asymmetric forces, such as membrane curvature and stretching, with a conformational change leading to channel pore opening and consequent ion uptake [46–50]. In morphogen gradient-noise correcting cell competition, Wnt-hyper-activated and -inhibited unfit cells would induce membrane stretching and curvature, respectively, in neighboring fit cells, and consequently, they would activate Piezo channels. In this way, Piezo channels convert the unfit cell-causing mechanical stress into calcium ion uptake in neighboring cells, resulting in the apoptosis of unfit cells [45] (Fig. 4).

3.3. AnnexinA1 (ANXA1) eliminates noisy cells

How do neighboring fit cells induce apoptosis in noisy cells with unfit Wnt signaling in response to calcium ion uptake? RNA-seq analysis of neighboring fit cells identified a secretory protein, ANXA1, as a mediator [45]. ANXA1, a member of the annexin family of proteins, binds to the plasma membrane in a calcium ion-dependent manner [51–53] and is reported to activate Smad signaling [54]. We observed that Piezo-mediated calcium influx specifically upregulated ANXA1 expression in cells adjacent to unfit cells with abnormally high or low Wnt activity [45]. ANXA1 induction in neighboring cells is essential for eliminating unfit cells because they appear to receive ANXA1 proteins secreted from neighboring cells to undergo apoptosis.

In summary, the Wnt morphogen gradient is converted into a gradient of intercellular tension, with neighboring cells sensing the morphogen gradient noise as a local alteration of the tension gradient,

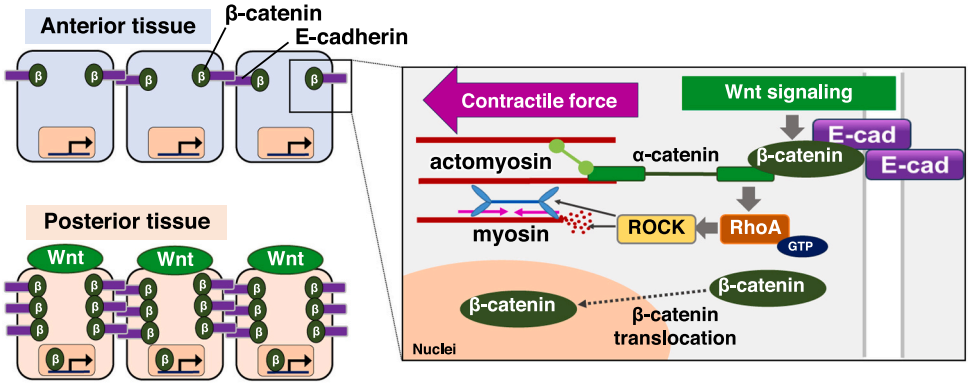

Fig. 3. Schematic illustration of Wnt/β-catenin signaling-mediated regulation of membrane E-cadherin and actomyosin contraction. (Left) Wnt signaling activity is converted to membrane E-cadherin levels. In the Wnt signaling-active posterior tissue, β-catenin accumulates in the nucleus and plasma membrane. β-catenin acts as a Wnt signaling transcription factor in the nucleus, whereas it also functions as a linker between the adhesion molecule E-cadherin and actin cytoskeleton in plasma membrane. (Right) In the presence of active Wnt/β-catenin signaling, β-catenin proteins accumulate in the membrane to positively regulate membrane E-cadherin levels and actomyosin contractile force at the adherens junctions. The RhoA-Rho-associated coiled-coil kinase (ROCK) signaling pathway activates actin polymerization and myosin activation underneath the adherens junctions. The contractile force generated by actomyosin activation is transmitted to adjacent cells as intercellular tension through E-cadherin.

