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Structure watch

UNMAKE A MARK

The Research Highlight 'Fine-tuning tools' in this issue discusses the identification of histone demethylases, one of which — the JmjC-domain-containing protein JMJD2A — is predominantly a Lys trimethyl-specific demethylase. In *Cell*, Zhang and colleagues provide insights into how this protein functions by describing crystal structures of the catalytic core of JMJD2A in the presence of Fe^{2+}, with and without α-ketoglutarate.

Several unique structural features of the catalytic core indicated that JMJD2A and possibly other JmjC-domain-containing proteins form a new subfamily within the large Fe^{2+}- and α-ketoglutarate-dependent oxygenase family. The features include a C-terminal domain that has a novel fold and an unexpected zinc-finger motif that is formed by a Cys and His residue from the JmjC domain and two Cys residues from the C-terminal domain. This unique zinc-finger structure ensures a tight association between these two domains and seems to create a rigid conformation around the catalytic centre. Structural data combined with mutagenesis studies enabled the authors to identify two potential binding pockets in JMJD2A — one for binding the peptide substrate and another for methyl-group recognition. They also identified structural features that contribute to the differential specificity of individual JMJD2-family members for different methyl groups.

REFERENCE Chen, Z. *et al.* Structural insights into histone demethylation by JMJD2 family members. *Cell* **125**, 691–702 (2006)

CAGE CONTROL

The GroEL–GroES chaperonin cage has an important role in folding proteins of up to ~60 kDa, but its role was thought to be passive, with the cage purely providing an environment that allows folding to occur unimpaired by aggregation. However, recent studies have indicated that the cage can alter the folding-energy landscape for some proteins, thereby accelerating their folding rate. Hayer-Hartl and colleagues therefore investigated the structural features of the cage that are essential for the rapid folding of encapsulated substrates.

Reporting in *Cell*, the authors describe how they analysed the effect of varying the volume of the chaperonin cage. Their results were consistent with theoretical confinement models, in that the proteins tested showed an increased folding rate with increasing confinement up to a point where further decreases in space would have limited essential reconfiguration steps. They further showed that interactions with the C-terminal, mildly hydrophobic Gly-Gly-Met repeats of GroEL, which protrude into the cage cavity, were required for the folding of some proteins. Several conserved negatively charged residues on the cavity wall were also essential for the folding of certain proteins. As the authors conclude, "…by combining these features, the chaperonin cage provides a physical environment optimized to catalyze the structural annealing of proteins with kinetically complex folding pathways."

REFERENCE Tang, Y.-C. *et al.* Structural features of the GroEL-GroES nano-cage required for rapid folding of encapsulated protein. *Cell* **125**, 903–914 (2006)