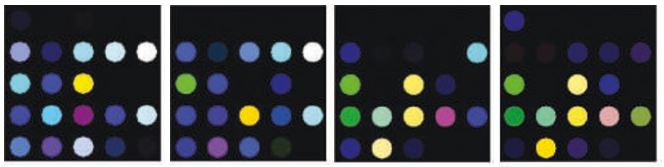
ORGANIC CHEMISTRY

Dotty solutions

What are you drinking? One answer to this frequently asked question might be found by a sensor that uses an array of chemically sensitive dyes to identify organic compounds dissolved in water.

The innovative array developed by Chen Zhang and Kenneth S. Suslick (see *J. Am. Chem. Soc.* doi:10.1021/ja052606z; 2005) uses 36 dots of dyes that change colour in response to pH, molecular polarity and Lewis basicity (how readily a molecule donates an electron pair). These properties are strongly influenced by water, making it tricky to identify trace molecules in solution. So Zhang and Suslick dampen the effects of water by using hydrophobic dyes on a hydrophobic membrane.

The combination of colour changes in the dye dots when they are dunked in solution forms a 'fingerprint' of the compounds present. The authors confirm this using a variety of common organic molecules at concentrations as low as one micromol per litre. And, although a breakdown of components is not possible with the array, complex mixtures of organic molecules do excite a unique response — as the authors show by testing a number of similar aqueous solutions found in their refrigerators (see images).



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Zhang and Suslick concede that the recognition of flavours is still some way off. That would require the incorporation into the array of hydrophobic dyes that are sensitive to salt or sugar, for instance. For now, answers to questions of taste, at least, will remain on the tip of the human tongue.

Richard Webb

activated only by wild-type MYC. The mutants' failure to activate BIM seems to contribute to their enhanced tumorigenicity, because both wild-type and mutant MYC were equally oncogenic when HSC lacking BIM were used. This implies that BIM normally constrains the carcinogenic potential of wild-type MYC, consistent with previous observations[3].

Activation of BIM by wild-type MYC does not require p53 signalling, as BIM levels were elevated in p53-deficient cells overexpressing wild-type MYC. Therefore, the oncogene activates BIM through an independent route. The authors' model predicts that BIM expression is not induced in Burkitt's lymphoma cells carrying MYC mutations. Indeed, high levels of BIM were found in all seven human Burkitt's lymphoma samples examined that carried a wild-type MYC gene, but in only one of seven Burkitt's lymphoma samples carrying a mutant gene.

Although the MYC mutants seemed to have little effect on p53 itself, they did activate one of its downstream effectors, an inhibitor of cell division called p21. How does this effect on p21 occur, and does it contribute to MYC-driven signals? Wild-type MYC inhibits p21 production by binding to the p21 gene promoter in a complex with the protein Miz-1 and recruiting further repressor proteins[4,5]. Perhaps the mutations disrupt MYC's interaction with the repressors. Or, as overexpression of mutant MYC also suppresses its own promoter, perhaps there is no wild-type MYC to form complexes with Miz-1, thereby relieving the suppression of p21. Consistent with this notion, overexpression of wild-type MYC reduced p21 levels.

BIM and p21 levels seem to be inversely regulated in this system, but it remains unclear whether wild-type MYC directly activates BIM or does so through p21. In the latter case, an interesting scenario emerges in which p21 acts upstream of BIM[6], serving as a switch to determine whether a cell will stop dividing or undergo apoptosis.

Both wild-type and mutant MYC have similar activating effects on three components of the p53-controlled apoptotic pathway — Bax, PUMA and NOXA. However, activation of these apoptosis-promoting factors does not trigger apoptosis if BIM activation is compromised (Fig. 1). Similarly, BIM activation by wild-type MYC does not induce apoptosis if the p53 pathway is disabled. The picture that emerges suggests that impairment of either the p53 or the BIM signalling route is enough to make wild-type MYC as oncogenic as the MYC mutants. The apoptotic signals conveyed by either pathway seem to be similar and additive. In mouse models, loss of one copy of the BIM gene confers strong resistance to apoptosis[3], and it will be interesting to learn whether such a loss is sufficient to abolish the difference between wild-type and mutant MYC in inducing lymphomas.

As chemotherapy usually activates the p53 pathway, these observations prompt a comparison of the response to chemotherapy between lymphoma patients carrying a translocated mutant MYC gene and normal p53 and patients carrying a translocated wild-type MYC and mutant p53. For patients with a mutant MYC, one might argue that, despite the reduced apoptosis resulting from suppression of BIM, forceful activation of the p53 pathway might potently induce apoptosis. However, it is possible that p21 would divert the signal towards cell-cycle arrest rather than death[6]. This comparison would also show whether the resistance to chemotherapy observed in mouse models of Burkitt's lymphoma[7] that overexpress MYC and are deficient in p53 faithfully mimics the response of human lymphomas with similar characteristics. If this is the case, it will offer the opportunity to refine the treatment of Burkitt's lymphoma. ■

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1. Hemann, M. T. *et al. Nature* **436,** 807–811 (2005).
2. Chang, D. W., Claassen, G. F., Hann, S. R. & Cole, M. D. *Mol. Cell. Biol.* **20,** 4309–4319 (2000).
3. Egle, A., Harris, A. W., Bouillet, P. & Cory, S. *Proc. Natl Acad. Sci. USA* **101,** 6164–6169 (2004).
4. Wu, S. *et al. Oncogene* **22,** 351–360 (2003).
5. Seoane, J., Le, H. V. & Massagué, J. *Nature* **419,** 729–734 (2002).
6. Collins, N. L. *et al. Mol. Cell. Biol.* **25,** 5282–5291 (2005).
7. Schmitt, C. A. *et al. Cell* **109,** 335–346 (2002).

MANTLE GEOCHEMISTRY

Big lessons from little droplets

Claude Herzberg

How does Hawaii look deep below the surface? Like viewing an object at a different magnification, studies of minuscule inclusions in volcanic rocks on the surface provide a fresh perspective on the question.

Mantle plumes are thought to be roughly elongate cylinders of rock that buoyantly rise up from deep within the Earth, manifesting themselves at the surface in features such as the Hawaiian islands and Iceland. Much attention has centred on Hawaii, because it is constructed from Earth's largest volcanoes distributed along two geochemically distinct alignments, and there is considerable debate about what these distinctions reveal about the underlying plume that feeds them. On page 837 of this issue[1], Ren *et al.* add to that