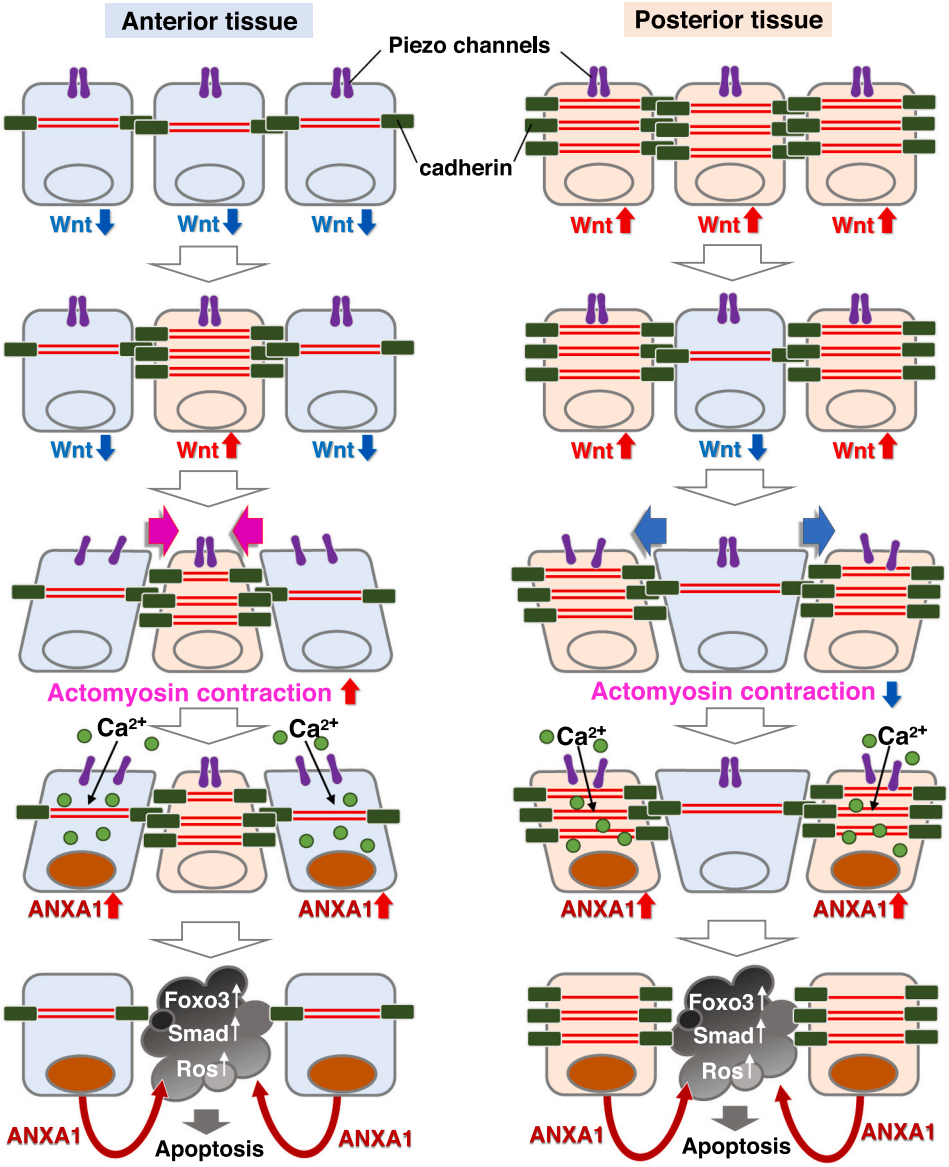

Fig. 4. Mechanical force drives morphogen gradient noise correction. Schematic illustration of the mechanical force-driven correction of noisy morphogen gradients. Wnt morphogen gradient is converted to an actomyosin-mediated mechano-gradient along the anterior-posterior axis. When cells with unfit Wnt activity are generated, this unfitness generates local tensile force alteration through the alteration of membrane E-cadherin levels. This local tension alteration applies mechanical stress to neighboring fit cells and activates the Piezo family of mechanosensitive channels to trigger rapid Ca^{2+} influx and consequent ANXA1 expression in neighboring cells. ANXA1 is secreted from neighboring cells and induces apoptosis in the unfit cells.

thereby initiating cell competition to eliminate unfit cells (Fig. 4). Therefore, the robustness of the morphogen gradient is supported by the conversion of chemical signals into mechanical signals [45].

4. Perspectives

4.1. Cell competition-mediated morphogen gradient correction

The morphogen gradient correction was firstly discovered through observation of *Drosophila* imaginal disc; where cells with either high or low bone morphogenic protein (BMP) signaling activity were introduced and underwent apoptosis through cell competition or its related system [55–59]. However, it is unclear whether cell competition corrects morphogen gradients in the physiological situation and vertebrate tissues. In addition, the detailed mechanisms of morphogen gradients-noise correction remain unknown. As described above, we recently discovered that physiological cell competition corrects Wnt and Shh morphogen gradient in zebrafish and that the mechano-chemical conversion mediated by Cadherin-Piezo-ANXA1-Foxo3-Smad-ROS-Bcl2 axis drives the noise correction [30,31,45]. This suggest that the cell competition-driven morphogen gradient correction system is evolutionarily conserved from flies to vertebrates and that the similar mechano-chemical conversion system may also be involved in above-mentioned *Drosophila* morphogen-noise correction. Further research on this correction mechanism will solve these questions and will allow us to understand morphogen activity and its regulation/dysregulation in pathologic situations.

4.2. Mechanical force-driven cell competition in other contexts

Morphogen gradients support both tissue patterning and adult tissue turnover, and the cells with abnormal morphogen signaling activity can cause various diseases [60–62]. Therefore, the mechanical force-mediated morphogen-noise correction system is essential for

embryogenesis, organogenesis, and adult tissue homeostasis. As mentioned above, Shh morphogen signaling negatively regulates membrane N-cadherin levels in the developing spinal cord and muscle [31,36] and N-cadherin also functions as a site of actomyosin assembly just like E-cadherin [43], indicating that N-cadherin-mediated mechano-gradients may be formed in these tissues. Actually, similar to Wnt morphogen gradients-noise correction, the noises in Shh morphogen gradients are also repaired via N-cadherin-Foxo3-Smad-ROS-Bcl2 axis [31]. Taken together, it is likely that N-cadherin-mediated mechano-gradients facilitate cell competition to ensure robust Shh morphogen gradients. Additionally, the adult intestine, which forms Wnt morphogen gradients, may use mechanical force-mediated cell competition. In the mouse intestines, artificially introduced Wnt-hyper-activated cells strongly upregulate E-cadherin levels and are eliminated through apoptosis from the tissue [63]. Notably, cells with abnormally high Wnt signaling can cause colorectal cancer [64,65]. The mediators of mechanical force-mediated cell competition, such as E-cadherin, Smads, and ANXA1, are tumor-suppressor genes [66–70], indicating a close relationship between the mechanism of mechano-driven cell competition and tumor suppression. Therefore, the mechanical force-mediated morphogen noise correction system may help prevent tumorigenesis in adult tissues.

