February 22, 2005 | vol. 102 | no. 8 | 2673–3170

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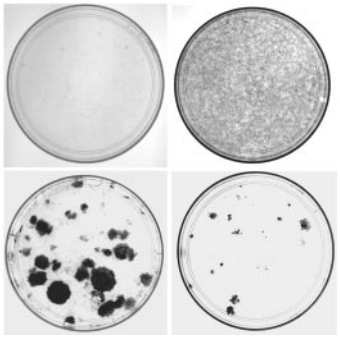
PNAS
Proceedings of the National Academy of Sciences of the United States of America
www.pnas.org

BIOCHEMISTRY

PTEN C-terminal domain suppresses transformation

According to Koichi Okumura *et al.*, the C-terminal domain of the PTEN (phosphatase and tensin homologue) tumor suppressor protein inhibits transformation by the oncogenic MSP58 protein. Normally, PTEN suppresses tumorigenesis by down-regulating the PI3K pathway and p53 regulation via the phosphatase activity of its catalytic domain. However, the C-terminal region of PTEN, which helps to stabilize the protein, is mutated in a variety of human cancers, suggesting an additional mechanism by which PTEN regulates transformation. To elucidate the function of the PTEN C-terminal region, the authors used a yeast two-hybrid screen to identify PTEN-interacting proteins. The researchers found that the PTEN C-terminal domain physically interacts with the forkhead-associated (FHA) domain of the oncogenic MSP58 protein, and this interaction requires PTEN threonine 366. MSP58 transformed PTEN-deficient mouse embryonic fibroblasts, but reintroducing wild-type PTEN dramatically reduced the number of transformed foci. Furthermore, a PTEN mutant clone with an inactive catalytic domain (G129R) was still able to suppress MSP58 oncogenicity. These results demonstrate that the PTEN C-terminal region inhibits the transformational potential of MSP58, and this attenuation does not require PTEN catalytic activity. The authors propose that PTEN suppression of MSP58 transformation through protein–protein interactions represents a previously unidentified ability of PTEN to interfere with tumorigenesis.



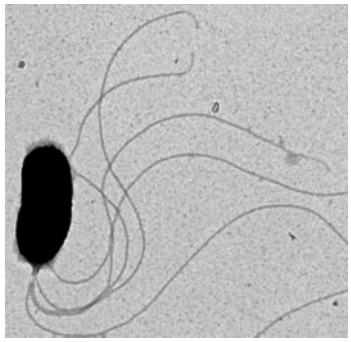
PTEN inhibits transformation by MSP58.

"Cellular transformation by the MSP58 oncogene is inhibited by its physical interaction with the PTEN tumor suppressor" by Koichi Okumura, Mujun Zhao, Ronald A. DePinho, Frank B. Furnari, and Webster K. Cavenee (see pages 2703–2706)

MICROBIOLOGY

Illuminating genes in *Vibrio*

The genome of the symbiotic marine bacterium *Vibrio fischeri*, known for producing luminescence in the light-emitting organs of various fish and squid, bears similarities to its pathogenic relatives, including *Vibrio cholerae*. Edward Ruby *et al.* shotgun sequenced the ES114 strain of *V. fischeri* and compared it with the genomes of *V. cholerae*, *Vibrio parahaemolyticus*, and *Vibrio vulnificus*. The comparison reveals genetic mainstays of the four *Vibrio* genomes and characteristics that differ between beneficial and pathogenic bacteria. *V. fischeri* has several noteworthy traits: the lowest G+C content of the 27 known species of Vibrionaceae; a 2-fold greater percentage of unique genes residing on chromosome II than *V. cholerae*; and a cholera-toxin (CTX) phage-like gene cluster on chromosome II. Although *V. fischeri* is not known to be pathogenic, its genome harbors homologues of *Vibrio* genes that may have toxin activity such as CTX phage-encoded genes, zona occludins toxin (zot), accessory cholera enterotoxin (ace), and repeats in structural toxins (RTX). The authors suggest that the activities of these proteins may be beneficial or produce a pathogenic outcome depending on the host and the tissue in which each *Vibrio* species resides.



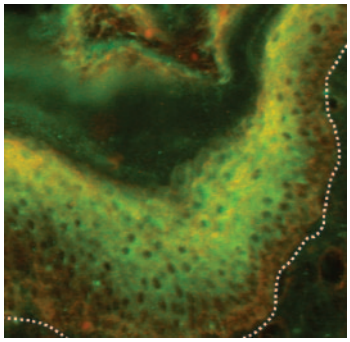
Vibrio fischeri.

