conclusion from studies by Kam *et al.*[2] was that PtdIns(3,4,5)P_3 is involved in neither recruitment nor activation of ASAP1, whereas PtdIns(4,5)P_2 is required for activation. Consistent with this, data from recent studies indicate that whereas the PH domain of ASAP1 shares some sequence similarity with targets of PtdIns(3,4,5)P_3, ASAP1 does not contain structural determinants of specific PtdIns(3,4,5)P_3 binding[3,4].

We felt this clarification was important to facilitate understanding of the regulation of Arf proteins by Arf GAPs. In addition, we wanted to emphasize the point that several Arf GAPs might be targets of PtdIns(3,4,5)P_3. Another family of Arf GAPs, the GITs, which do not contain PH domains[1,5], are activated to a small extent (2–3-fold) by 100–200 μM PtdIns(3,4,5)P_3. One of our laboratories has also identified a PH domain-containing Arf GAP that is specifically activated by PtdIns(3,4,5)P_3, and is currently testing whether this protein might be a target *in vivo* (K. Miura and P.A. Randazzo, unpublished). Other phosphoinositide isomers are probably important for other Arf GAPS; for example PtdIns(4,5)P_2 activates ASAP1. The Arf GAP ACAP1 (Ref. 6) (referred to as centaurin β1 in Ref. 1) is activated by PtdIns(4,5)P_2 and PtdIns(3,5)P_2, but not PtdIns(3,4,5)P_3, *in vitro* (P.A. Randazzo, unpublished). Based on these differences, we propose that discriminate regulation of the Arf GAPs is achieved through unique lipid dependencies of activation. We look forward to further results from work on the phosphoinositide-dependent Arf GAPs and to descriptions of possible interactions linking Arf GAPs with the PI 3-kinase signaling pathway.

Paul A. Randazzo*
Koichi Miura
Zhongzhen Nie
Ann Orr
Laboratory of Cellular Oncology, National Cancer Institute, Bethesda, MD, USA.
*e-mail: randazzo@helix.nih.gov

Anne B. Theibert
Brian G. Kearns
Dept of Neurobiology, University of Alabama at Birmingham, Birmingham, AL 35294, USA.

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In Brief

The protein folds how Rosetta predicts

A promising computational method for predicting protein folding, called Rosetta, has been developed by David A. Baker and co-workers (Howard Hughes Medical Institute, Chevy Chase, MD, USA), and their colleagues at the University of Washington (Seattle, WA, USA). The correct prediction of the 3D structure of a folded protein *ab initio* (i.e. starting from only the amino acid sequence) has been a long-pursued problem for computational biologists. However, during the fourth Critical Assessment of Techniques for Protein Structure Prediction (CASP4), held at the Asilomar Conference Center (California, CA, USA) from 3–7 December 2000, Rosetta proved strikingly successful in deducing protein structures from linear sequences of amino acids. Rosetta functions by searching for the lowest overall energy combination of the conformations adopted by the local segments of a protein during folding, taking the distribution of conformations observed for short sequence segments in known protein structures as an approximation. Considering the wealth of raw gene sequence data being continuously produced by genome sequencing efforts, the possible implications of an *ab initio* computational technique such as Rosetta are far reaching, as Baker underlined '…one can conceive of going through a genome and generating structures and possibly functional insights for every protein'. *AR* (http://www.hhmi.org/news/baker.html; http://www.hhmi.org/research/investigators/bakerd.html)

Sweet, sweet chemistry

A major leap in automating the production of synthetic complex carbohydrates could cut the time required to make an oligosaccharide by a factor of one hundred! Scientists investigating the sophisticated and multifaceted biochemistry of oligosaccharides, a class of biomolecules notoriously difficult to produce, have longed for a technology that enables complex sugars to be synthesized on a par with the relatively easy construction of oligopeptides and oligonucleotides. By modifying a commercially available peptide synthesizer, a group led by Peter H. Seeberger at the Massachusetts Institute of Technology (Cambridge, MA, USA) has described the automated synthesis of several oligosaccharides, including a branched dodecasaccharide, on an octenediol-functionalized resin [*Science* (2001) 291, 1523–1527]. *AR* (http://web.mit.edu/newsoffice/tt/2001/feb07/carbs.html)

Sorting DNA molecules with a nanotechnological sieve

Biochemistry will be a first-line target of the tsunami wave caused by the nanotechnology revolution. This novel technology has an unprecedented ability to work at the molecular level, atom by atom, to create large structures with fundamentally new molecular organization. The manufacturing of several silicon-based devices by