4.3. Unsolved mechanism in mechanical force-driven cell competition

Although we demonstrated that the unfit cell-generating mechanical force activates the Piezo channel, further studies are required to clarify the detailed mechanisms underlying Piezo activation in neighboring cells, its role in ANXA1 expression, and how ANXA1 specifically eliminates unfit cells. Additionally, it may be valuable to assess whether the mechanical force-Piezo-ANXA1 axis mediates other types of cell competition. Because actomyosin systems that generate mechanical force interact with various cellular signaling and metabolism [71–74], unfit cells with abnormal signaling and metabolic activity may trigger cell competition by altering mechanical force. It is worth noting that a recent study reported that AnnexinA2 (ANXA2) is involved in the elimination process of Ras-hyper-activated oncogenic cells [75], suggesting the possibility that the ANXA family proteins may commonly mediate various types of cell competition.

4.4. Mechano-sensing of unfit cells: a novel mechanism of cell competition

Numerous studies have reported that mechanical force drives unfit cell elimination during cell competition. For example, in mammalian cell cultures, Ras-hyper-activated oncogenic cells are physically eliminated by the contractile force that is generated by cytoskeletal proteins (filamin and vimentin) expressed in neighboring normal cells [76]. In *Drosophila* pupal notum, tissue crowding-induced mechanical stress stimulates the cell competition-mediated elimination of cells with lower proliferative activity [77]. Similarly, crowding-induced cell competition, which is triggered by stretch-induced Piezo1 activation, contributes to homeostasis in zebrafish fin [78,79]. In *Xenopus* embryos, Piezo1-driven apical cell extrusion plays an essential role in the epithelium remodeling [80]. However, the role of mechanical force in sensing unfit cells remains unclear. Our recent study is the first to demonstrate that mechanical force mediates unfit cell sensing during cell competition [45]. By focusing on mechano-sensing, we can also understand the unfit cell-sensing mechanisms in other types of cell competition.

4.5. Interaction between morphogen and mechanical force

Similar to our findings, recent studies have revealed interactions between morphogens and mechanical forces. For example, during zebrafish gastrulation, Nodal signaling acts as a chemical morphogen to control gene expression and as a “mechanogen” triggering collective cell migration through motility-driven (un)jamming [81–83]. In zebrafish blastoderm spreading, Wnt11 morphogen signaling generates spatial pattern of tissue fluidization via enhancing actomyosin contractility [84]. In *Xenopus* animal cap experiments, mechanical stimulation of the ectoderm activated β-catenin and induced head organizer gene expression, thereby regulating AP axis formation [85]. Therefore, morphogens and mechanical forces regulate embryogenesis. Future research should explore the interaction of mechanical forces with Wnt and other morphogens because similar regulatory mechanisms are likely to be involved in organogenesis and adult tissue homeostasis. Additionally, although we revealed a part of the significance of the mechano-gradient (cell competition driver), this gradient likely plays other yet unknown roles. In the future, we may aim to unravel these roles to enhance our understanding of mechanical force-morphogen interactions during tissue development and regeneration.

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Author contributions

K.A., and T.I. wrote the main manuscript text; K.A. prepared the figures. All authors have reviewed the manuscript.

Declaration of Competing Interest

The authors declare no competing interests.

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References

[1] K.W. Rogers, A.F. Schier, Morphogen gradients: from generation to interpretation, Annu Rev. Cell Dev. Biol. 27 (2011) 377–407, https://doi.org/10.1146/annurev-cellbio-092910-154148.
[2] J.B. Gurdon, P.Y. Bourillot, Morphogen gradient interpretation, Oct 25, Nature 413 (6858) (2001) 797–803, https://doi.org/10.1038/35101500.
[3] A.M. Turing, The chemical basis of morphogenesis, discussion 119-52, Bull. Math. Biol. 52 (1-2) (1990) 153–197, https://doi.org/10.1007/BF02459572.
[4] L. Wolpert, Positional information and the spatial pattern of cellular differentiation (Oct), J. Theor. Biol. 25 (1) (1969) 1–47, https://doi.org/10.1016/s0022-5193(69)80016-0.
[5] F. Crick, Diffusion in embryogenesis, Jan 31, Nature 225 (5231) (1970) 420–422, https://doi.org/10.1038/225420a0.
[6] C. Guillot, T. Lecuit, Mechanics of epithelial tissue homeostasis and morphogenesis, Jun 7, Science 340 (6137) (2013) 1185–1189, https://doi.org/10.1126/science.1235249.
[7] A. Stathopoulos, D. Iber, Studies of morphogens: keep calm and carry on (Oct), Development 140 (20) (2013) 4119–4124, https://doi.org/10.1242/dev.095141.
[8] K.S. Stapornwongkul, J.P. Vincent, Generation of extracellular morphogen gradients: the case for diffusion (Jun), Nat. Rev. Genet 22 (6) (2021) 393–411, https://doi.org/10.1038/s41576-021-00342-y.
[9] C.P. Petersen, P.W. Reddien, Wnt signaling and the polarity of the primary body axis, Dec 11, Cell 139 (6) (2009) 1056–1068, https://doi.org/10.1016/j.cell.2009.11.035.

