ner leaflet of the plasma membrane (see figure) (*15*, *17*). Palmitoylation of yeast Ras2p is required for membrane binding and glucose signaling (*18*). So why farnesylate H-Ras if palmitoylation is required for membrane binding? Perhaps palmitoylation alone is not sufficient to anchor Ras to membranes. This notion has not been tested directly because in cells farnesylation is a prerequisite for palmitoylation (*6*, *7*). Palmitoylation of H-Ras may occur only in plasma membranes by a putative palmitoyltransferase that is bound to the plasma membrane. Farnesylation may bring a finite amount of H-Ras to all cellular membranes, and palmitoylation may then be required to trap it in the plasma membrane. Our understanding of the enzymology of protein palmitoylation has only just begun (*19*); however, we do know that H-Ras palmitoylation, like G protein α-subunit palmitoylation, is a reversible event and so may regulate signal transduction (*20*). Some transfection studies have led to the suggestion that H-Ras palmitoylation is not required for cellular transformation (*6*), but studies in *Xenopus* oocytes with more physiological amounts of H-Ras indicate that Ras activates oocytes very poorly, if at all, unless it is palmitoylated (*16*).

In addition to palmitoylation, prenylated proteins are subject to COOH-terminal proteolysis and methylation. Are these modifications necessary for function of the protein? In this context, the new studies in yeast by Boyartchuk (*4*) are providing some insights. Two genes, *RCE1* and *AFC1*, are responsible for COOH-terminal proteolysis of prenylated proteins in yeast. In yeast that lack these functional proteases, Ras2p, which normally localizes to the plasma membrane, mislocalizes to the interior of the cell, at least when overexpressed. Loss of proteolysis reduces but does not eliminate Ras2p function in yeast expressing either high or endogenous levels of the protein. In *Xenopus*, proteolysis and methylation are required for palmitoylation, membrane binding, and the function of Ras (*21*). These studies suggest that the prenyl protein–specific protease and methyltransferase, like FTase, may be good targets for antioncogenic therapeutics, especially because yeast lacking prenyl protein–specific protease activity are viable.

References

1. J. A. Glomset, M. H. Gelb, C. C. Farnsworth, *Trends Biochem. Sci.* **15**, 139 (1990).
2. F. L. Zhang and P. J. Casey, *Annu. Rev. Biochem.* **65**, 241 (1996).
3. H.-W. Park, S. R. Boduluri, J. F. Moomaw, P. J. Casey, L. S. Beese, *Science* **275**, 1800 (1997).
4. V. L. Boyartchuk, M. N. Ashby, J. Rine, *ibid.*, p. 1796.
5. H. K. Yamane *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **87**, 5868 (1990); S. M. Mumby, P. J. Casey, A. G. Gilman, S. Gutowski, P. C. Sternweis, *ibid.*, p. 5873; R. K. Lai, D. Perez-Sala, F. J. Canada, R. R. Rando, *ibid.*, p. 7673.
6. J. F. Hancock, A. I. Magee, J. E. Childs, C. J. Marshall, *Cell* **57**, 1167 (1989).
7. P. J. Casey, P. A. Solski, C. J. Der, J. E. Buss, *Proc. Natl. Acad. Sci. U.S.A.* **86**, 8323 (1989); W. E. Schafer *et al.*, *Science* **245**, 379 (1989).
8. K. S. Koblan *et al.*, *Biochem. Soc. Trans.* **24**, 688 (1996).
9. Y. Reiss, J. L. Goldstein, M. C. Seabra, P. J. Casey, M. S. Brown, *Cell* **62**, 81 (1990).
10. K. Yokoyama and M. H. Gelb, *J. Biol. Chem.* **268**, 4055 (1993); J. F. Moomaw and P. J. Casey, *ibid.* **267**, 17438 (1992); M. C. Seabra, J. L. Goldstein, T. C. Sudhof, M. S. Brown, *ibid.*, p. 14497.
11. K. Yokoyama, K. Zimmerman, J. Scholten, M. H. Gelb, *ibid.* **272**, 3944 (1997).
12. J. A. Glomset and C. C. Farnsworth, *Annu. Rev. Cell Biol.* **10**, 181 (1994).
13. C. C. Farnsworth *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **88**, 6196 (1991).
14. M. H. Gelb and O. G. Berg, unpublished data.
15. J. F. Hancock, K. Cadwallader, C. J. Marshall, *EMBO J.* **10**, 641 (1991).
16. T. Dudler and M. H. Gelb, *J. Biol. Chem.* **271**, 11541 (1996).
17. F. Ghomashchi, X. Zhang, M. H. Gelb, *Biochemistry* **34**, 11910 (1995).
18. S. Bhattacharya, L. Chen, J. R. Broach, S. Powers, *Proc. Natl. Acad. Sci. U.S.A.* **92**, 2984 (1995).
19. L. Liu, T. Dudler, M. H. Gelb, *J. Biol. Chem.*, in press.
20. P. T. Wilson and H. R. Bourne, *ibid.* **270**, 9667 (1995).
21. T. Dudler and M. H. Gelb, unpublished data.

