relatively large eukaryotic cell without harming the cell. This last experiment demonstrated that optical tweezers could be used as a gentle non-invasive method to study the force generation inside a cell.

Reports of such studies quickly followed: Block and colleagues[6] reported the measurements of torsional compliance of bacterial flagella in 1989. In 1990, Ashkin *et al.*[7] used optical tweezers to study the force driving active organelle movement along microtubules, whereas Block and coworkers[8] monitored the movement of kinesin along microtubules by trapping silica beads coated with carrier protein. These results highlight some of the questions that can be studied using optical tweezers, which are becoming an important tool in the biologist's arsenal.

Hwa-ping Feng

1. Ashkin, A. *Phys. Rev. Lett.* **24**, 156–159 (1970).
2. Ashkin, A. & Dziedzic, J.M. *Science* **235**, 1517–1520 (1987).
3. Chu, S., Bjorkholm, J.E., Ashkin, A. & Cable, A. *Phys. Rev. Lett.* **57**, 314–317 (1986).
4. Chu, S., Hollberg, L., Bjorkholm, J.E., Cable, A. & Ashkin, A. *Phys. Rev. Lett.* **55**, 48–51 (1985).
5. Ashkin, A., Dziedzic, J.M. & Yamane, T. *Nature* **330**, 769–771 (1987).
6. Block, S.M., Blair, D.F. & Berg, H.C. *Nature* **338**, 514–518 (1989).
7. Ashkin, A. Schütze, K., Dziedzic, J.M., Euteneuer, U. & Schliwa, M. *Nature* **348**, 346–348 (1990).
8. Block, S.M., Goldstein, L.S.B. &Schnapp, B.J. *Nature* **348**, 348–352 (1990).

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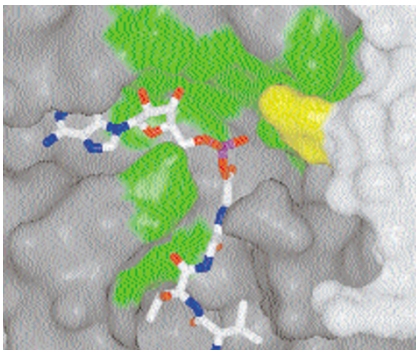
picture story

Making Moco

The sulfur-containing molybdenum cofactor (Moco) is an essential component of a number of redox enzymes involved in sulfite detoxification and the metabolism of xenobiotics; defects in its biosynthesis usually lead to fatal disease in humans. It has recently become clear that its biosynthetic pathway has quite a bit in common with another important pathway, namely the activation of ubiquitin used in tagging proteins for degradation and signaling. MoeB, a required sulfurtransferase in Moco biosynthesis, has significant sequence similarity to the ubiquitin activating enzyme E1, responsible for the initial steps in ubiquitination. Both enzymes catalyze the C-terminal adenylation of their small protein targets, MoaD and ubiquitin, which also share a common fold and a common C-terminal Gly-Gly motif. In fact, it has been proposed that Moco biosynthesis, present in bacteria, archaea and eukarya, represents an evolutionary precursor to the ubiquitin pathway, found only in eukaryotes.

As described recently in *Nature* (Lake *et al.*, **in the press**), Schindelin and colleagues have solved X-ray crystal structures of MoaD in complex with MoeB, representing the first structures of a ubiquitin-like protein bound to its activating enzyme. Three structures — of the apo-complex, the ATP-bound form and the adenylated MoaD form (shown here) — provide an evolving picture of the adenylation reaction. The structures reveal a $MoaD_2$–$MoeB_2$ tetramer, in which both of the MoeB subunits (dark and light gray) contribute to each active site. Several active site residues are strictly conserved between MoeB and E1 (these are shown in green for one monomer and yellow for the other). Based on their structures, Lake *et al.* propose a reaction mechanism for the adenylation of MoaD, and by analogy, ubiquitin.

In the proposed mechanism, a carboxylate oxygen of the C-terminal Gly 81 of MoaD (the adenylated MoaD is shown in an all-bonds representation) directly attacks the α-phosphate of the ATP molecule. The repulsion between these two negatively charged species is presumably mitigated by a nearby Mg^{2+} ion, predicted to be coordinated by Asp 130 of MoeB (green, to the left of MoaD). Consistent with this, the authors show that mutation of Asp 130 severely reduces the activity of the enzyme. Binding of ATP appears to induce a kink at the α-phosphate, which promotes cleavage of the bond between the α- and β-phosphates. Several conserved residues in MoeB, including Arg 14 (yellow) and Arg 73 (green residue behind Arg 14) are proposed to stabilize the negative charge on the β-phosphate of the leaving group; the authors show through mutagenesis that at least one positive charge in this region is required for activity.



These three structures thus provide new mechanistic insights into the biosynthesis of this important cofactor; and given the identification of a growing number of ubiquitin-like proteins, they may serve as a starting point for understanding the activation of a large class of proteins involved in a variety of functions.

Julie Hollien