[10] J.O. Russell, S.P. Monga, Wnt/β-Catenin Signaling in Liver Development, Homeostasis, and Pathobiology, Jan 24, Annu Rev. Pathol. 13 (2018) 351–378, https://doi.org/10.1146/annurev-pathol-020117-044010.
[11] R.M. Houtekamer, M.C. van der Net, M.M. Maurice, M. Gloerich, Mechanical forces directing intestinal form and function, Jul 25, Curr. Biol. 32 (14) (2022) R791–R805, https://doi.org/10.1016/j.cub.2022.05.041.
[12] M. Valet, E.D. Siggia, A.H. Brivanlou, Mechanical regulation of early vertebrate embryogenesis (Mar), Nat. Rev. Mol. Cell Biol. 23 (3) (2022) 169–184, https://doi.org/10.1038/s41580-021-00424-z.
[13] T. Duncan, T.T. Su, Embryogenesis: coordinating cell division with gastrulation, Apr 20, Curr. Biol. 14 (8) (2004) R305–R307, https://doi.org/10.1016/j.cub.2004.03.050.
[14] S. Kurosaka, A. Kashina, Cell biology of embryonic migration (Jun), Birth Defects Res C. Embryo Today 84 (2) (2008) 102–122, https://doi.org/10.1002/bdrc.20125.
[15] G. Reig, E. Pulgar, M.L. Concha, Cell migration: from tissue culture to embryos (May), Development 141 (10) (2014) 1999–2013, https://doi.org/10.1242/dev.101451.
[16] G. Morata, M. Calleja, Cell competition and tumorigenesis in the imaginal discs of Drosophila (Jun), Semin Cancer Biol. 63 (2020) 19–26, https://doi.org/10.1016/j.semcancer.2019.06.010.
[17] C. Clavería, M. Torres, Cell Competition: Mechanisms and Physiological Roles, Oct 6, Annu Rev. Cell Dev. Biol. 32 (2016) 411–439, https://doi.org/10.1146/annurev-cellbio-111315-125142.
[18] C. Díaz-Díaz, M. Torres, Insights into the quantitative and dynamic aspects of Cell Competition, Curr. Opin. Cell Biol. 60 (2019) 68–74 (Oct).
[19] R. Levayer, E. Moreno, Mechanisms of cell competition: themes and variations, Mar 18, J. Cell Biol. 200 (6) (2013) 689–698, https://doi.org/10.1083/jcb.201301051.
[20] G. Morata, P. Ripoll, Minutes: mutants of drosophila autonomously affecting cell division rate (Feb), Dev. Biol. 42 (2) (1975) 211–221, https://doi.org/10.1016/0012-1606(75)90330-9.
[21] G. Morata, Cell competition: A historical perspective (Aug), Dev. Biol. 476 (2021) 33–40, https://doi.org/10.1016/j.ydbio.2021.02.012.
[22] M. Kajita, Y. Fujita, EDAC: Epithelial defence against cancer-cell competition between normal and transformed epithelial cells in mammals (Jul), J. Biochem 158 (1) (2015) 15–23, https://doi.org/10.1093/jb/mvv050.
[23] A. Di Gregorio, S. Bowling, T.A. Rodriguez, Cell Competition and Its Role in the Regulation of Cell Fitness from Development to Cancer, Sep 26, Dev. Cell 38 (6) (2016) 621–634, https://doi.org/10.1016/j.devcel.2016.08.012.
[24] S. Kon, K. Ishibashi, H. Katoh, S. Kitamoto, T. Shirai, S. Tanaka, M. Kajita, S. Ishikawa, H. Yamauchi, Y. Yako, T. Kamasaki, T. Matsumoto, H. Watanabe, R. Egami, A. Sasaki, A. Nishikawa, I. Kameda, T. Maruyama, R. Narumi, T. Morita, Y. Sasaki, R. Enoki, S. Honma, H. Imamura, M. Oshima, T. Soga, J.I. Miyazaki, M. R. Duchen, J.M. Nam, Y. Onodera, S. Yoshioka, J. Kikuta, M. Ishii, M. Imajo, E. Nishida, Y. Fujioka, Y. Ohba, T. Sato, Y. Fujita, Cell competition with normal epithelial cells promotes apical extrusion of transformed cells through metabolic changes (May), Nat. Cell Biol. 19 (5) (2017) 530–541, https://doi.org/10.1038/ncb3509.
[25] C. Villa Del Campo, C. Clavería, R. Sierra, M. Torres, Cell competition promotes phenotypically silent cardiomyocyte replacement in the mammalian heart, Sep 25, Cell Rep. 8 (6) (2014) 1741–1751, https://doi.org/10.1016/j.celrep.2014.08.005.
[26] A. Sasaki, T. Nagatake, R. Egami, G. Gu, I. Takigawa, W. Ikeda, T. Nakatani, J. Kunisawa, Y. Fujita, Obesity Suppresses Cell-Competition-Mediated Apical Elimination of RasV12-Transformed Cells from Epithelial Tissues, Apr 24, Cell Rep. 23 (4) (2018) 974–982, https://doi.org/10.1016/j.celrep.2018.03.104.
[27] C. Clavería, G. Giovinazzo, R. Sierra, M. Torres, Myc-driven endogenous cell competition in the early mammalian embryo, Aug 1, Nature 500 (7460) (2013) 39–44, https://doi.org/10.1038/nature12389.
