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IN BRIEF

CELL SIGNALLING

Antagonizing and amplifying EGF signalling

Activation of epidermal growth factor receptor (EGFR) is associated with many human tumours, but no extracellular antagonist for EGFR in human cells was known. Here, the authors report that the macrophage migration inhibitory factor (MIF), which is a cytokine also implicated in tumorigenesis, binds to the extracellular domain of EGFR and blocks EGF binding, thereby inhibiting EGFR activation and signalling. The authors found that MIF is *O*-GlcNAcylated at Ser112 and Thr113, and that these modifications are required for EGFR inhibition and for reducing EGF-induced tumour cell invasion in mice. Furthermore, EGFR activation led to the degradation of extracellular MIF, owing to enhanced secretion of matrix metalloproteinase 13. This uncovers a positive feedback loop, by which EGFR signalling can be amplified in heterogeneous tumour microenvironments.

ORIGINAL RESEARCH PAPER Zheng, Y. *et al.* Secreted and *O*-GlcNAcylated MIF binds to the human EGF receptor and inhibits its activation. *Nat. Cell Biol.* http://dx.doi.org/10.1038/ncb3222 (2015)

GENE EXPRESSION

Integrator enhances enhancers

The expression of enhancer RNAs (eRNAs) is important for enhancer activation. As eRNAs are non-polyadenylated, Shiekhattar and colleagues studied the role of the Integrator complex, which is required for the 3′-end processing of other non-polyadenylated RNAs, in their biogenesis. They found that addition of epidermal growth factor (EGF) to HeLa cells resulted in Integrator recruitment to EGF-responsive enhancers and the induction of eRNA expression. When the Integrator subunit INTS11 was depleted, unprocessed eRNAs accumulated, the formation of EGF-dependent interactions between enhancers and promoters was abrogated, and the expression of EGF-responsive genes was reduced. The ectopic expression of wild-type, but not catalytically inactive, INTS11 restored EGF-dependent eRNA and gene expression, indicating that defects in eRNA processing contribute to the loss of transcriptional responsiveness to signalling cues.

ORIGINAL RESEARCH PAPER Lai, F. *et al.* Integrator mediates the biogenesis of enhancer RNAs. *Nature* http://dx.doi.org/10.1038/nature14906 (2015)

TRANSLATION

Regulating the proteome in and out of mitosis

During the cell cycle, protein levels are thought to be controlled mainly by regulating transcription and protein degradation. The importance of translation regulation during somatic mitotic divisions remains unclear. Using ribosome profiling and metabolic labelling in cells synchronized with a small-molecule CDK1 inhibitor, Tanenbaum *et al.* found that translation is globally reduced by ~35% during mitosis. Moreover, 199 genes showed specific translation regulation: they were all translationally repressed at mitotic entry and re-activated at mitotic exit. The authors then focused on EMI1, which is an inhibitor of the anaphase-promoting complex (APC/C) that is degraded early during mitosis to enable mitotic progression. They found that translational repression of EMI1, mediated through its 3′ UTR, was required for the efficient activation of APC/C, revealing that translational repression cooperates with protein degradation to regulate protein activity during mitosis.

ORIGINAL RESEARCH PAPER Tanenbaum, M. E. *et al.* Regulation of mRNA translation during mitosis. *eLife* **4**, e07957 (2015)