Multi-cellular polarity lit search (2019)

- Intracellular polarity of neighbors often aligns according to a common axis (e.g. apicobasal or planar) (Abley et al. 2013)
- Vectored distribution of cell identity or positional information within the tissue (Wopert199

J Cell Biol. 2018 May 7;217(5):1827-1845. doi: 10.1083/jcb.201708103. Epub 2018 Mar 5.

Branched actin networks push against each other at adherens junctions to maintain cell-cell adhesion.

Efimova N[1], Svitkina TM[2].

Nat Commun. 2019 Aug 23;10(1):3800. doi: 10.1038/s41467-019-11716-6.

Rebalancing of actomyosin contractility enables mammary tumor formation upon loss of E-cadherin.

Schipper K[1], Seinstra D[1], Paulien Drenth A[1], van der Burg E[1], Ramovs V[2], Sonnenberg A[2], van Rheenen J[1], Nethe M[3,4], Jonkers J[5].

Exp Cell Res. 2019 Mar 1;376(1):86-91. doi: 10.1016/j.yexcr.2019.01.006. Epub 2019 Jan 8.

Cadherin mechanotransduction in leader-follower cell specification during collective migration.

Khalil AA[1], de Rooij J[2].

Sci Rep. 2017 Apr 13;7:46326. doi: 10.1038/srep46326.

Actomyosin contractility provokes contact inhibition in E-cadherin-ligated keratinocytes.

Hirata H[1,2], Samsonov M[3], Sokabe M[2].

Curr Opin Cell Biol. 2018 Dec;55:104-110. doi: 10.1016/j.ceb.2018.07.001. Epub 2018 Jul 18.

Alignment of cytoskeletal structures across cell boundaries generates tissue cohesion during organ formation.

Sánchez-Corrales YE[1], Röper K[2].

Dev Biol. 2018 Feb 1;434(1):133-148. doi: 10.1016/j.ydbio.2017.12.002. Epub 2017 Dec 6.

WAVE regulates Cadherin junction assembly and turnover during epithelial polarization.

Sasidharan S[1], Borinskaya S[1], Patel F[1], Bernadskaya Y[1], Mandalapu S[1], Agapito M[1], Soto MC[2].

Nat Cell Biol. 2016 Dec;18(12):1311-1323. doi: 10.1038/ncb3438. Epub 2016 Nov 14.

Engulfed cadherin fingers are polarized junctional structures between collectively migrating endothelial cells.

Hayer A[1], Shao L[2], Chung M[1], Joubert LM[3], Yang HW[1], Tsai FC[1], Bisaria A[1], Betzig E[2], Meyer T[1].

Nat Commun. 2018 Nov 27;9(1):5021. doi: 10.1038/s41467-018-07448-8.

Distinct contributions of tensile and shear stress on E-cadherin levels during morphogenesis.

Kale GR[1,2], Yang X[3,4], Philippe JM[1], Mani M[3], Lenne PF[5], Lecuit T[6,7].

J Cell Sci. 2018 Jun 27;131(12). pii: jcs211334. doi: 10.1242/jcs.211334.

Myosin-1c promotes E-cadherin tension and force-dependent recruitment of α-actinin to the epithelial cell junction.

Kannan N[1], Tang VW[2].

Experimentally-observed hypotheses for effect of cadherin on cell-cell junction: (6/1/2023)

1. Suppress RhoA following Rac1 activation (through p190RhoGAP recruitment to cadherin complexes)

G.A. Wildenberg, et al., p120-catenin and p190RhoGAP regulate cell-cell adhesion by coordinating antagonism between Rac and Rho, Cell 127 (2006) 1027–1039.

2. Suppress RhoA activation

P.Z. Anastasiadis, et al., Inhibition of RhoA by p120 catenin, Nat. Cell Biol. 2 (2000) 637–644.

R.A. van de Ven, et al., p120-catenin prevents multinucleation through control of MKLP1-dependent RhoA activity during cytokinesis, Nat. Commun. 7 (2016) 13874.

3. Activation of Rac1 and Cdc42 (through association of p120 to the RhoGEF Vav2)

N.K. Noren, B.P. Liu, K. Burridge, B. Kreft, p120 catenin regulates the actin cytoskeleton via Rho family GTPases, J. Cell Biol. 150 (2000) 567–580.

- In border cell migration, Rac1 activation in leader cells is proposed to be dependent on the increase in E-cadherin tension in leader cells as compared to the follower cells. Citation: D. Cai, et al., Mechanical feedback through E-cadherin promotes direction sensing during collective cell migration, Cell 157 (5) (2014) 1146–1159.
- In MDCK sheets, Rac1 activity is controlled by the tight junction adhesion complex which releases Merlin in a tension-dependent manner into the cytoplasm of follower cells, resulting in a front-rear gradient of Rac activity that promotes migration in the direction of the leader cell. Citation: T. Das, et al., A molecular mechanotransduction pathway regulates collective migration of epithelial cells, Nat. Cell Biol. 17 (3) (2015), 276–287.

4. Positive feedback systems appear to exist where increasing tension on cadherin-based junctions drives Rho GTPase signaling to increase global cellular contractility leading to a further increase in junctional tension.

A.A. Khalil, J. de Rooij. Cadherin mechanotransduction in leader-follower cell specification during collective migration, Exp Cell Res. 376 (2019) 86-91.

5. KIF17 activates RhoA at cell-cell contacts and/or bundled actin

B.R. Acharya et al. KIF17 regulates RhoA-dependent actin remodeling at epithelial cell–cell adhesions, J. Cell Sci. 129 (2016), 957-970.

