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

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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

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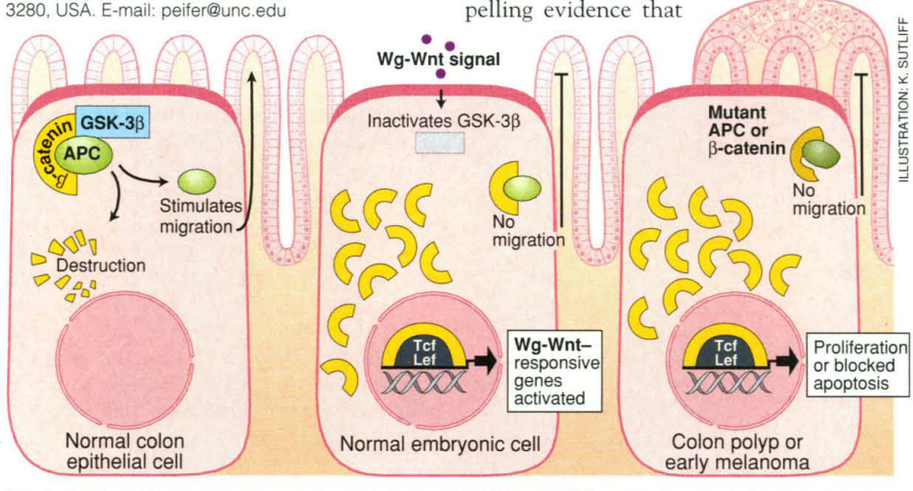

Incriminating β-catenin. In normal colon cells, GSK-3β and APC target β-catenin for degradation. In both normal embryonic cells and colon or melanoma cells, β-catenin is not degraded and accumulates, binding to Tcf-Lef and triggering gene expression.

a fly Tcf family member, *dTcf* (also called *pangolin*), plays a key role in transduction of Wingless signal in vivo (6). Loss-of-function mutations in *dTcf* disrupt normal anterior-posterior patterning, and epistasis analysis places *dTcf* downstream of *armadillo* in the Wingless signal transduction pathway. Mutations in *dTcf* block expression of Wingless-responsive genes, and analysis of a Wingless-response element revealed an essential dTcf binding site. dTcf alone is inactive, even though it binds DNA. The active transcription factor is a bipartite complex, with dTcf contributing the DNA binding domain and Armadillo a potential transactivation domain.

This brings us back to the scene of the crime, suggesting that β-catenin cooperates with Tcf family proteins to alter gene expression in human colon. This thesis was tested and extended in the three reports in this issue. In colon cancer cell lines (*1*), and surprisingly also in many melanoma cell lines (*2*), high levels of free β-catenin drive formation of complexes with Tcf-4 or Lef-1, activating gene expression. The genes activated may include those stimulating cell proliferation or inhibiting apoptosis. There are at least two ways to increase levels of free β-catenin. The first is due to the previously described mutations in APC. The second is to mutate β-catenin itself, altering an NH_2-terminal domain that down-regulates β-catenin stability in cell lines (*7*) and up-regulates Wg-Wnt signaling ability in vivo (*6*, *8*). Thus β-catenin itself is an oncogene.

These data firmly establish APC as a negative regulator of β-catenin signaling. However, APC likely has additional abilities. It localizes in vivo to the end of cell processes, clustering at the tips of microtubule bundles (*9*). This suggests that APC regulates migration by regulation of the cytoskeleton. This model was tested by manipulating APC activity in cultured epithelial cells. APC promotes cell migration and regulates cell adhesion both of individual cells and of cells cooperating to form epithelial tubules (*10*). This is consistent with the behavior of normal colon epithelial cells, which migrate from crypt to villus, where they die and are sloughed off. These data also suggest that free β-catenin prevents APC from stimulating migration. The APC–β-catenin complex appears to be a binary switch. In the absence of outside input, APC mediates β-catenin degradation and promotes cell migration. In contrast, in the presence of Wg-Wnt signal, β-catenin is stabilized (perhaps by inactivation of GSK kinase). This inactivates APC, down-regulating migration and promoting formation of β-catenin–Tcf complexes, thereby altering gene expression. Mutations in either APC or β-catenin mimic Wg-Wnt signaling, stimulating proliferation or antagonizing apoptosis.

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PHYSICS

Atomic Parity Violation and the Nuclear Anapole Moment

W. C. Haxton

Until 40 years ago, physicists had assumed that the fundamental forces of nature did not distinguish between left and right. That is, it was believed that the laws of physics in a mirror-symmetric universe would be the same as in ours. Then in 1957, following a suggestion by Lee and Yang (*1*), experimenters discovered that the weak nuclear force, which is responsible for beta decay, violated this conservation of parity (*2*). Shortly thereafter, Vaks and Zeldovich (*3*) independently noted that particles could therefore have parity-violating couplings to the electromagnetic field. Such "anapole moments"—in the more modern language of today's standard model—would arise from very small effects associated with weak forces among, for example, the quarks within a nucleon or nucleus. On page 1759 of this issue, the first definitive measurement of an anapole moment is reported by Wood *et al.* (*4*).

Some nuclear interactions with the electromagnetic field are quite familiar. As a charged object, the nucleus accelerates when an electric field is applied. If the nucleus has a nonzero spin **I**, it also has an interaction with an applied magnetic field **B** of the form $\mu\mathbf{B}\cdot\mathbf{I}$, where μ is the magnetic moment. More exotic interactions can arise when symmetries preserved by electromagnetism are violated by other, weaker forces. Perhaps the best known of these interactions is that of the electric dipole moment d (which can be visualized as an asymmetric distribution of charge along a particle's spin axis) with an electromagnetic field. A particle with an intrinsic dipole moment will experience an interaction $d\mathbf{E}\cdot\mathbf{I}$ when placed in an electric field **E**. Electric dipole moments arise only if the laws of physics are asymmetric under both parity inversion and time reversal. Studies of the decays of the long-lived neutral K meson have shown that this combination of symmetries is violated, although only weakly. Consequently, despite considerable effort, no one has succeeded in detecting a nonzero nuclear electric dipole moment.

This had also been the case for the anapole moment, which can be generated by parity violation in the weak interaction but does not require time reversal violation. This moment has a number of curious properties. It vanishes when probed by real photons (that is, photons satisfying the usual energy-momentum relation). Thus, the anapole moment of a nucleus, for example, can be measured only in processes where virtual photons are exchanged with some interacting particle, such as an atomic electron. The resulting electron-nucleus interaction is point-like: The atomic cloud feels the nuclear anapole moment only to the extent that the wave functions of the orbiting electrons penetrate the nucleus. Although the exchanged photon is electric dipole in nature, its absorption by the nucleus takes place through parity-violating components of the nuclear wave function. The combination of the usual nuclear current and the parity violation produces a current configuration similar to a winding about a torus.

Exquisitely precise (1%) measurements of atomic parity violation have been made in recent years. It is now widely recognized that these efforts are important not only as tests of the standard electroweak model, determining parameters, such as the weak mixing angle θ_W, but also as crucial searches for new physics beyond the standard model, complementing the efforts at high-energy colliders. The dominant contribution to atomic parity violation comes from direct Z_0 exchange between electrons and a nucleus, with the elec-

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