METAL TRANSPORT

A boron chaperone?

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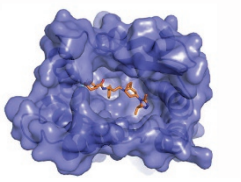
Boron is present at relatively high concentrations in the ocean and has been shown to influence expression of iron uptake genes from *Marinobacter algicola*: the majority of these genes were upregulated, but the gene encoding the periplasmic binding protein Mb-FbpA was substantially downregulated. As Mb-FbpA homologs can transport free Fe^{3+} when paired with a synergistic anion, Weerasinghe *et al.* suspected that this differential regulation might be explained if Mb-FbpA was using a borate anion in a similar manner. Structural alignments suggested the Fe^{3+}-binding site in Mb-FbpA would have sufficient room to accommodate $B(OH)_4^-$, as the protein mapped more closely to the homologous *Mannheimia hemolytica* protein—which has a C-terminal domain binding site—than the *Neisseria gonorrheae* protein, in which the binding site is buried. *In vitro* characterization confirmed that Mb-FbpA does bind a boron-containing compound, with a K_d comparable to environmental concentrations, but not at acidic pH values, consistent with the relevant species being borate. Analysis of Fe^{3+} binding in the presence and absence of borate or other anions demonstrated that boron increases the iron affinity of Mb-FbpA at comparable levels to citrate and carbonate, known biologically relevant anions. These results shed new light on a ubiquitous marine element, suggesting further functions may await discovery. *CG*

STRUCTURAL BIOLOGY

HIV-1 and its tropes

Science **341**, 1387–1390 (2013)



BEILI WU

The HIV-1 envelope glycoprotein gp120 acts as a receptor for binding immune cells that express the chemokine receptors CCR5 and/or CXCR4, which act as gp120 co-receptors for viral entry into host cells. Being able to bind either CCR5 or CXCR4 or both is a result of HIV tropism, the virus's ability to evolve its co-receptor specificity, driven primarily by gp120, to infect a greater variety of cells. To better to understand HIV tropism, Tan *et al.* first solved the structure of CCR5 with maraviroc, a CCR5 inverse agonist that allosterically stabilizes the receptor in an inactive conformation. Confirming this mechanism of action, the CCR5-maraviroc structure shows specific residues in conformations similar to those observed in other inactive structures. The maraviroc-binding site is different from a chemokine ligand-binding site in the 7-transmembrane region, which helps to explain its allosteric action, whereas some specific maraviroc interactions within CCR5 helices I-III and V-VII are supported by previous SAR data and mutagenesis studies. The authors next built models of the interaction between the co-receptors and each of two variable loop (V3) region variants of gp120, one specific for CCR5 and one for CXCR4. These structural studies, combined with sequence analysis of charge distribution of the two gp120 V3 regions, suggest that different charge distributions and steric hindrances in the chemokine receptor-binding pockets could be important in HIV tropism. *MB*

PLANT BIOLOGY

Tomatoes quit smoking

Plant Cell, doi:10.1105/tpc.113.114231

YURY TIKUNOV

Volatile organic compounds influence how humans perceive and evaluate fruit. For instance, phenylpropanoid volatiles such as guaiacol contribute to the 'smoky' aroma of certain tomato varieties. These compounds are stored as disaccharide glycoconjugates during fruit development and are released upon consumption by the action of glycosyl hydrolases. Previous work has shown that in 'non-smoky' tomatoes, these glycoconjugates are converted to trisaccharides that are resistant to hydrolysis and prevent release of smoky volatiles. Tikunov *et al.* now report the identification of the glycosyltransferase that controls tomato smokiness. Unbiased gene expression analysis using next-generation sequencing of tissue from a panel of smoky and non-smoky tomato cultivars identified two linked genes associated with the non-smoky phenotype, which the authors termed NON-SMOKY GLYCOSYLTRANSFERASE 1 and 2 (*NSGT1* and *NSGT2*). Though *NSGT* genes were found in some smoky cultivars, they seem to be nonfunctional. Metabolic profiling reveals that expression of *NSGT1* in non-smoky cultivars correlates with increased trisaccharide conjugates and reduced volatile emission. *In vitro* assays with expressed enzyme confirmed that NSGT1 is a glucosyltransferase that uses disaccharide-phenylpropanoid substrates. Expression of NSGT1 in a smoky line engenders a non-smoky phenotype, a property that was detected by sensory analysis of tomato aromas by a panel of experts. In addition to revealing that NSGT1 regulates smoky aroma expression in tomatoes, the study highlights a potential horticultural strategy for breeding tomatoes with desired aroma properties. *TLS*

CANCER THERAPEUTICS

Online matchmaker

Cell **154**, 1151–1161 (2013)

Matching a genetically defined cancer cell line (CCL) with a specific drug to elicit optimal growth inhibition is often a good indicator for future clinical efficacy. Although current genetically matched therapies target oncogenes themselves, targeting genes that cooperate with oncogenes to ensure survival and proliferation (oncogene-induced dependencies) may potentially form the basis for additional effective therapies. To identify these dependencies, Basu *et al.* embarked on a large-scale analysis measuring the cell growth of 242 characterized CCLs in response to a set of 354 well-annotated small molecules. These findings were translated into an online portal called the Cancer Therapeutics Response Portal (CTRP) (http://www.broadinstitute.org/ctrp/), which contains more than 70,000 connections between drug sensitivities and the genetic features of CCLs. This resource was successful in identifying common features in particular groups of CCLs that were either responsive or unresponsive to a particular drug, creating potential new therapies. For example, CCLs containing activating mutations in *β-catenin* (*CTNNB1*) exhibited strong sensitivity in response to the Bcl-2 family antagonist navitoclax. The data set also identified compounds with strong potency for specific lineages; for example, RSL3 and related probes for ferroptosis potently caused cell death in a group of ovarian CCLs. Thus, the CTRP, which will be updated with additional data in the future, can assist researchers in developing new drugs and combinations to improve cancer therapy. *GM*

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