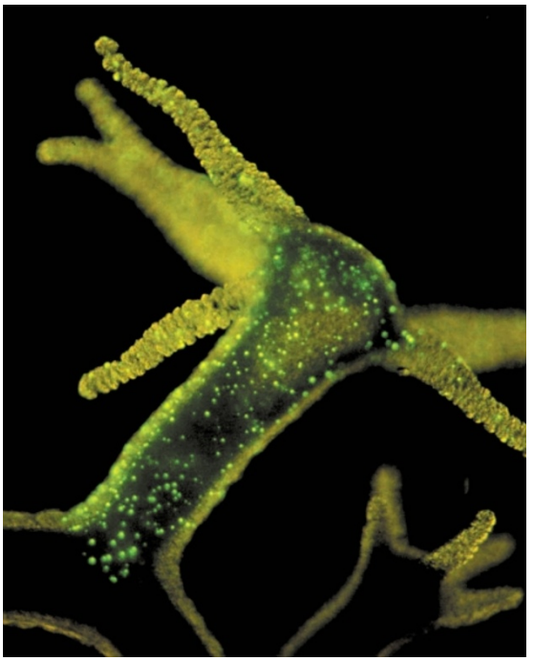
DEVELOPMENTAL BIOLOGY

Headless Hydra get Heady



Hydra's remarkable ability to regenerate lost body parts means that these simple metazoans, unlike their more complex relatives, have morphogenic mechanisms that are continuously active throughout life. Like other cnidarians, Hydra are radially symmetric and have only one body axis — the apical–basal axis. The head and foot at the opposite ends of this axis are Hydra's only differentiated body parts. Hydra's cells continuously proliferate and are displaced towards these structures, where they differentiate to replace lost cells. The molecular mechanisms that control this cell proliferation and differentiation remain largely unknown, but a newly discovered, 23-amino-acid peptide, HEADY, sheds light on this and on how Hydra specify a head.

HEADY was identified in a screen for differentially expressed RNAs in dissociated Hydra cells undergoing reaggregation and *de novo* axis formation. *HEADY* RNA is only weakly expressed in intact Hydra but is transiently upregulated on removal of their heads, when it accumulates at its highest levels in the apical-most cells. This induction remains unchanged regardless of how far along the anterior–posterior axis decapitation takes place, which is unusual because the induction of other head-differentiation genes is delayed by basally positioned decapitations. Furthermore, HEADY transcripts and protein do not localize to the intact adult head. These results gave the first indication that HEADY is not involved in head differentiation but in the early specificiation of apical cell fate.

RNA interference experiments confirmed that HEADY is required for specifying apical fate and for head regeneration. So HEADY is necessary, but is it sufficient for apical specification? To answer this, the authors grafted small pieces of gastric tissue from a HEADY-treated Hydra into the same gastric region of an untreated Hydra. The result was that a secondary axis with head morphology often formed from the HEADY-treated grafts —the picture shows such a graft with HEADY labelled in green (image courtesy of the authors, reproduced with permission, CSH Press, ©2000). These and other data confirmed that HEADY is necessary and sufficient for specifying and organizing the apical axis. But how this transiently activated, small peptide fits into current models of Hydra's continuously active morphogen gradients remains to be resolved.

Jane Alfred

References and links

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WEB SITE The cnidaria homepage

CANCER

The trouble with smoking

Among the 3,000 mutagens in tobacco smoke is benzo[*a*]pyrene diol epoxide (BPDE). This compound forms bulky adducts on G residues in DNA, leading mainly to G→T mutations, which are much more common in lung cancer than in other cancers. Furthermore, in the *p53* (*TP53*) oncogene, BPDE interacts preferentially with the specific G residues that are frequently mutated in the lung cancers of smokers. So, BPDE stands convicted — an open and shut case — that is, until Rodin and Rodin reopened it.

In their most recent work, the authors examined a weak link in the BPDE story — the *p53* mutation spectrum in lung cancers from non-smokers. This has been investigated previously, but with small sample numbers. Rodin and Rodin do report evidence for an overall difference in the *p53* mutation spectrum between smokers and non-smokers. However, this difference can be accounted for by DNA strand-specific differences, which could reflect the activities of strand-specific DNA repair mechanisms in smokers versus non-smokers. They find no evidence that G→T mutations arise more frequently in smoke-exposed versus non-exposed cancer tissue. And, strikingly, one particular G→T mutation is prevalent not only in lung cancer but also in other tumours such as colon cancer, suggesting that this mutation is found frequently because it is more tumorigenic than other mutations — not because it arises more often.

Rodin and Rodin conclude that physiological stresses in smoke-exposed tissue lead to selection pressures on cells that, in turn, affect the type of mutations that are identified in lung cancers. So mutagenesis by BPDE seems less important, although it might still have a role in lung cancer — after all, there's no smoke without fire.

Mark Patterson

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ENCYCLOPEDIA OF LIFE SCIENCES DNA damage
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