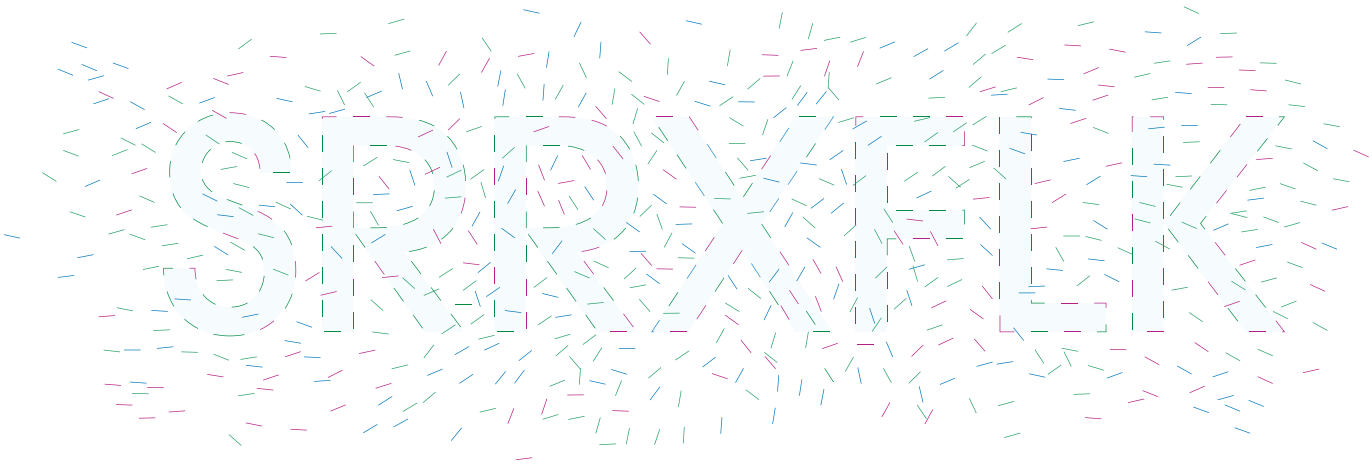

BACTERIAL SECRETION

Respiratory remnants

Some non-exported bacterial redox enzymes contain remnant twin-arginine signal peptides that can be reactivated into functional twin-arginine transport (Tat) export signals, according to a report in the latest issue of *Microbiology*.

The Tat pathway is a general secretory pathway that transports fully folded proteins across the cytoplasmic membrane of prokaryotes and the thylakoid membrane of chloroplasts. Substrate recognition occurs through a conserved amino-terminal tripartite signal peptide, which contains a canonical twin-arginine motif. In *Escherichia coli*, Tat substrates tend to be complex, oligomeric proteins such as respiratory enzymes, many of which contain a molybdenum cofactor. Previously, however, sequence analysis had revealed that in *E. coli* some non-exported molybdenum-dependent proteins, including the respiratory nitrate reductase NarG and biotin sulphoxide reductase BisC, contain an amino acid signature that resembles the twin-arginine motif. This led to the hypothesis that these so-called N-tail regions are remnants of Tat signal peptides that might have been active in a common ancestor.

Bérengère Ize and colleagues set out to investigate this hypothesis. They found that the N-tails of both NarG and BisC could be reactivated to form active Tat export signals by site-directed and random mutagenesis. For NarG, mutation of just 6 out of the 36 residues restored transport activity, and for BisC only 5 out of the 36 residues had to be mutated. However, these changes had profound implications for the functionality of both proteins. The mutated NarG could no longer bind to its chaperone, NarJ, so was unable to form a functional dimer with NarH and was rapidly degraded. The mutated BisC was also not functional, leading authors to speculate that the BisC N-tail contains a chaperone binding site, although a binding partner could not be identified.

> “the N-tails of both NarG and BisC could be reactivated to form active Tat export signals”

The authors conclude by addressing the obvious question of which came first, the Tat pathway or the non-exported enzymes? A basic local alignment search tool (BLAST) search revealed that most prokaryotic genomes that encode NarG also encode the TatC translocase. This indicates that the Tat system came first, and that the N-tail regions of proteins such as NarG represent remnant Tat signal peptides that have been retained as they are essential for key functions such as chaperone binding.

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ORIGINAL RESEARCH PAPER Ize, B. *et al.* Remnant signal peptides on non-exported enzymes: implications for the evolution of prokaryotic respiratory chains. *Microbiology* **155**, 3992–4004 (2009)