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Metastatic teamwork

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Oncogenes such as Ras are thought to be involved in both tumorigenesis and metastasis, but the specific involvement of Ras in tumor progression has been difficult to identify, as the effects of Ras in cell culture depend greatly upon the cell line used. In the October 09 Sciencexpress, Raymond A. Pagliarini and Tian Xu at Yale University School of Medicine show that Ras mutations and genetic alterations promoting noninvasive tumor growth have a synergistic effect in the development of metastatic behavior (*Science*, DOI:10.1126/science.1088474, October 09, 2003).

Pagliarini and Xu designed a genetic screen in *Drosophila* to interrogate the genome for mutations that caused noninvasive tumors of the eye disc to invade neighboring or distant tissues. They observed that cooperation between oncogenic RasV12 expression and inactivation of any one of a number of genes affecting cell polarity led to metastatic behavior, including basement membrane degradation, loss of E-cadherin expression, migration, invasion, and secondary tumor formation. In addition, the authors showed that inactivation of cell polarity genes could not drive metastatic behavior alone or in combination with other tumor-initiating alterations.

"[This] may provide an explanation for the different metastatic potential observed in tumors of distinctive origins. It will be greatly informative using the advantages of *Drosophila* genetics to analyze the specific targets of RasV12 in metastatic cells, to identify other genes that cooperate with RasV12 or other oncogenic alterations in promoting metastasis, and to elucidate the cellular processes that go awry during metastatic progression," conclude the authors.

References

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