"Complete genome sequence of Vibrio fischeri*: A symbiotic bacterium with pathogenic congeners" by E. G. Ruby, M. Urbanowski, J. Campbell, A. Dunn, M. Faini, R. Gunsalus, P. Lostroh, C. Lupp, J. McCann, D. Millikan, A. Schaefer, E. Stabb, A. Stevens, K. Visick, C. Whistler, and E. P. Greenberg* (see pages 3004–3009)

PHARMACOLOGY

CB_2 receptor activation inhibits pain via β-endorphin release

CB_2 cannabinoid receptor activation inhibits acute, inflammatory, and neuropathic pain without causing central nervous system effects, but the mechanism of CB_2 receptor-mediated antinociception (pain inhibition) is not known. Previous research has shown that keratinocyte skin cells express CB_2 receptors and contain opioid peptides, presumably to activate opioid receptors on primary afferent neurons to inhibit pain. These findings prompted Mohab Ibrahim *et al.* to hypothesize that keratinocytes are responsible for the antinociceptive effects of CB_2 receptor activation. The researchers demonstrated that subcutaneous injection of either a CB_2 receptor agonist or the opioid β-endorphin increased paw withdrawal delay to thermal pain stimulus. However, injection of antiserum to β-endorphin or the opioid receptor antagonist naxalone prevented CB_2 receptor agonist-mediated antinociception. The CB_2 receptor agonist did not inhibit nociception in μ-opioid receptor-deficient mice. In addition, the CB_2 receptor agonist stimulated β-endorphin release from rat skin and human keratinocytes *in vitro*, whereas a CB_2 receptor antagonist blocked β-endorphin release. These data suggest that CB_2 receptor activation on keratinocytes stimulates release of β-endorphin, which acts on local neuronal μ-opioid receptors to inhibit nociception. The authors propose that CB_2 receptor agonists are promising candidates for the treatment of pain.



CB_2 receptor-mediated pain inhibition.

"CB_2 cannabinoid receptor activation produces antinociception by stimulating peripheral release of endogenous opioids" by Mohab M. Ibrahim, Frank Porreca, Josephine Lai, Phillip J. Albrecht, Frank L. Rice, Alla Khodorova, Gudarz Davar, Alexandros Makriyannis, Todd W. Vanderah, Heriberto P. Mata, and T. Philip Malan, Jr. (see pages 3093–3098)

PHYSIOLOGY

Peripheral pathways of circadian rhythms

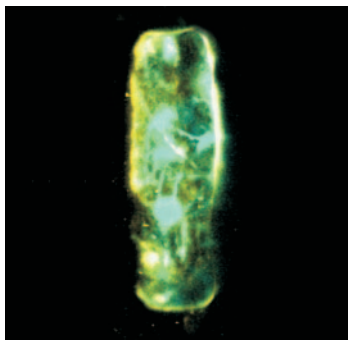
Nonneural signals in mice appear to be adequate to maintain circadian rhythms of clock gene expression in liver and kidney, but not in heart, spleen, or skeletal muscle, according to Hongnian Guo *et al*. Circadian rhythms are expressed in a wide variety of peripheral organs and are known to be controlled by the suprachiasmatic nucleus (SCN) of the hypothalamus. However, the pathways with which the SCN controls the peripheral organs are unclear. The authors used parabiosis (surgical conjoining of two organisms) techniques in mice, such that in each experimental pair, one mouse with its SCN removed was conjoined with another mouse with its SCN intact. Nine pairs of SCN-lesioned and SCN-intact mice and eight pairs of SCN-intact mice were included in the study. Northern blots were used to measure the abundance of transcripts of *mPer1*, *mPer2*, and *mBmal1*, which are critical to the generation of circadian rhythms. The results showed that SCN-driven behavioral or hormonal cues may ensure persistence of circadian rhythms of *mPer1*, *mPer2*, or *mBmal1* expression in liver and kidney. By contrast, circadian rhythms of clock gene expression were not maintained in spleen, heart, or skeletal muscle of the same SCN-lesioned mice parabiosed to SCN-intact partners. These findings suggest that SCN-dependent neural input is required for these tissues.

"Differential control of peripheral circadian rhythms by suprachiasmatic-dependent neural signals" by Hongnian Guo, Judy McKinley Brewer, Ameya Champhekar, Ruth B. S. Harris, and Eric L. Bittman (see pages 3111–3116)

PLANT BIOLOGY

Pathogen portals in plants and animals

Biologists have discovered that pathogens of plants and animals use similar molecular portals for entry into host cells. Riyaz Bhat *et al.* tracked the cellular movement of the plant protein mildew resistance locus O (MLO), which is coopted by a widespread fungal parasite for host cell invasion. The authors found that fluorescently tagged MLO migrated in the plant cell membrane and concentrated in an area where fungi attached themselves to the cell's outer surface. This directed movement to pathogen entry sites was also seen for an intracellular plant protein, calmodulin, which interacts with and up-regulates MLO. The authors found that the calmodulin/MLO complex forms part of a microdomain in the plasma membrane that is similar to microdomains formed by animal cells upon assault by pathogenic bacteria. Clustering of lipid rafts is believed to drive the formation of these pathogen-triggered microdomains. A third plant protein, syntaxin, also becomes recruited to the fungus-induced pathogen portal. Unlike MLO and calmodulin, syntaxin directs a vesicle-associated defense response to the intruder at the cell periphery, leading to localized discharge of antifungal vesicle cargo. Thus, plant cells appear to have invented a strategy that aims to eliminate infective agents at pathogen portals before host cell entry.



Plant pathogen portals.

"Recruitment and interaction dynamics of plant penetration resistance components in a plasma membrane microdomain" by Riyaz A. Bhat, Marco Miklis, Elmon Schmelzer, Paul Schulze-Lefert, and Ralph Panstruga (see pages 3135–3140)