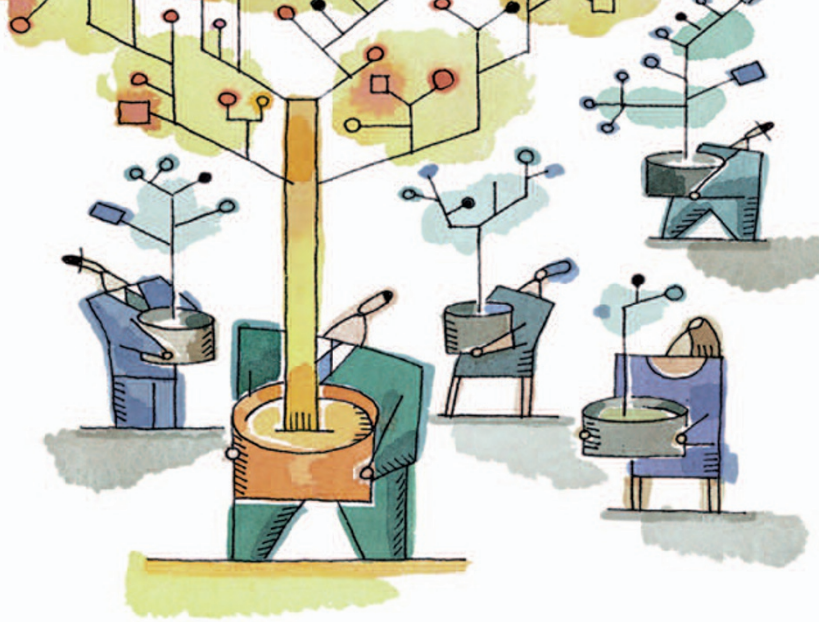

GENE REGULATION

The logic of sharing

By implementing a systematic chromatin immunoprecipitation-microarray (ChIP-chip) analysis of the heat-shock σ-factor regulon (σ^{32}) of *Escherchia coli*, Wade *et al.* reveal the surprising finding that there is functional overlap between σ factors.

Sigma factors confer specificity on the bacterial RNA polymerase (RNAP), directing this enzyme to promoter sequences, positioning the RNAP at the promoter and effecting local unwinding of the DNA duplex near to the transcription start site. In addition to the main σ^{70} factor that directs transcription of housekeeping genes, most bacteria synthesize alternative σ factors that enable recognition of different sets of promoters by the RNAP — a neat solution to the problem of how to rapidly modulate global transcription in response to changing conditions.

The availability of whole-genome microarrays has allowed researchers to attempt to exhaustively catalogue all the members of the σ^{32} regulon. ChIP-chip studies are an ideal tool for delineating regulons, since they do not rely on artificially overproducing proteins in cells, but instead can detect DNA sequences that are bound by physiological levels of regulatory proteins. Using this approach, the authors identified a minimum of 87 promoters — they estimate that the true number might be closer to 120–150 — that are bound by σ^{32}-RNAP ($E\sigma^{32}$), a massive increase on the previous known size of this regulon.

Perhaps it is not surprising that the heat-shock regulon is large, given that heat shock is a drastic environmental shift, but close inspection of the promoters recognized by $E\sigma^{32}$ led the researchers to some surprising conclusions. First, 22 heat-shock promoters were located in coding or intergenic regions rather than promoter regions, with 3 promoters postulated to transcribe regulatory RNAs. Second, by comparing the regulon with the predicted σ^{70} regulon (not yet published) the authors found significant overlap in targets that are bound by both σ^{32} and σ^{70}. Traditional biochemistry confirmed that $E\sigma^{70}$ can indeed transcribe from five selected $E\sigma^{32}$ promoters. In addition, comparing the σ^{70} and previously published σ^{24} (σ^{E}) regulons also revealed an extensive overlap between target promoters.

The hypothesis arising from this research is that alternative σ factors primarily evolved to augment σ^{70} transcription and generate complex regulatory patterns, and the authors argue that this is a key feature of transcriptional logic. The power of using a systems-wide approach to detect regulatory networks is clearly shown by these unexpected findings.

Susan Jones

ORIGINAL RESEARCH PAPER Wade, J.T. *et al.* Extensive functional overlap between σ factors in *Escherichia coli*. *Nature Struct. Mol. Biol.* 06 Aug 2006 (doi:10.1038/nsmb1130)

IN BRIEF

BACTERIAL SECRETION

Signal sequence directs localized secretion of bacterial surface proteins

Carlsson, F. *et al. Nature* **442**, 943–946 (2006)

In bacteria, the presence of a signal sequence at the amino terminus of a nascent protein tags this protein for secretion across the cytoplasmic membrane. Secretion is not uniform, however, and some bacterial cell-surface proteins show distinct localization patterns. What determines this localized secretion? Carlsson *et al.* suggest that the answer lies in the signal sequence. They examined the secretion of two *Streptococcus pyogenes* proteins that are known to have different localization patterns — the M protein localizes to the septum whereas PrtF localizes to the old poles of growing cells. The signal sequences of these two proteins were swapped and the localization of the hybrid proteins was analysed using quantitative immunogold electron microscopy. It was shown that the signal sequence of the M protein directs secretion to the septum (perhaps promoting binding of the M protein to the cell division complex) and the signal sequence of PrtF directs secretion to the old poles. Work to determine the exact motifs responsible is ongoing.

HOST RESPONSE

Natural killer T cells recognize diacylglycerol antigens from pathogenic bacteria

Kinjo, Y. *et al. Nature Immunol.* **7**, 978–986 (2006)

Natural killer T (NKT) cells, a specialized T-cell subset, do not recognize conventional peptide antigens presented by major histocompatibility complex molecules. Instead, NKT cells have been shown to recognize glycosphingolipid antigens from non-pathogenic *Sphingomonas* bacteria presented by CD1d, but researchers have been keen to identify any NKT-cell antigens expressed by pathogenic species. Kinjo *et al.* have now identified a new class of NKT-cell antigens expressed by the spirochaete *Borrelia burgdorferi*, the causative agent of Lyme disease. *B. burgdorferi* has an unusual outer membrane that contains no lipopolysaccharide but instead contains two glycolipids, a cholesteryl galactoside and a galactosyl diacylglycerol. Kinjo *et al.* found that the diacylglycerol activates both mouse and human NKT cells. The extent of activation is determined by the length of the acyl chain and the authors speculate that pathogenic bacteria could use alterations in chain composition as an immune evasion mechanism.

HIV

Autophagy is involved in T cell death after binding of HIV-1 envelope proteins to CXCR4

Espert, L. *et al. J. Clin. Invest.* **116**, 2161–2172 (2006)

Although the decline of uninfected and infected $CD4^+$ T-cell populations is a well-known consequence of HIV-1 infection, our knowledge of this process remains incomplete. It was previously known that HIV-1-infected $CD4^+$ T cells can trigger the apoptosis of bystander uninfected $CD4^+$ T cells through an interaction between the HIV envelope glycoprotein (Env) and the CXCR4 chemokine receptor. Now, reporting in the *Journal of Clinical Investigation*, Espert *et al.* provide *in vitro* evidence that the Env–CXCR4 interaction triggers autophagy and that the autophagic response not only leads directly to the death of uninfected cells but is also a prerequisite for the death of uninfected cells by apoptotic pathways. Further studies are required to determine whether this process contributes to $CD4^+$ T-cell depletion *in vivo*.