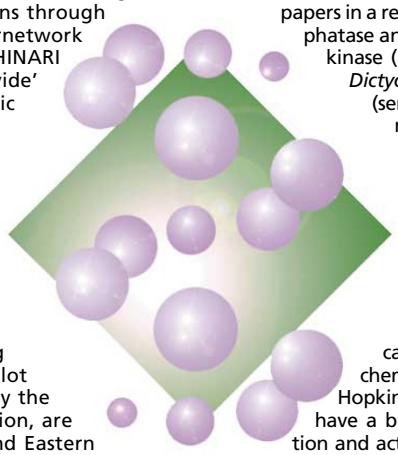
TOUCHING**base**

Science and development

A leader in a recent issue of *Nature* (vol. 417, 365; 2002) announced the free availability of all Nature Publishing Group journals to the world's poorest nations through the World Health Organization's Health Internetwork Access to Research Initiative (HINARI). The HINARI was created in 2000 to bridge the 'digital divide' that impedes the flow of health and scientific information from the developed to developing world. Through the HINARI web portal, 490 registered libraries from 106 nations with a gross national product of less than US$1,000 per head are able to access over 1,000 scientific publications. For this resource to be effective, significant improvements in computer infrastructure and reductions in computing costs are required — a far greater task than arranging for free access to journals. At this point, pilot efforts to improve connectivity, sponsored by the Open Society Institute of the Soros Foundation, are underway in eight African, Central Asian and Eastern European countries; however, such improvements will require a much greater effort by governments and corporations. The argument has been made that providing computers and Internet access to developing countries is foolish, as these nations must first contend with more immediate problems such as famine and epidemics. However, building a health and information infrastructure is essential if we are to move beyond band-aid remedies. As the editor of SciDev.net, David Dickson, states, "those who stand to benefit most from modern science and technology are also those who have least access to information about it". Thus, bridging the digital divide is essential to bridging the health divide.

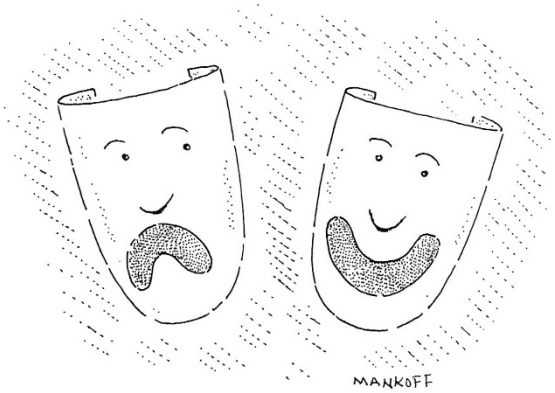


Chemotaxis á la *PTEN*

The role of PTEN phosphatase as a tumor suppressor is well established, but what else can this handy little molecule do? Two papers in a recent issue of of *Cell* outline the role of the phosphatase and its kinase counterpart phosphatidylinositol 3-kinase (PI3K) in regulating chemotaxis in the amoeba *Dictyostelium discoideum*. The ability to chemotax (sense extracellular chemical gradients and migrate in response) is essential for cellular functions including wound repair, pathogen defense by leukocytes, axon guidance and localization of unicellular organisms such as *D. discoideum* to food sources. Proteins with pleckstrin homology (PH) domains localize at the leading edge of the cell in response to chemoattractant. As PH-domain proteins interact with 3-phosphoinositides, it was logical to examine the roles of PI3K and PTEN in chemotaxis. Miho Iijima and Peter Devreotes (Johns Hopkins Univ.) show that amoebae that lack PTEN have a broader swathe of PH-domain protein localization and actin polymerization regions at the leading edge of the cell, causing it to take a more circuitous route toward the attractant (*Cell* **109**, 599–610; 2002). Using GFP-tagged PTEN, they were then able to show that the phosphatase localizes to the rear of the cell. Another study, carried out by Satoru Funamoto and colleagues (Univ. California, San Diego) establishes that PI3K localizes to the leading edge of the cell in response to chemoattractant exposure (*Cell* **109**, 611–623; 2002). When PI3K is forced to 'mislocalize' so that it has a uniform distribution along the plasma membrane, pseudopodia form—so the kinase may have an instructive role in the formation of pseudopodia. Now that it is established that PTEN and PI3K coordinate chemotaxis in *D. discoideum*, one wonders about their role in mammalian cellular chemotaxis.

Interfering with HIV

The potential use of small interfering RNAs (siRNAs) as a means to manipulate gene expression seems to have fired the imagination of geneticists in recent months. Reports in *Science* (vol. 296, 550–553; 2002) and *Genes & Development* (vol. 16, 948–958; 2002) have described new vectors that allow stable suppression of target genes (*TP53* in each case). The therapeutic application of siRNA has now taken a step forward through two additional studies. Writing in *Nature Biotechnology* (vol. 20, 500–505), Nan Sook Lee and colleagues (Graduate School of Biological Sciences) present another new siRNA vector that they use to suppress expression of the HIV *rev* transcript. The vector contains the human U6 snRNA promoter, followed by 21-mers that are complementary to different regions of *rev*. When co-transfected into cells, the combination of two different U6-driven siRNAs dramatically reduces *rev* expression and HIV replication. In another paper, published by *Nature Medicine* (vol. 8, 681–686; 2002), Carl Novina (Massachusetts Institute of Technology) and colleagues show that the delivery of siRNAs targeted to either the gene encoding the CD4 receptor or viral *gag* can inhibit the replication of HIV in cell culture. The inhibition can occur either before or after proviral integration, suggesting that anti-HIV siRNA can be effective at more than one stage of the viral life cycle. These siRNAs were delivered the 'old-fashioned' way—by transfection in cationic lipid complexes; however, the vector-based approach of Lee *et al*. suggests that the stable delivery of siRNA inhibitors of HIV is possible. One is tempted to propose (as the authors do) that 'combination therapy' with several siRNAs targeted to different regions of the HIV genome could be an important new approach in fighting the replication of drug-resistant viruses.



"Oh, yeah? Well, I think you're the one with the biochemical imbalance."