Structure watch

COPI VESICLE ASSEMBLY

The coat proteins COPI, COPII and clathrin mediate the formation of transport vesicles from distinct membranes: COPI triggers vesicle formation at the Golgi, COPII works at the endoplasmic reticulum and clathrin acts at the plasma membrane. Lee and Goldberg now determine the structure of a COPI subcomplex and find that it shares key features of both the COPII and clathrin coats. The authors used proteolysis to isolate COPI subcomplexes in baculovirus-infected insect cells. Crystallization of one of these — the αβ′-COP subcomplex — in *Saccharomyces cerevisiae* at 2.5 Å resolution revealed that, similarly to COPII and clathrin coats, the αβ′-COP core consists of α-solenoid and β-propeller protein domains. The αβ′-COP subcomplex is similar to that of COPII in that its β-propeller domains converge at the vertices of the lattice. But, like clathrin, these vertices of the COPI subcomplexes are arranged in three-way intersections; this suggests that the COPI cage may also form a 'football-type' triskelion lattice.

ORIGINAL RESEARCH PAPER Lee, C. & Goldberg, J. Structure of coatomer cage proteins and the relationship among COPI, COPII, and clathrin vesicle coats. *Cell* **142**, 1–10 (2010)

DNA LESION BYPASS

The Y-family polymerases specialize in replication past DNA lesions. In this family, polymerase η (Pol η) has the unique ability to allow the bypass of *cis-syn* T dimers created on exposure to ultraviolet radiation. Deficiency of Pol η causes the human syndrome xeroderma pigmentosum (XPV), which is characterized by increased skin malignancies. Two groups now determine crystal structures for Pol η in complex with the DNA template and incoming nucleotide — Silverstein *et al.* working with yeast Pol η and Biertümpfel *et al.* with human Pol η. Together, they provide insights into how Pol η achieves specific and efficient bypass of damaged DNA. By comparing the structural complexes formed between Pol η and normal T bases versus a *cis-syn* T dimer, both groups find that Pol η has a more open active site compared with high-fidelity polymerases, which allows it to accommodate the *cis-syn* T dimer. Silverstein *et al.* used this structure to identify Gln55, Arg73 and Met74 as key residues that maintain the T dimers in a stable conformation in the active site. By comparing a structure of Pol η in which replication has proceeded to allow further nucleotide incorporation, Biertümpfel *et al.* identify a 'molecular splint' structure that keeps the growing chain in the correct conformation and allows rapid extension past the DNA lesion. They also model mutations observed in patients with XPV onto these structures and find that they may target either the molecular splint structure or the active site itself.

ORIGINAL RESEARCH PAPERS Silverstein, T. D. *et al.* Structural basis for the suppression of skin cancers by DNA polymerase η. *Nature* **465**, 1039–1043 (2010) | Biertümpfel, C. *et al.* Structure and mechanism of human DNA polymerase η. *Nature* **465**, 1044–1049 (2010)