IMMUNOLOGY

Gut Reaction

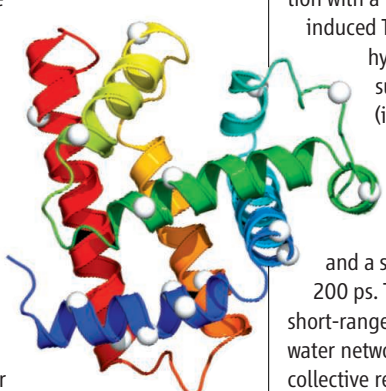
The intestine, as well as providing the wherewithal to digest food, is a dynamic immunological site—and indeed, is the largest in the body. The oral delivery of vaccines has the potential to provide an extremely effective means of immunizing against infection. However, to improve on the few currently successful oral vaccines, new approaches will be needed to deliver antigens selectively to the relevant intestine-situated immune cells. A distinct class of epithelial cells, called M cells, have been seen as ideal targets for some time, because they are specialists in the transfer of antigens from the lumen of the gut to the underlying mucosa. By attaching antigens to a monoclonal antibody that is able to latch selectively onto M cells, Nochi *et al*. achieved specific delivery to these cells. When compared with antigens that had been coupled to nonspecific immunoglobulin, oral administration of the antigen-conjugated monoclonal led to an increase in elicited antibodies and protection from a normally lethal bacterial challenge. The M-cell specificity of the monoclonal was due to a difference associated with a carbohydrate moiety present on epithelial cells, suggesting that looking for similar targets on human M cells might be beneficial in human vaccine development. — SJS

J. Exp. Med. 10.1084/jem.20070607 (2007).

BIOPHYSICS

Shining Light on Hydration

Proteins derive a substantial degree of their form and function from the presence or absence of water molecules swarming about the amino acids in various parts of the structure. The hydration process is highly dynamic, and ultrafast laser spectroscopy has recently proved useful in exploring the detailed interactions between protein and solvent. In this vein, Zhang *et al.* undertook a systematic study of water motion in distinct regions of the eight helices constituting the native conformation of apomyoglobin, as well as the molten globular form of the protein accessed at low pH. To introduce local probes, they prepared a series of mutants with tryptophan (Trp) residues substituted at 16 different sites; excitation with a femtosecond ultraviolet pulse then induced Trp fluorescence that varied with the hydration environment. Increased exposure to water led to a higher Stokes shift (i.e., longer wavelength emission), as well as a shorter fluorescence lifetime. In general, the emission decays were biexponential, with a fast time constant that ranged from ~1 to 8 ps and a slow component ranging from ~20 to 200 ps. The fast process could be attributed to short-range fluctuations of the hydrogen-bonded water network, and the slower process to more collective restructuring as exchange with bulk solvent starts to come into play. — JSY



Mutated sites (white) in myoglobin.

Proc. Natl. Acad. Sci. U.S.A. **104**, 18461 (2007).

CHEMISTRY

Triangle Triumph

How does an extra proton latch onto an ethylene? If one thinks about the $H_2C{=}CH_2$ molecule grasping H^+, the logical structure would seem to be a triangle with the proton shared between the two carbons, because that's where the electrons doing the grasping are already mostly confined. On the other hand, the same cation should result from stripping H^- off ethane ($H_3C\text{-}CH_3$), and in that context it seems as though the extra H should stay on one carbon or the other, in a more classical bonding arrangement. Chemists have long puzzled over this question, and the highest-level quantum mechanical calculations favor the triangular H-sharing structure. However, direct experimental evidence has been elusive. Andrei *et al.* have now measured the vibrational spectrum of the $C_2H_5^+$ cation in gas phase and confirmed the nonclassical geometry. The experiment relied on a highly sensitive technique in which an argon atom loosely bound to the cation is ejected (and the naked cation then mass-detected) by the energy dissipated when C-H

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Sniffing mice.