[28] C. Díaz-Díaz, L. Fernandez de Manuel, D. Jimenez-Carretero, M.C. Montoya, C. Clavería, M. Torres, Pluripotency Surveillance by Myc-Driven Competitive Elimination of Differentiating Cells, Sep 25, Dev. Cell 42 (6) (2017) 585–599.e4, https://doi.org/10.1016/j.devcel.2017.08.011.
[29] M. Hashimoto, H. Sasaki, Epiblast Formation by TEAD-YAP-Dependent Expression of Pluripotency Factors and Competitive Elimination of Unspecified Cells, Jul 22, Dev. Cell 50 (2) (2019) 139–154.e5, https://doi.org/10.1016/j.devcel.2019.05.024.
[30] Y. Akieda, S. Ogamino, H. Furuie, S. Ishitani, R. Akiyoshi, J. Nogami, T. Masuda, N. Shimizu, Y. Ohkawa, T. Ishitani, Cell competition corrects noisy Wnt morphogen gradients to achieve robust patterning in the zebrafish embryo, Oct 17, Nat. Commun. 10 (1) (2019) 4710, https://doi.org/10.1038/s41467-019-12609-4.
[31] K. Matsumoto, Y. Akieda, Y. Haraoka, N. Hirono, H. Sasaki, T. Ishitani, Foxo3-mediated physiological cell competition ensures robust tissue patterning throughout vertebrate development, Dec 17, Nat. Commun. 15 (1) (2024) 10662, https://doi.org/10.1038/s41467-024-55108-x.
[32] H.L. Stickney, M.J. Barresi, S.H. Devoto, Somite development in zebrafish (Nov;), Dev. Dyn. 219 (3) (2000) 287–303, https://doi.org/10.1002/1097-0177 (2000) 9999:9999< ::AID-DVDY1065> 3.0.CO;2-A.
[33] C.S. Blagden, P.D. Currie, P.W. Ingham, S.M. Hughes, Notochord induction of zebrafish slow muscle mediated by Sonic hedgehog, Sep 1, Genes Dev. 11 (17) (1997) 2163–2175, https://doi.org/10.1101/gad.11.17.2163.
[34] T.M. Jessell, Neuronal specification in the spinal cord: inductive signals and transcriptional codes (Oct), Nat. Rev. Genet 1 (1) (2000) 20–29, https://doi.org/10.1038/35049541.
[35] E. Dessaud, A.P. McMahon, J. Briscoe, Pattern formation in the vertebrate neural tube: a sonic hedgehog morphogen-regulated transcriptional network (Aug), Development 135 (15) (2008) 2489–2503, https://doi.org/10.1242/dev.009324.
[36] T.Y. Tsai, M. Sikora, P. Xia, T. Colak-Champollion, H. Knaut, C.P. Heisenberg, S. G. Megason, An adhesion code ensures robust pattern formation during tissue morphogenesis, Oct 2;, Science 370 (6512) (2020) 113–116, https://doi.org/10.1126/science.aba6637.
[37] E.T. Hall, E. Hoesing, E. Sinkovics, E.M. Verheyen, Actomyosin contractility modulates Wnt signaling through adherens junction stability, Feb 1, Mol. Biol. Cell 30 (3) (2019) 411–426, https://doi.org/10.1091/mbc.E18-06-0345.
[38] C.P. Heisenberg, Y. Bellaïche, Forces in tissue morphogenesis and patterning, May 23, Cell 153 (5) (2013) 948–962, https://doi.org/10.1016/j.cell.2013.05.008.
[39] J. Howard, S.W. Grill, J.S. Bois, Turing's next steps: the mechanochemical basis of morphogenesis (Jun), Nat. Rev. Mol. Cell Biol. 12 (6) (2011) 392–398, https://doi.org/10.1038/nrm3120.
[40] M. Amano, M. Nakayama, K. Kaibuchi, Rho-kinase/ROCK: A key regulator of the cytoskeleton and cell polarity (Sep), Cytoskelet. (Hoboken) 67 (9) (2010) 545–554, https://doi.org/10.1002/cm.20472.
[41] R.J. Marjoram, E.C. Lessey, K. Burridge, Regulation of RhoA Activity by Adhesion Molecules and Mechanotransduction (Feb), Curr. Mol. Med 14 (2) (2014) 199–208, https://doi.org/10.2174/1566524014666140128104541.
[42] G. Salbreux, G. Charras, E. Paluch, Actin cortex mechanics and cellular morphogenesis (Oct), Trends Cell Biol. 22 (10) (2012) 536–545, https://doi.org/10.1016/j.tcb.2012.07.001.
[43] S. Nandadasa, Q. Tao, N.R. Menon, J. Heasman, C. Wylie, N- and E-cadherins in Xenopus are specifically required in the neural and non-neural ectoderm, respectively, for F-actin assembly and morphogenetic movements (Apr), Development 136 (8) (2009) 1327–1338, https://doi.org/10.1242/dev.031203.
[44] O. Campàs, I. Noordstra, A.S. Yap, Adherens junctions as molecular regulators of emergent tissue mechanics (Apr), Nat. Rev. Mol. Cell Biol. 25 (4) (2024) 252–269, https://doi.org/10.1038/s41580-023-00688-7.
