IN BRIEF

GENE EXPRESSION

DNMT1 learns to be picky

DNA methyltransferase 1 (DNMT1) primarily methylates hemimethylated CpG sites on DNA following replication and has a key role in regulating gene expression. Previous work had identified the DNMT1 protein domains that recognize unmethylated DNA and prevent DNA methylation. This study reveals a complementary mechanism that governs the specificity of DNMT1 for hemimethylated DNA. The authors determined the crystal structure of mouse DNMT1 in complex with DNA containing a hemimethylated CpG site on the parental strand. They observed that hemimethylated DNA is recognized by the target recognition domain (TRD) within the methyltransferase domain, which forms a shallow concave surface that harbours the 5-methyl group of methylcytosine from the parental DNA strand. Biochemical analysis indicated that the hydrophobic environment generated by the residues lining the concave surface probably also has a role in determining substrate specificity.

ORIGINAL RESEARCH PAPER Song, J. *et al.* Structure-based mechanistic insights into DNMT1-mediated maintenance DNA methylation. *Science* **335**, 709–712 (2012)

TRANSCRIPTION

PKM2 as a protein kinase

Pyruvate kinase isoform M2 (PKM2) is a glycolytic enzyme that mediates the conversion of phosphoenolpyruvate (PEP) to pyruvate. It has been suggested that PKM2 may have additional enzymatic activities and localizes to the nucleus to regulate transcription. Here, the authors show that PKM2 can act as a kinase in the nucleus. They found that nuclear PKM2 affected the expression of many genes; one of its targets was *Mek5* (also known as *Map2k5*), the expression of which was increased following an interaction of PKM2 with signal transducer and activator of transcription 3 (STAT3). Specifically, PKM2 was found to phosphorylate STAT3 on Tyr705, leading to STAT3 activation and increased DNA binding affinity. Importantly, the authors observed that dimeric PKM2 localizes to the nucleus and is the active protein kinase, whereas the tetramer is found in the cytoplasm and acts as a pyruvate kinase.

ORIGINAL RESEARCH PAPER Gao, X. *et al.* Pyruvate kinase M2 regulates gene transcription by acting as a protein kinase. *Mol. Cell* 2 Feb 2012 (doi:10.1016/j.molcel.2012.01.001)

MEMBRANE TRAFFICKING

Adaptor waves at the Golgi

During membrane trafficking between the *trans* Golgi network (TGN) and endosomes, clathrin-coated vesicles are formed through the concerted action of adaptor proteins that link clathrin, membrane and cargo. Here, Daboussi *et al.* use live cell imaging and super-resolution microscopy to dissect the relationship between the adaptor proteins Ap1 and Gga2 in budding yeast. They find that these proteins are recruited to the TGN in two waves during coat assembly, with Gga2 arriving first. Levels of the phosphoinositide PtdIns4P, which mediates the localization of these adaptors to the TGN, are important for ensuring the proper rate of adaptor progression. In addition, Gga2 recruits Pik1, a kinase that generates PtdIns4P, through a direct interaction. Thus, this mechanism may provide a means of generating adaptor-specific coats and coated vesicles with distinct target destinations.

ORIGINAL RESEARCH PAPER Daboussi, L. *et al.* Phosphoinositide-mediated clathrin adaptor progression at the *trans* Golgi network. *Nature Cell Biol.* 19 Feb 2012 (doi:10.1038/ncb2427)