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Controlling CFTR protein folding

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Tudor Toma

Email: t.toma@ic.ac.uk

The mechanism by which a linear sequence of amino acids controls the folding of a protein into its unique three-dimensional structure remains incompletely understood. In the April 8 online edition [Nature Structural Biology](#), Christian Wigley and colleagues from [University of Texas Southwestern Medical Center](#), Dallas, show that a protein sequence can encode the native structure by preventing the formation of a misfolded structure.

Wigley *et al.* observed that a proline residue in the center of the third transmembrane helix of the cystic fibrosis transmembrane conductance regulator promotes correct folding by disfavoring alternate conformations. A genome-wide sequence analysis of transmembrane domains revealed a correlation between certain residues and proline, supporting the idea that this mechanism is a general one (*Nat Struct Biol* 2002, DOI: 10.1038/nsb784).

"Incorporation by nature of such 'negative folding determinants', aimed at preventing the formation of off-pathway structures, represents an additional mechanism by which folding information is encoded within the evolved sequences of proteins", concluded the authors.

References

1. Wigley WC, Corboy MJ, Cutler TD, Thibodeau PH, Oldan J, Lee MG, Rizo J, Hunt JF, Thomas PJ: A protein sequence that can encode native structure by disfavoring alternate conformations. *Nat Struct Biol* 2002, DOI: 10.1038/nsb784., [<http://www.nature.com/nsb/>]
2. University of Texas Southwestern Medical Center, [<http://www3.utsouthwestern.edu/>]