[45] K. Aoki, T. Higuchi, Y. Akieda, K. Matsubara, Y. Ohkawa, T. Ishitani, Mechano-gradients drive morphogen-noise correction to ensure robust patterning, Nov 15, Sci. Adv. 10 (46) (2024) eadp2357, https://doi.org/10.1126/sciadv.adp2357.
[46] J. Ge, W. Li, Q. Zhao, N. Li, M. Chen, P. Zhi, R. Li, N. Gao, B. Xiao, M. Yang, Architecture of the mammalian mechanosensitive Piezo1 channel, Nov 5, Nature 527 (7576) (2015) 64–69, https://doi.org/10.1038/nature15247.
[47] K. Saotome, S.E. Murthy, J.M. Kefauver, T. Whitwam, A. Patapoutian, A.B. Ward, Structure of the mechanically activated ion channel Piezo1, Feb 22, Nature 554 (7693) (2018) 481–486, https://doi.org/10.1038/nature25453.
[48] Y. Wang, S. Chi, H. Guo, G. Li, L. Wang, Q. Zhao, Y. Rao, L. Zu, W. He, B. Xiao, A lever-like transduction pathway for long-distance chemical- and mechano-gating of the mechanosensitive Piezo1 channel, Apr 3, Nat. Commun. 9 (1) (2018) 1300, https://doi.org/10.1038/s41467-018-03570-9.
[49] Q. Zhao, H. Zhou, S. Chi, Y. Wang, J. Wang, J. Geng, K. Wu, W. Liu, T. Zhang, M. Q. Dong, J. Wang, X. Li, B. Xiao, Structure and mechanogating mechanism of the Piezo1 channel, Feb 22, Nature 554 (7693) (2018) 487–492, https://doi.org/10.1038/nature25743 (E).
[50] R. Syeda, M.N. Florendo, C.D. Cox, J.M. Kefauver, J.S. Santos, B. Martinac, A. Patapoutian, Piezo1 Channels Are Inherently Mechanosensitive, Nov 8, Cell Rep. 17 (7) (2016) 1739–1746, https://doi.org/10.1016/j.celrep.2016.10.033.
[51] U. Rescher, N. Zobiack, V. Gerke, Intact Ca(2+)-binding sites are required for targeting of annexin 1 to endosomal membranes in living HeLa cells (Nov), J. Cell Sci. 113 (Pt 22) (2000) 3931–3938, https://doi.org/10.1242/jcs.113.22.3931.
[52] S.L. Foo, G. Yap, J. Cui, L.H.K. Lim, Annexin-A1-A Blessing or a Curse in Cancer? (Apr), Trends Mol. Med 25 (4) (2019) 315–327, https://doi.org/10.1016/j.molmed.2019.02.004.
[53] W.W. Yim, H. Yamamoto, N. Mizushima, Annexins A1 and A2 are recruited to larger lysosomal injuries independently of ESCRTs to promote repair (Apr), FEBS Lett. 596 (8) (2022) 991–1003, https://doi.org/10.1002/1873-3468.14329.
[54] M. de Graauw, M.H. van Miltenburg, M.K. Schmidt, C. Pont, R. Lalai, J. Kartopawiro, E. Pardali, S.E. Le Dévédec, V.T. Smit, A. van der Wal, L.J. Van't Veer, A.M. Cleton-Jansen, P. ten Dijke, B. van de Water, Annexin A1 regulates TGF-beta signaling and promotes metastasis formation of basal-like breast cancer cells, Apr 6;, Proc. Natl. Acad. Sci. USA 107 (14) (2010) 6340–6345, https://doi.org/10.1073/pnas.0913360107.
[55] T. Adachi-Yamada, K. Fujimura-Kamada, Y. Nishida, K. Matsumoto, Distortion of proximodistal information causes JNK-dependent apoptosis in Drosophila wing, Jul 8, Nature 400 (6740) (1999) 166–169, https://doi.org/10.1038/22112.
[56] T. Adachi-Yamada, M.B. O'Connor. Morphogenetic apoptosis: a mechanism for correcting discontinuities in morphogen gradients, Nov 1, Dev. Biol. 251 (1) (2002) 74–90, https://doi.org/10.1006/dbio.2002.0821.
[57] E. Moreno, K. Basler, G. Morata, Cells compete for decapentaplegic survival factor to prevent apoptosis in Drosophila wing development, Apr 18, Nature 416 (6882) (2002) 755–759, https://doi.org/10.1038/416755a.
[58] J.P. Vincent, G. Kolahgar, M. Gagliardi, E. Piddini, Steep differences in wingless signaling trigger Myc-independent competitive cell interactions, Aug 16, Dev. Cell 21 (2) (2011) 366–374, https://doi.org/10.1016/j.devcel.2011.06.021.
[59] M.M. Merino, C. Seum, M. Dubois, M. Gonzalez-Gaitan, A role for Flower and cell death in controlling morphogen gradient scaling (Apr), Nat. Cell Biol. 24 (4) (2022) 424–433, https://doi.org/10.1038/s41556-022-00858-3.
[60] J. Taipale, P.A. Beachy, The Hedgehog and Wnt signalling pathways in cancer, May 17, Nature 411 (6835) (2001) 349–354, https://doi.org/10.1038/35077219.
[61] Y. Yang, Wnt signaling in development and disease, Apr 20, Cell Biosci. 2 (1) (2012) 14, https://doi.org/10.1186/2045-3701-2-14.
[62] H. Clevers, R. Nusse, Wnt/β-catenin signaling and disease, Jun 8, Cell 149 (6) (2012) 1192–1205, https://doi.org/10.1016/j.cell.2012.05.012. PMID: 22682243..

