PHOTOSENSORS

## Hold your tongue

*Nature* **509**, 245–248 (2014)

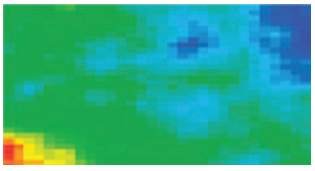
Phytochromes are red light–sensing kinases found primarily as dimers in plants and bacteria and are composed of a sensory domain (chromophore) consisting of PAS, GAF and PHY domains and a regulatory domain, which transmits the light signal output to downstream regulators. Exposure of phytochromes to red light produces a shift from a relaxed conformation (Pr) to an illuminated conformation (Pfr). Recent structural studies have identified a tongue-like loop within the PHY domain that stabilizes the chromophore, creates contacts with the PAS and GAF domains and ensures the transition from Pf to Pfr. However, the detailed structural changes between Pf and Pfr remain unclear. Takala *et al.* exposed the chromophore domain from *D. radiodurans* to laser flashes of red light and detected immediate nanometer-scale structural changes by time-resolved solution X-ray scattering and X-ray crystallography. Light exposure caused the dimer to change from a closed to an open Y-shaped conformation. This change was primarily driven by transition of the PHY tongue secondary structure from a β-sheet to an α-helix. These new structural data provide new insight on how phytochrome proteins can transmit their signal to downstream mediators upon exposure to red light. *GM*

TOXICOLOGY

## Toxicity biomaps

*Nat. Biotechnol.* doi:10.1038/nbt.2914

NATURE BIOTECHNOLOGY



Assessing the safety of drugs and other chemicals can be time consuming and expensive. Kleinstreuer *et al.* now report the use of a panel of eight complex primary human cell culture systems called BioMAP Systems to detect chemical toxicities and distinguish chemicals acting via different pathological mechanisms. The authors assessed 87 biological readouts each for four concentrations of 776 chemical compounds, including colorants, food additives, fragrances, pesticides and pharmaceuticals, in the eight systems. Unsupervised clustering of the data revealed compounds with similar activity with potentially predictable mechanisms. The researchers then used support vector machine learning to test the classification of the chemicals into 28 classes based on training from a reference compound database. Mechanisms for 26 of 33 compounds with known modes of action were correctly predicted. For example, estrogen receptor modulators, aryl hydrocarbon receptor activators and mTOR inhibitors all increased levels of tissue factor (TF) in the venular endothelial cell system. TF is involved in blood coagulation and is a clinical risk factor for thrombosis. Increased risk of thrombosis has been associated with the use of pharmaceuticals from all three of these compound classes. Taken together, the data suggest panels of primary human cells can be used to predict potential mechanisms of toxicity for chemical compounds. *AD*

MEMBRANES

## A measure of fluid

*Phys. Rev. Lett.* **112**, 188101 (2014)

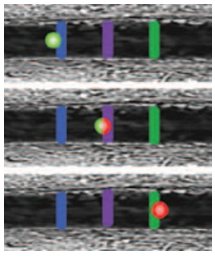
Cell membrane components can recognize and interact with one another because the underlying lipid membrane is a two-dimensional fluid. Dependent on membrane viscosity, phospholipids and membrane-bound proteins exhibit lateral and rotational diffusion behavior that alters a membrane's physiological properties and activities. Current strategies to measure membrane viscosity using routine lipid- and protein-diffusion coefficient measurements are inadequate because they involve problematic assumptions and difficulty in controlling the generation of probes. To overcome these issues, Hormel *et al.* developed a model membrane system using planar bilayers that are probed with fluorescent microspheres that can be visualized by fluorescence microscopy to determine the orientation and position of the beads. Viewed in the context of two mathematical models describing diffusion in a planar membrane, the data provide rotational and translational diffusion coefficients of the tracers and tracer radii as well as measurements of viscosity. The viscosity measurements were approximately ten times larger than what has been reported for other fluid membranes, which may relate to the membrane geometry used here. The authors also used their methodology to show that Sar1p, a small GTPase that can induce membrane curvature during vesicle traffic, markedly increases the viscosity of the bilayers, which should be sufficient to affect vesicle trafficking dynamics. *MB*

CANCER TUMOR IMAGING

## Catch me if you can

*Chem. Biol.* doi:10.1016/j.chembiol.2014.03.012

ELSEVIER



Circulating tumor cells (CTCs) are responsible for metastasis that decreases survival for patients with cancer. The dissemination of these cells remains poorly understood owing to the inability to track the CTCs once they enter the circulation. Nedosekin *et al.* have developed a method that combines the ultrafast photoswitching of Dendra2 fluorescent protein with *in vivo* flow cytometry to enable labeling and tracking of a single CTC in the bloodstream. The authors focused their lasers on blood vessels where the blood flow allowed the CTC to pass through three laser beams, causing the cell to photoconvert from green to red. Once the cell changes its color, it can be tracked *in vivo*. In addition, the efficiency of photoconversion determined by the ratio of green to red fluorescence can be used as a unique fingerprint to follow individual CTCs that differ in their ratios. The authors wanted to use this system to determine pathways of recirculation and final destinations of CTCs when they exit from the primary tumor. They examined a mouse model of metastatic carcinoma in the ear, which released Dendra2-expressing CTCs. Upon photoconversion of these cells specifically in the tail vein, the authors found that some CTCs ended up residing not only in intact tissue and primary tumor, as established before, but also in existing metastases. This new technology will reveal more information about the behavior of CTCs, which may inspire new strategies for cancer therapeutics. *GM*

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