Title:	Replacement of the active surface of a thermophile protein by that of a homologous mesophile protein through structure-guided 'protein surface grafting
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Abstract:	Using several tens of rationally-selected substitutions, insertions and deletions of predominantly non-contiguous residues, we have remodeled the solvent-exposed face of a beta sheet functioning as the substrate-binding and catalytically-active groove of a thermophile cellulase (Rhodothermus marinus Cel12A) to cause it to resemble, both in its structure and function, the equivalent groove of a mesophile homolog (Trichoderma reesei Cel12A). The engineered protein, a mesoactive-thermostable cellulase (MT Cel12A) displays the temperature of optimal function of its mesophile ancestor and the temperature of melting of its thermophile ancestor, suggesting that such 'grafting' of a mesophile-derived surface onto a thermophile-derived structural scaffold can potentially help generate novel enzymes that recombine structural and functional features of homologous proteins sourced from different domains of life.
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