[63] M.H. Wong, B. Rubinfeld, J.I. Gordon, Effects of forced expression of an NH2-terminal truncated beta-Catenin on mouse intestinal epithelial homeostasis, May 4, J. Cell Biol. 141 (3) (1998) 765–777, https://doi.org/10.1083/jcb.141.3.765.
[64] K.W. Kinzler, M.C. Nilbert, L.K. Su, B. Vogelstein, T.M. Bryan, D.B. Levy, K. J. Smith, A.C. Preisinger, P. Hedge, D. McKechnie, R. Finniear, A. Markham, J. Groffen, M.S. Boguski, S.F. Altschul, A. Horii, H. Ando, Y. Miyoshi, Y. Miki, I. Nishisho, Y. Nakamura, Identification of FAP locus genes from chromosome 5q21, Aug 9, Science 253 (5020) (1991) 661–665, https://doi.org/10.1126/science.1651562.
[65] I. Nishisho, Y. Nakamura, Y. Miyoshi, Y. Miki, H. Ando, A. Horii, K. Koyama, j Utsunomiya, S. Baba, P. Hedge, Mutations of chromosome 5q21 genes in FAP and colorectal cancer patients, Aug 9, Science 253 (5020) (1991) 665–669, https://doi.org/10.1126/science.1651563.
[66] G. Christofori, H. Semb, The role of the cell-adhesion molecule E-cadherin as a tumour-suppressor gene (Feb), Trends Biochem Sci. 24 (2) (1999) 73–76, https://doi.org/10.1016/s0968-0004(98)01343-7.
[67] R. Derynck, R.J. Akhurst, A. Balmain, TGF-beta signaling in tumor suppression and cancer progression (Oct), Nat. Genet 29 (2) (2001) 117–129, https://doi.org/10.1038/ng1001-117.
[68] C. Guo, S. Liu, M.Z. Sun, Potential role of Anxa1 in cancer (Nov), Future Oncol. 9 (11) (2013) 1773–1793, https://doi.org/10.2217/fon.13.114.
[69] Z. Fu, S. Zhang, B. Wang, W. Huang, L. Zheng, ACheng, Annexin A1: A double-edged sword as novel cancer biomarker (May), Clin. Chim. Acta 504 (2020) 36–42, https://doi.org/10.1016/j.cca.2020.01.022.
[70] T.G. Araújo, S.T.S. Mota, H.S.V. Ferreira, M.A. Ribeiro, L.R. Goulart, L. Vecchi, Annexin A1 as a Regulator of Immune Response in Cancer, Aug 30, Cells 10 (9) (2021) 2245, https://doi.org/10.3390/cells10092245.
[71] K.M. Tharp, M.S. Kang, G.A. Timblin, J. Dempersmier, G.E. Dempsey, P.H. Zushin, J. Benavides, C. Choi, C.X. Li, A.K. Jha, S. Kajimura, K.E. Healy, H.S. Sul, K. Saijo, S. Kumar, A. Stahl, Actomyosin-Mediated Tension Orchestrates Uncoupled Respiration in Adipose Tissues, Mar 6, Cell Metab. 27 (3) (2018) 602–615.e4, https://doi.org/10.1016/j.cmet.2018.02.005.
[72] J.S. Park, C.J. Burckhardt, R. Lazcano, L.M. Solis, T. Isogai, L. Li, C.S. Chen, B. Gao, J.D. Minna, R. Bachoo, R.J. DeBerardinis, G. Danuser, Mechanical regulation of glycolysis via cytoskeleton architecture (Feb), Nature 578 (7796) (2020) 621–626, https://doi.org/10.1038/s41586-020-1998-1.
[73] R. Santos, L. Lokmane, D. Ozdemir, C. Traoré, A. Agesilas, C. Hakibilen, Z. Lenkei, D. Zala, Local glycolysis fuels actomyosin contraction during axonal retraction, Dec 4, J. Cell Biol. 222 (12) (2023) e202206133, https://doi.org/10.1083/jcb.202206133.
[74] E. Crosas-Molist, V. Graziani, O. Maiques, P. Pandya, J. Monger, R. Samain, S. L. George, S. Malik, J. Salise, V. Morales, Le.A. Guennec, A.R.A. tkinson, R. M. Marti, X. Matias-Guiu, G. Charras, M.R. Conte, A. Elosegui-Artola, M. Holt, V. Sanz-Moreno, AMPK is a mechano-metabolic sensor linking cell adhesion and mitochondrial dynamics to Myosin-dependent cell migration, May 22;, Nat. Commun. 14 (1) (2023) 2740, https://doi.org/10.1038/s41467-023-38292-0.
[75] S. Ito, K. Kuromiya, M. Sekai, H. Sako, K. Sai, R. Morikawa, Y. Mukai, Y. Ida, M. Anzai, S. Ishikawa, K. Kozawa, T. Shirai, N. Tanimura, K. Sugie, J. Ikenouchi, M. Ogawa, I. Naguro, H. Ichijo, Y. Fujita, Accumulation of annexin A2 and S100A10 prevents apoptosis of apically delaminated, transformed epithelial cells, Oct 24, Proc. Natl. Acad. Sci. USA 120 (43) (2023) e2307118120, https://doi.org/10.1073/pnas.2307118120.
[76] M. Kajita, K. Sugimura, A. Ohoka, J. Burden, H. Suganuma, M. Ikegawa, T. Shimada, T. Kitamura, M. Shindoh, S. Ishikawa, S. Yamamoto, S. Saitoh, Y. Yako, R. Takahashi, T. Okajima, J. Kikuta, Y. Maijima, M. Ishii, M. Tada, Y. Fujita, Filamin acts as a key regulator in epithelial defence against transformed cells, Jul 31, Nat. Commun. 5 (2014) 4428, https://doi.org/10.1038/ncomms5428.
[77] R. Levayer, C. Dupont, E. Moreno, Tissue Crowding Induces Caspase-Dependent Competition for Space, Mar 7, Curr. Biol. 26 (5) (2016) 670–677, https://doi.org/10.1016/j.cub.2015.12.072.
[78] G.T. Eisenhoffer, P.D. Loftus, M. Yoshigi, H. Otsuna, C.B. Chien, P.A. Morcos, J. Rosenblatt, Crowding induces live cell extrusion to maintain homeostatic cell numbers in epithelia, Apr 15, Nature 484 (7395) (2012) 546–549, https://doi.org/10.1038/nature10999.
[79] G.T. Eisenhoffer, J. Rosenblatt, Bringing balance by force: live cell extrusion controls epithelial cell numbers (Apr), Trends Cell Biol. 23 (4) (2013) 185–192, https://doi.org/10.1016/j.tcb.2012.11.006.
[80] R. Ventrella, S.K. Kim, J. Sheridan, A. Grata, E. Bresteau, O.A. Hassan, E.E. Suva, P. Walentek, B.J. Mitchell, Bidirectional multiciliated cell extrusion is controlled by Notch-driven basal extrusion and Piezo1-driven apical extrusion, Sep 1, Development 150 (17) (2023) dev201612, https://doi.org/10.1242/dev.201612.
[81] K. Dasbiswas, E. Alster, S. Safran, Mechanobiological induction of long-range contractility by diffusing biomolecules and size scaling in cell assemblies, Jun 10, Sci. Rep. 6 (2016) 27692, https://doi.org/10.1038/srep27692.
[82] K. Dasbiswas, E. Hannezo, N.S. Gov, Theory of Epithelial Cell Shape Transitions Induced by Mechanoactive Chemical Gradients, Feb 27, Biophys. J. 114 (4) (2018) 968–977, https://doi.org/10.1016/j.bpj.2017.12.022.
[83] D. Pinheiro, R. Kardos, É . Hannezo, C.P. Heisenberg, Morphogen gradient orchestrates pattern-preserving tissue morphogenesis via motility-driven unjamming, Nat. Phys. 18 (2022) 1482–1493, https://doi.org/10.1038/s41567-022-01787-6.
[84] N.I. Petridou, S. Grigolon, G. Salbreux, E. Hannezo, C.P. Heisenberg, Fluidization-mediated tissue spreading by mitotic cell rounding and non-canonical Wnt signalling (Feb), Nat. Cell Biol. 21 (2) (2019) 169–178, https://doi.org/10.1038/s41556-018-0247-4.
[85] M. Bubna-Litic, G. Charras, R. Mayor, Tissue mechanics modulate morphogen signalling to induce the head organiser, Dec 2, Cells Dev. (2024) 203984, https://doi.org/10.1016/j.cdev.2024.203984.