ECOLOGY

Nothing to Sniff at…

In many animals, the major histocompatibility complex (MHC) has been thought to be responsible for the generation of signals that inform the status of relationship among individuals. The similarity of MHC complexes, which is detectable by scent, were believed to be a means by which mice, and potentially other mammals, recognize and avoid breeding with close relatives. However, Cheetham *et al.* now find that female mice could not differentiate between individuals that differed solely on the basis of their MHC type. Instead, the mice showed preferences between a choice of half-sibling males on the basis of direct contact with another set of species-specific variable markers—their major urinary proteins. This suggests that the factors used by many animals to recognize specific individuals may not in fact be controlled by their MHC profile. — LMZ

Curr. Biol. **17**, 1771 (2007).

CREDITS (TOP TO BOTTOM): MICHAEL THOM, UNIVERSITY OF LIVERPOOL; ZHANG *ET AL., PROC. NATL. ACAD. SCI. U.S.A.* **104**, 18461 (2007)

Continued from page 1351

bonds in the compound resonantly absorb infrared light. Spectral shifts of the primary bands relative to ethylene were relatively small (<50 cm^{-1}). — JSY

Angew. Chem. Int. Ed. **46**, 10.1002/anie.200704163 (2007).

CHEMISTRY

Tougher Liposomes

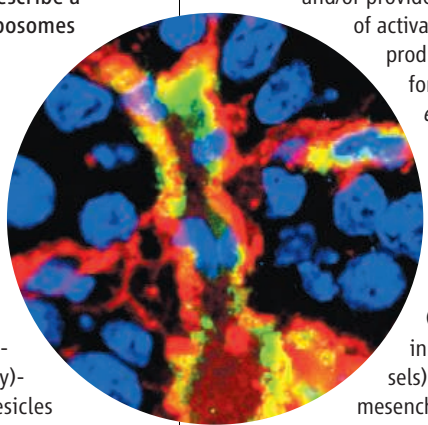
Although liposomes can be used for drug delivery, efforts continue toward improving both the stability of these spherical bilayer structures and the control over how they release their aqueous contents. Lee *et al*. **describe a method to generate caged liposomes surrounded by a cholesterol-anchored polymer** coating whose stability is pH dependent. Cholesterol-terminated poly(acrylic acid) was mixed with dipalmitoyl-phosphatidylcholine liposomes. After an overnight incubation period, these coated liposomes, which had a mean diameter of 90 nm, were cross-linked with 2,2′-(ethylenedioxy)-bis(ethylamine). The coated vesicles retained their spherical shape after freeze-drying and were resistant to leakage after 500 hours in bovine calf serum. However, the carboxylic acid cross-links helped facilitate release of the vesicles' content through compressive rupture after introduction into modestly acidic solutions (pH range of 4.0 to 5.5) over periods of 150 hours. This type of modified liposome has the potential to provide a stable, controllable drug-delivery vehicle. — PDS

J. Am. Chem. Soc. **129**, 10.1021/ja070748i (2007).

BIOMEDICINE

Another Case of Cellular Identity Theft

Solid tumors use a variety of crafty mechanisms to optimize their growth, invasion, and metastasis. One unusual mechanism that has attracted much recent interest is a form of cellular identity theft whereby tumor cells morph into a different cell type or induce surrounding normal cells to do so. The best characterized of these phenotypic changes is EMT, or "epithelial-mesenchymal transition," a process thought to endow tumor epithelial cells with migratory and invasive features and/or provide the tumor with a pool of activated fibroblasts that produce molecules required for metastasis. Zeisberg *et al*. describe a new variation on this theme. Using genetically marked transgenic mice, they show that proliferating endothelial cells (the cells that form the inner layer of blood vessels) can also morph into mesenchymal cells resembling activated fibroblasts and that the latter cells are present in at least two distinct tumor types in mice. This "endothelial-mesenchymal" transition is promoted by transforming growth factor–1β1, a cytokine that also promotes EMT and that is abundant in many tumors. The next question is whether and how these intriguing cells contribute to tumor progression. — PAK



Multicolor "endothelial-mesenchymal" transition–derived cells.

CREDIT: ZEISBERG *ET AL.*, *CANCER RES.* **67**, 10123 (2007)

Cancer Res. **67**, 10123 (2007).