WEB WATCH

Let's get together

Protein–protein interactions literally hold cellular processes together, but keeping up with the ever-expanding literature on what might bind what is enough to make you fall apart, and it's likely to get worse as whole-genome scans for protein–protein interactions churn them out in bulk (see the review by Albertha J. M. Walthout and Marc Vidal on page 55 of our January issue). PreBIND — a new adjunct to the Biomolecular Interaction Network Database (BIND) built by researchers at the Samuel Lunenfeld Research Institute in Toronto — helps you to search the literature for possible interactions and then submit bona fide interactions to BIND.

The version now available is a prototype that searches for protein–protein interactions in the yeast *Saccharomyces cerevisiae*, using proteins described in the NCBI's RefSeq database, but there are plans to add more organisms. PreBIND is simple to use, and the help page is a model of clarity. You can search PreBIND by entering a protein name or RefSeq accession number. PreBIND then returns a list of papers that discuss other molecules that interact with your protein of interest. The power behind PreBIND is a trained alogorithm that allows it to recognize papers that discuss interactions. For that reason, it searches much more thoroughly than you could doing a simple PubMed search. For each paper that it finds, PreBIND lists the proteins discussed in the paper and provides a score of the likelihood that the paper contains interaction information. You can then review the paper, decide whether or not it discusses a true interaction, and submit your response to BIND. This will then be refereed by a moderator before being added to BIND. Over time, PreBIND and BIND should help us to gain valuable and reliable insights into molecular interactions.

Cath Brooksbank

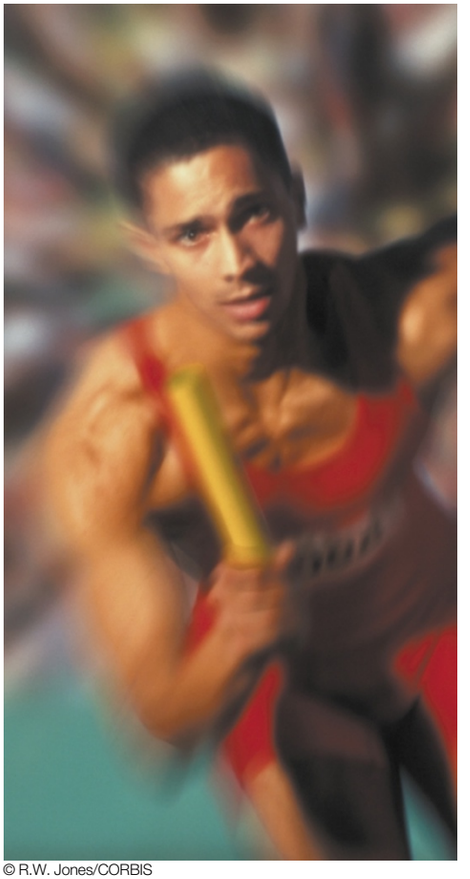
CELL MOVEMENT

Take steroids to move faster

As well as being important regulators of developmental and physiological processes, steroid hormones have a darker side — in the development and progression of breast, ovarian and prostate cancer. This was believed to be due to stimulation of proliferation, but evidence presented by Jianwu Bai and colleagues in *Cell* suggests a new function for steroid hormones: making cells move.

Using the *Drosophila melanogaster* egg chamber, this group has identified mutants that block movement towards the oocyte of a group of cells called border cells. Genes previously identified using this system include *slow border cells* (*slbo*), which encodes a transcription factor, and the *Drosophila* E-cadherin gene. Their latest screen has identified *taiman* (*tai*) — meaning 'too slow': mutant clones typically remain stuck at the anterior end of the egg chamber instead of moving towards the oocyte. *tai* mutants had normal expression levels of SLBO, indicating that TAI might be involved in a different pathway from SLBO, but E-cadherin was mislocalized.

So what is TAI? It turns out to belong to a family of steroid-receptor co-activator (SRC) proteins previously not thought to exist in *Drosophila*. Its closest relative in mammals is AIB1, a SRC that is amplified in breast and ovarian cancer. Which steroid hormone receptor does TAI interact with? Several genes for steroid hormone receptors have been identified in the *Drosophila* genome but only one of these, the ecdysone receptor (a heterodimer of the USP and EcR proteins), has a known ligand, which is synthesized by the ovary. USP and EcR were expressed together with TAI in wild-type border cells, and TAI, USP and EcR colocalized exactly on *Drosophila* polytene chromosomes, indicating that the three proteins form a complex. Furthermore, provided that SLBO was also expressed, treatment with ecdysone caused precocious migration of border cells whereas migration was abrogated in an *ecdysoneless* mutant.



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What next? As well as identifying the targets of the ecdysone receptor–taiman complex, it will be important to determine whether AIB1 has similar effects on cell motility in vertebrates. If so, it could explain the increased invasiveness of

PROTEIN TRAFFICKING

Made for export

Without plasma membrane proteins, every cell would be an island, unable to communicate with the outside world. So how does the cell ensure that newly synthesized plasma membrane proteins reach their destination? Proteins that don't fold properly or aren't correctly glycosylated are held back in the endoplasmic reticulum (ER), and an emerging mechanism that prevents the untimely escape of proteins from the ER is an ER-retention signal, RXR(R), which has to be masked by another protein to allow exit from the ER. But Ma and colleagues, reporting in the 12 January issue of *Science*, have found a new signal that, instead of holding proteins back, pushes them out.

The authors stumbled on this mechanism when they were trying to express different K^+ channels in *Xenopus* oocytes. Two of the channels, Kir1.1 and Kir2.1, were efficiently expressed at the surface but others were not. So they swapped the carboxyl termini of the poorly expressed channels for those of the efficiently expressed channels, and got efficient expression. Conversely, removal of the C terminus of Kir2.1 beyond residue 374 reduced trafficking to the surface. This did not seem to be due to a fault in folding or assembly, because the small amount of surface-expressed truncated Kir2.1 had identical conductance properties to wild-type Kir2.1. Surface levels could also be restored by expression of full-length Kir2.1 together with truncated Kir2.1, indicating that the two forms could assemble to create functional channels.

Scanning mutagenesis narrowed the signal down to *FCYENE*: even conservative mutations in the italicized residues abolished surface expression of green-fluorescent-protein (GFP)-tagged Kir2.1. The position of the sequence seemed unimportant: it worked when inserted between GFP and Kir2.1, or at the extreme C terminus of Kir2.1. But does the export sequence work for other proteins? A truncated form of Kir3.1 normally remains stuck in the ER but adding FCYENE to its C terminus allowed it to escape. Likewise, FCYENE facilitated the export of a distantly related K^+ channel, Kv1.2, which is normally helped to the surface by its partner, Kvβ2.