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Drosophila APC2 and APC1 Play Overlapping Roles in Wingless Signaling in the Embryo and Imaginal Discs

Kathryn Akong [a] … Mark Peifer [a, b, c, 1]

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Abstract

The regulation of signal transduction plays a key role in cell fate choices, and its disregulation contributes to oncogenesis. This duality is exemplified by the tumor suppressor APC. Originally identified for its role in colon tumors, APC family members were subsequently shown to negatively regulate Wnt signaling in both development and disease. The analysis of the normal roles of APC proteins is complicated by the presence of two APC family members in flies and mice. Previous work demonstrated that, in some tissues, single mutations in each gene have no effect, raising the question of whether there is functional overlap between the two APCs or whether APC-independent mechanisms of Wnt regulation exist. We addressed this by eliminating the function of both *Drosophila* APC genes simultaneously. We find that APC1 and APC2 play overlapping roles in regulating Wingless signaling in the embryonic epidermis and the imaginal discs. Surprisingly, APC1 function in embryos occurs at levels of expression nearly too low to detect. Further, the overlapping functions exist despite striking differences in the intracellular localization of the two APC family members.

Keywords

APC; β-catenin; Armadillo; Wnt; Wingless; *Drosophila*; tumor suppressor

References

REFERENCES

1 Y. Ahmed, S. Hayashi, A. Levine, E. Wieschaus
Regulation of Armadillo by a *Drosophila* APC inhibits neuronal apoptosis during retinal development
Cell, 93 (1998), pp. 1171-1182
Article PDF (886KB)

2 Y. Ahmed, A. Nouri, E. Wieschaus
Drosophila Apc1 and Apc2 regulate Wingless transduction throughout development
Development, 129 (2002), pp. 1751-1762

3 S.S. Blair

3 S.S. Blair
Shaggy (zeste-white 3) and the formation of supernumerary bristle precursors in the developing wing blade of Drosophila
Dev. Biol., 152 (1992), pp. 263-278
Article PDF (16MB)

4 C.L. Day, T. Alber
Crystal structure of the amino-terminal coiled-coil domain of the APC tumor suppressor
J. Mol. Biol., 301 (2000), pp. 147-156
Article PDF (405KB)

5 R. Fodde, W. Edelmann, K. Yang, C. van Leeuwen, C. Carlson, B. Renault, C. Breukel, E. Alt, M. Lipkin, P.M. Khan
A targeted chain-termination mutation in the mouse Apc gene results in multiple intestinal tumors
Proc. Natl. Acad. Sci. USA, 91 (1994), pp. 8969-8973

6 F. Hamada, Y. Murata, A. Nishida, F. Fujita, Y. Tomoyasu, M. Nakamura, K. Toyoshima, T. Tabata, N. Ueno, T. Akiyama
Identification and characterization of E-APC, a novel Drosophila homologue of the tumour suppressor APC
Genes Cells, 4 (1999), pp. 465-474

7 F. Hamada, M. Bienz
A Drosophila APC tumour suppressor homologue functions in cellular adhesion
Nat. Cell Biol., 4 (2002), pp. 208-213

8 S. Hayashi, B. Rubinfeld, B. Souza, P. Polakis, E. Wieschaus, A. Levine
A *Drosophila* homolog of the tumor suppressor gene adenomatous polyposis coli down-regulates β-catenin but its zygotic expression is not essential for the regulation of Armadillo
Proc. Natl. Acad. Sci. USA, 94 (1997), pp. 242-247

9 B.M. McCartney, H.A. Dierick, C. Kirkpatrick, M.M. Moline, A. Baas, M. Peifer, A. Bejsovec
***Drosophila* APC2 is a cytoskeletally-associated protein that regulates Wingless signaling in the embryonic epidermis**
J. Cell Biol., 146 (1999), pp. 1303-1318

10 B.M. McCartney, D.G. McEwen, E. Grevengoed, P. Maddox, A. Bejsovec, M. Peifer
***Drosophila* APC2 and Armadillo participate in tethering mitotic spindles to cortical actin**
Nat. Cell Biol., 3 (2001), pp. 933-938

11 A.R. Moser, A.R. Shoemaker, C.S. Connelly, L. Clipson, K.A. Gould, C. Luongo, W. Dove, P.H. Siggers, R.L. Gardner
Homozygosity for the Min allele of Apc results in disruption of mouse development prior to gastrulation
Dev. Dyn., 203 (1995), pp. 422-433

12 H. Nakagawa, Y. Murata, K. Koyama, A. Fujiyama, Y. Miyoshi, M. Monden, T. Akiyama, Y. Nakamura
Identification of a brain-specific APC homologue, APCL, and its interaction with beta-catenin
Cancer Res., 58 (1998), pp. 5176-5181

13 M. Peifer, D. Sweeton, M. Casey, E. Wieschaus
***wingless* signal and Zeste-white 3 kinase trigger opposing changes in the intracellular distribution of Armadillo**
Development, 120 (1994), pp. 369-380

14 P. Polakis
Wnt signaling and cancer
Genes Dev., 14 (2000), pp. 1837-1851

15 R. Rosin-Arbesfeld, G. Ihrke, M. Bienz
Actin-dependent membrane association of the APC tumour suppressor in polarized mammalian epithelial cells
EMBO J., 20 (2001), pp. 5929-5939

16 E. Siegfried, T.-B. Chou, N. Perrimon
***wingless* signaling acts through *zeste-white 3*, the *Drosophila* homolog of *glycogen synthase kinase-3*, to regulate *engrailed* and establish cell fate**
Cell, 71 (1992), pp. 1167-1179
Article PDF (10MB)

17 P. Simpson, C. Cateret
A study of *shaggy* reveals spatial domains of expression of *achaete-scute* alleles on the thorax of *Drosophila*
Development, 106 (1989), pp. 57-66

18 N.S. Tolwinski, E. Wieschaus
Armadillo nuclear import is regulated by cytoplasmic anchor Axin and nuclear anchor dTCF/Pan
Development, 128 (2001), pp. 2107-2117

19 J.H. van Es, C. Kirkpatrick, M. van de Wetering, M. Molenaar, A. Miles, J. Kuipers, O. Destrée, M. Peifer, H. Clevers
Identification of APC2, a homologue of the adenomatous polyposis coli tumour suppressor
Curr. Biol., 9 (1999), pp. 105-108

20 J.P. von Kries, G. Winbeck, C. Asbrand, T. Schwarz-Romond, N. Sochnikova, A. Dell'Oro, J. Behrens, W. Birchmeier
Hot spots in beta-catenin for interactions with LEF-1, conductin and APC
Nat. Struct. Biol., 7 (2000), pp. 800-807

21 X. Yu, L. Waltzer, M. Bienz
A new Drosophila APC homologue associated with adhesive zones of epithelial cells
Nat. Cell Biol., 1 (1999), pp. 144-151

1 To whom correspondence should be addressed. Fax: (919) 962-1625. E-mail: peifer@unc.edu.