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IN BRIEF

GENOME ENGINEERING

Presenting Argonaute, the genome editor

Argonaute proteins are endonucleases that typically require 5′-phosphorylated, short single-stranded guide RNAs (gRNA) for targeting and cleavage of transcripts; however, some prokaryotic Argonautes cleave DNA, similarly to the endonuclease Cas9. Unlike Cas9, DNA-cleaving Argonautes use gDNA rather than gRNA and do not require auxiliary sequences in targets or secondary structures in guides for cleavage. Gao *et al.* identified an Argonaute from the archaebacterium *Natronobacterium gregoryi* (NgAgo). They found that, when expressed in human cells, NgAgo did not associate with endogenous nucleic acids and was targeted to DNA only when the gDNA was delivered concomitantly with its expression, thereby minimizing the risk of guide swapping. NgAgo formed double-strand breaks (with nucleotide removal) and also mediated genome editing though homology-directed repair with donor DNA. The NgAgo–gDNA system was at least as efficient as Cas9–gRNA and, importantly, had lower off-targeting levels.

ORIGINAL ARTICLE Gao, F. *et al.* DNA-guided genome editing using the *Natronobacterium gregoryi* Argonaute. *Nat. Biotechnol.* http://dx.doi.org/10.1038/nbt.3547 (2016)

ION TRANSPORTERS

Potassium channel regulates ciliogenesis

K_v10.1 is a voltage-gated potassium channel, whose upregulation can lead to severe developmental disorders and to cancer. Sánchez *et al.* found that in mammalian cells, K_v10.1 can localize to primary cilia, where it promotes cilia disassembly — a process that is thought to be required for mitosis. Accordingly, K_v10.1 knockdown increased cilia numbers and length, and this caused the hyperactivation of cilia-mediated Sonic hedgehog signalling, prolonged the cell cycle and forced mitosis in the presence of cilia. When implanted into mice, cells overexpressing K_v10.1 lacking the cilia-targeting motif had reduced tumorigenic potential compared to cells overexpressing the full-length protein, indicating that this previously unrecognized function of K_v10.1 in ciliogenesis is important for the pathologic effects associated with K_v10.1 misexpression.

ORIGINAL ARTICLE Sánchez, A., Urrego, D. & Pardo, L. A. Cyclic expression of the voltage-gated potassium channel K_v10.1 promotes disassembly of the primary cilium. *EMBO Rep.* **17**, 708–723 (2016)

DNA DAMAGE RESPONSE

p53 curbs topological stress

Excessive DNA unwinding in S phase by DNA and RNA polymerases causes topological stress which, if not relieved by topoisomerase II (Topo II), can lead to DNA damage. Investigating why p53-deficient cells are more sensitive to Topo II inhibitors, Yeo *et al.* showed that treating p53-deficient human and mouse cells with Topo II poisons resulted in higher levels of catalytically inhibited DNA–Topo IIα complexes and of replication-mediated double-strand breaks (DSBs). Notably, inhibition of RNA polymerase II substantially decreased the formation of DNA–Topo IIα complexes and DSBs. Furthermore, even without Topo II inhibition, p53 deficiency impaired replication fork progression, and this was relieved by transcription inhibition. Thus, p53 is important for preventing transcription-induced topological stress that interferes with replication and causes DNA damage.

ORIGINAL ARTICLE Yeo, C. Q. *et al.* p53 maintains genomic stability by preventing interference between transcription and replication. *Cell Rep.* **15**, 132–146 (2016)

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