- Also, RhoB deflection reduces cell-cell adhesion and down-regulates E-cadherin levels. Citation: F. M. Vega. The Rho GTPase RhoB regulates cadherin expression and epithelial cell-cell interaction, Cell Commun. Signal. 13 (2015), 1-9.

6. Branched actin is up-regulated at cell-cell contacts

J. X. H. Li, V. W. Tang, W. M. Brieher. Actin protrusions push at apical junctions to maintain E-cadherin adhesion, PNAS. 117 (2020) 432-438.

- Related, WAVE regulates cadherin dynamics at cell-cell junction. Citation: S. Sasidharan et al. WAVE regulates Cadherin junction assembly and turnover during epithelial polarization, Dev. Biol. 434 (2018), 133-148.
- Related, Citation: M. V. Rao, R. Zaidel-Bar. Formin-mediated actin polymerization at cell–cell junctions stabilizes E-cadherin and maintains monolayer integrity during wound repair, MBOC. 27 (2016) 2803-2883.
- Related, Citation: Q. Yu et al. Cortical tension initiates the positive feedback loop between cadherin and F-actin, Biophys. J. 121 (2022) 596-606.

“Seems important but unsure of its effect” category:

** Myosin-1c promotes E-cadherin tension and force-dependent recruitment of α-actinin to the epithelial cell junction. Citation: https://pubmed.ncbi.nlm.nih.gov/29748378/

** Binding of cytoplasmic p120 to MPRIP increases ROCK signaling (MLC and Rho activation). Citation: R.C. Schackmann, et al., Cytosolic p120-catenin regulates growth of metastatic lobular carcinoma through Rock1-mediated anoikis resistance, J. Clin. Investig. 121 (2011) 3176–318.

** Binding of p120 to ROCK1 recruits ROCK1. Citation: A.L. Smith, M.R. Dohn, M.V. Brown, A.B. Reynolds, Association of Rho-associated protein kinase 1 with E-cadherin complexes is mediated by p120-catenin, Mol. Biol. Cell 23 (2012) 99–110.
**Junction-based lamellipodia drive endothelial cell rearrangements in vivo via a VE-cadherin-F-actin based oscillatory cell-cell interaction. Citation. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6119192/

	Cell 1	**Cell 2**	10x	100x	1000x
0	uncoupled				
2	Rho ↓	Rho ↓			
5	Rho ↑	Rho ↑			
5	Bundled ↑	Bundled ↑			
3	Rac ↑	Rac ↑			
6	Branched ↑	Branched ↑			
1					
4	?				

$r_{\text{on}} = 0.001, r_{\text{fb}} = 1.0, r_{\text{off}} = 0.9$

Multi-cellular polarity lit search (2023)

Paper	Finding	Cell type
Dev Cell. 2012 Jan 17;22(1):104-15. doi: 10.1016/j.devcel.2011.10.013. Epub 2011 Dec 8. A mechanoresponsive cadherin-keratin complex directs polarized protrusive behavior and collective cell migration Gregory F Weber, Maureen A Bjerke, Douglas W DeSimone	Tension -> cadherin -> keratin IF (local inhibition of Rac by PG (plakoglobin) at sites of stressed cell-cell contacts)	Xenopus mesendoderm cells
Integrating chemotaxis and contact-inhibition during collective cell migration small GTPases at work Eric Theveneau &**Roberto Mayor** Pages 113-117 | Received 02 Sep 2010, Accepted 20 Sep 2010, Published online: 01 Sep 2010	Cadherin is required for contact specific Rac inhibition	Neural crest cells

Dev Cell. 2010 Jul 20;19(1):39-53. doi: 10.1016/j.devcel.2010.06.012. Collective chemotaxis requires contact-dependent cell polarity Eric Theveneau, Lorena Marchant, Sei Kuriyama, Mazhar Gull, Barbara Moepps, Maddy Parsons, Roberto Mayor	Reviewed in above (Cadherin is required for contact specific Rac inhibition)	Neural crest cells
Nat Cell Biol. 2010 Jun;12(6):591-7. doi: 10.1038/ncb2061. Epub 2010 May 16. Light-mediated activation reveals a key role for Rac in collective guidance of cell movement in vivo Xiaobo Wang, Li He, Yi I Wu, Klaus M Hahn, Denise J Montell	Activation of Rac is sufficient to polarize and entree group of cells	Border cells in Drosophila ovary
Sci Rep. 2015 Jan 7;5:7656. doi: 10.1038/srep07656. Leader cells regulate collective cell migration via Rac activation in the downstream signaling of integrin β1 and PI3K Naoya Yamaguchi 1, Takeomi Mizutani 1, Kazushige Kawabata 1, Hisashi Haga	Supports above	MDCK epithelial cells
Nat Cell Biol. 2014 Mar;16(3):217-23. doi: 10.1038/ncb2917. Interplay of RhoA and mechanical forces in collective cell migration driven by leader cells M Reffay, M C Parrini, O Cochet-Escartin, B Ladoux, A Buguin, S Coscoy, F Amblard, J Camonis, P Silberzan		

Biophysical Journal. Volume 121, Issue 4, 15 February 2022, Pages 596-606. Cortical tension initiates the positive feedback loop between cadherin and F-actin. Qilin Yu 1, William R. Holmes 2, Jean P. Thiery 4 5, Rodney B. Luwor 3, Vijay Rajagopal 1	Theory paper:	