Glossary

Morphogen: A signaling molecule that diffuses through tissues in a concentration-dependent manner to provide positional data, guiding cell differentiation and tissue patterning during development.
Morphogen gradient: A spatial distribution of morphogen concentration across a tissue, where cells interpret different morphogen levels to adopt specific fates.
Wnt/β-Catenin pathway: A signaling pathway that regulates cell fate, proliferation, and differentiation.
Anterior-posterior axis: A directional axis in an embryo that defines the head-to-tail orientation.
Cadherin: A type of cell adhesion molecule (e.g. E-cadherin and N-cadherin) that mediates calcium-dependent intercellular adhesion, playing a role in tissue integrity and morphogenesis.
Actomyosin: A complex of actin filaments and myosin motor proteins that generates contractile force within cells, contributing to cellular and tissue mechanics.
Mechano-gradients: Gradients of mechanical tension or force generated within tissues, often regulated by cellular interactions involving the actomyosin system.
Piezo channels: Mechanosensitive ion channels that open in response to mechanical forces, such as pressure or tension, enabling calcium ions to enter cells and trigger downstream signaling.
Annexin A1 (ANXA1): A secretory protein involved in resolving inflammation and facilitating apoptosis.
Cell competition: A process where fitter cells eliminate less fit (unfit) neighboring cells through molecular or mechanical interactions, maintaining tissue homeostasis and developmental robustness.
Sonic hedgehog (Shh) morphogen: A signaling molecule crucial for patterning and growth during embryogenesis, specifically in the development of the nervous system and limbs.
E-cadherin and N-cadherin: Specific types of cadherins involved in cell-cell adhesion. E-cadherin is often expressed in epithelial tissues, whereas N-cadherin is common in neural and mesenchymal tissues.
Small mothers against decapentaplegic (Smads): Intracellular proteins that mediate signal transduction for the transforming growth factor-beta (TGF-β) superfamily, playing roles in cell growth, differentiation, and apoptosis.
Tumor-suppressor genes: Genes that protect cells from cancer by regulating cell division, promoting apoptosis, or maintaining DNA repair.
Nodal signaling: A signaling pathway involved in embryonic patterning, specifically in mesoderm and endoderm formation and left-right asymmetry.
Blastoderm: A layer of cells formed during early embryogenesis, specifically in vertebrates, that spreads and differentiates into distinct tissues.
Jamming: A process that takes place when cells become tightly packed and less mobile, often due to increased cell-cell adhesion or reduced motility, leading to a solid-like state
Unjamming: Transition from a jammed to an unjammed state, allowing cells to move more freely and facilitating tissue fluidity.