preservation of the protein structure in metal-free forms is a preferred feature in biological systems, it imposes constraints on the evolution of these proteins and may explain why evolution seems to have disfavoured highly charged metal clusters and why the more hydrophobic porphyrin systems dominate in higher organisms^{17,18}.

The observed structure of apoR2 raises the question of how a polypeptide can fold into a globular protein with an interior of several carboxyl residues (Fig. 3b), a situation that may be analogous to carboxyl group clustering in, for example, some ion channels¹⁹. The folding of a protein is a highly cooperative process; in the case of R2 the energy cost of the clustering of carboxyl side chains in the interior of the protein²⁰ must have been accounted for by other means. Hydrogen-bonding to polar side chains in the vicinity of the carboxyl residues partly reduces the effect of the charges (Fig. 3a). Most importantly, the folded state of the subunit is stabilized by extensive van der Waals interactions and hydrogen bonds between the unusually long helices of R2. These interactions must then stabilize the structure sufficiently for the energetically unfavourable clustering of internal carboxyl residues to be tolerated. □

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ERRATUM

Phosphorylation of the *S. cerevisiae* Cdc25 in response to glucose results in its dissociation from Ras

Eitan Gross, Doron Goldberg & Alexander Levitzki

Nature **360**, 762-765 (1992)

THE sentence starting on line 29 of this letter should read "After 1 min the cAMP levels decay to an intermediate level and, in parallel, Cdc25 reaches an intermediate state of phosphorylation that is higher than the state of phosphorylation of Cdc25 in glucose-starved cells (Fig. 1b, lanes 5 and 1, respectively)."

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