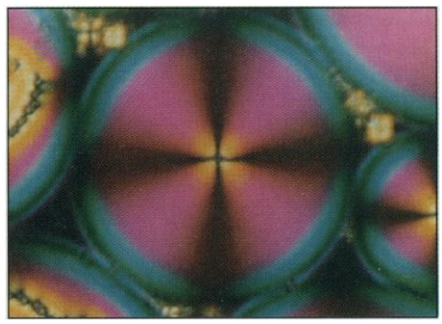
LIQUID CRYSTALS

Nematic Emulsions

J. F. Joanny

Emulsions are dispersions of liquid droplets, hundreds of nanometers to a micrometer in size, in a continuous liquid solvent. A typical example would be a dispersion of oil droplets in water (oil-in-water emulsion) or a dispersion of water droplets in an oil (water-in-oil emulsion). Many kinds of emulsions are encountered in the food or cosmetics industries, so understanding their behavior is of both scientific and technological importance. In general, emulsions are only metastable, and the droplets tend to coalesce. A large part of the research on emulsions (*1*) is thus devoted to the stability of the dispersion, to the monitoring of the interactions between droplets, and to the tailoring of surface active agents that prevent the rupture of a solvent film between two droplets. Emulsions stable over days or more are quite common. More recent work (*2*) deals with model emulsions with a monodisperse droplet size distribution, with the packing of droplets in a dense emulsion, or with emulsions having specific properties. An example would be magnetic emulsions, where the droplets are made of a magnetic fluid. Under the action of a magnetic field, the ferrofluid becomes polarized and each droplet acquires a dipole moment parallel to the field. The attractive interactions between the dipole moments induces the formation of chains of droplets.

On page 1770 of this issue, Poulin *et al.* (*3*) report a new type of emulsion in which the continuous solvent phase is not an isotropic liquid but a nematic liquid crystal, the dispersed phase being water droplets. The nematic liquid-crystal order parameter is its director field, which gives the local average orientation of the molecules. At the surface of each water droplet, the nematic director has a preferential orientation, and thus, the presence of the water droplets perturbs the nematic ordering. The distortion of the nematic field costs elastic energy and induces an interaction between the droplets. The nematic interaction between droplets depends not only on the bending constants of the nematic liquid crystal that measure the energy cost of the director distortion but also on the boundary conditions given by the orientation of the director at the surface of each droplet and at the external surface of the nematic liquid (which imposes the director field in the absence of the water droplets). A wide variety of behaviors can be expected when all of these parameters are varied.



Stalking the wild hedgehog. Viewed between crossed polarizers, the water droplets dispersed in liquid-crystal solvent exhibit unusual colloidal interactions. Black regions are water; colored regions are nematic liquid crystal. The orientation of the liquid crystal on the water droplet leads to the formation of topological defects called hedgehogs. A hedgehog (hyperbolic hedgehog) is seen in between two neighboring water droplets. [Reprinted from Poulin *et al.* (*3*)]

The author is at the Institut Charles Sadron, 6 rue Boussingault, 67083 Strasbourg, France. E-mail: joanny@janus.u-strasb.fr

The geometry chosen by Poulin *et al.* (*3*) is that of a multiple emulsion: Large droplets of a nematic liquid (50 μm across) are dispersed in water, and small water droplets are dispersed in these large droplets. The molecular interactions at the interface between water and the liquid crystal (in the presence of a surfactant) impose an orientation of the nematic molecules perpendicular to the interface. If there is only one water droplet, the equilibrium position of the droplet is at the center of the nematic drop, and the nematic director is radial. The central water droplet then acts as a defect in the director field called a (positive) hedgehog defect (*4*). This geometry is beautifully confirmed by optical microscopy images (see figure). When more water droplets are contained in the liquid-crystalline drop, these droplets form chains, similarly to what is observed with magnetic emulsions. Topological considerations impose constraints on the number of defects in a sphere where the nematic director is orthogonal to the surface. If each water droplet is associated with a positive hedgehog defect, one way to satisfy the topological constraints is to create for each of the droplets except the first a hyperbolic (negative) hedgehog defect. Each droplet is thus associated with a dipole of defects (positive and negative hedgehogs). A very elegant analogy with electrostatic dipoles shows that the interaction between these dipoles is attractive and leads to chain formation. This picture is confirmed by observation, where the hyperbolic hedgehogs are seen as smaller dots in between the water droplets.

This spectacular experiment takes advantage of the geometry of the multiple emulsion to impose a well-defined defect texture on the liquid-crystalline drop. It is the interaction between defects that drives the chain formation. It opens the way to a whole new field of emulsions with nonisotropic fluids. From the emulsion point of view, it involves a whole new class of systems showing nonclassical interactions and nonclassical structures [for example, chaining, as in Poulin *et al.* (*3*)]. From the liquid-crystal point of view, it provides a controlled and well-defined way to produce and study various kinds of point defects, their stability, and their interactions.

References and Notes

1. A. W. Adamson, *Physical Chemistry of Surfaces* (Wiley, New York, 1996).
2. J. Bibette, *J. Colloid Interface Sci.* **147**, 474 (1991); F. L. Calderon *et al.*, *Phys. Rev. Lett.* **72**, 2959 (1994).
3. P. Poulin *et al.*, *Science* **275**, 1770 (1997).
4. Hedgehogs are point defects in a nematic liquid crystal where all directions are swept out on the unit sphere. The simplest type of hedgehog is the radial hedgehog, in which the director points radially to the defect center. For a discussion of defects in nematic liquid crystals see: J. Prost and P. G. de Gennes, *The Physics of Liquid Crystals* (Clarendon, Oxford, 1993).

CANCER

β-Catenin as Oncogene: The Smoking Gun

Mark Peifer

Science and detective fiction share many features: a mysterious event, suspects with motive and opportunity, and a collection of evidence. The best cases end with a smoking gun, clinching the guilt of a suspect. This issue of *Science* contains three such smoking guns (*1*, *2*), on pages 1784, 1787, and 1790, firmly establishing β-catenin as an accomplice in causing colon cancer and as a strong suspect in melanoma. As in many crimes, however, β-catenin did not act alone but with a set of partners.

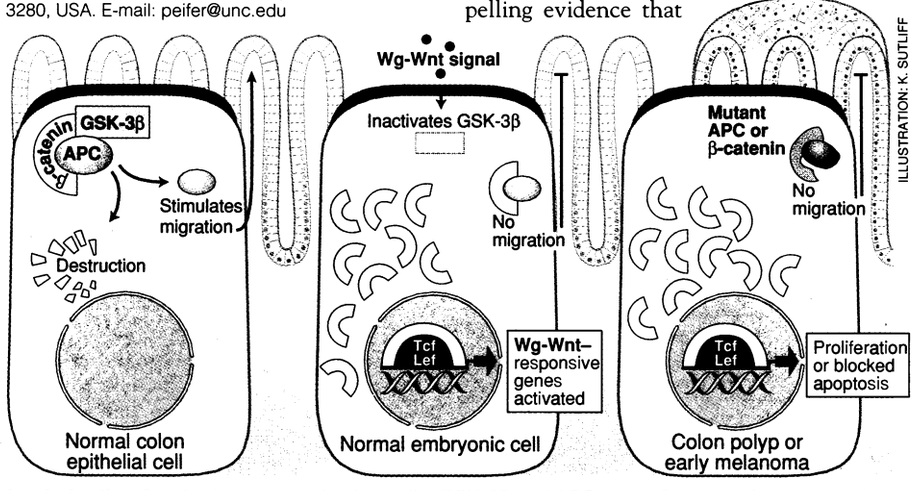
An enhanced version of this Perspective, with live links, can be seen in *Science* Online on the Web at http://www.sciencemag.org/

Suspicion initially fell on β-catenin through association with a known criminal (*3*). Adenomatous polyposis coli (APC), familial predisposition to colon cancer, is caused by *APC* mutations. *APC* encodes a large multidomain protein that binds β-catenin. APC, together with the serine-threonine glycogen synthase kinase (GSK)–3β, regulates the levels of free β-catenin. Normally these levels are quite low, as APC and GSK bind β-catenin, targeting it for destruction. However, in *APC* mutant colon cells, degradation is disrupted, and levels of free β-catenin rise dramatically. Thus β-catenin is a suspect as the cause of the benign colon polyps resulting from *APC* mutations.

β-Catenin and its homolog Armadillo in the fruitfly *Drosophila* are multifunctional proteins (*4*): Both are key components of cell-cell adhesive junctions and also participate in transduction of Wingless-Wnt cell-cell signals. Wingless-Wnt signals direct many key developmental decisions, regulating anterior-posterior and dorsal-ventral pattern in both flies and vertebrates. β-Catenin–Armadillo is a key effector of signal transduction. In the absence of signal, levels of free β-catenin–Armadillo are low; the Wingless-Wnt signal stabilizes free β-catenin–Armadillo.

Until recently, the trail ended there. A breakthrough came with the discovery of a new family of protein partners for β-catenin, DNA binding proteins of the T cell factor–lymphoid enhancer factor (Tcf-Lef) family (*5*). These proteins bind to β-catenin in vivo and when misexpressed in *Xenopus* eggs alter dorsal-ventral polarity, suggesting a possible role in Wnt signaling. Extending this work in *Drosophila*, three groups using different approaches provided compelling evidence that

The author is in the Department of Biology, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599–3280, USA. E-mail: peifer@unc.edu



Incriminating β-catenin. In normal colon cells, GSK-3β and APC target β-catenin for degradation. In both normal embryonic cells and colon or melanoma cells, β-catenin is not degraded and accumulates, binding to Tcf-Lef and triggering gene expression.