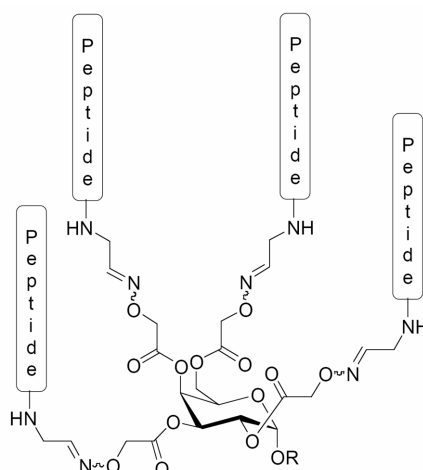


## CARBOPROTEINS: CARBOHYDRATES AS TEMPLATES FOR *DE NOVO* DESIGN OF PROTEINS

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*De novo* design of model proteins holds great promise for study of protein folding and for new tailored protein structural motifs [1]. It is also likely to become a powerful tool in nanobioscience and material science. We have recently described [2] the concept of carbohydrates as templates for *de novo* design of proteins and introduced the terms *carbopeptides* and *carboproteins* for this class of template-assembled synthetic proteins. The chemoselective oxime ligation of tetra-aminoxyacetyl functionalized carbohydrates and amphiphilic C-terminal peptide aldehydes provided 8 kDa carboproteins that fold to form 4- $\alpha$ -helix bundles according to CD spectroscopy and NMR H-D exchange studies. Interestingly, for some carboproteins we observed a clear effect by the template on the degree of  $\alpha$ -helicity. In one application towards nanobioscience, a thiol-functionalized carboprotein was shown to form self-assembled monolayers on Au surfaces and was extensively studied by scanning tunnelling microscopy (STM).



Here we report the synthesis of novel functionalized carboproteins comprised of peptide helices with His moieties or pyridyl substituents. We also introduce the use of new templates. A combinatorial ensemble of carboproteins, combining sets of peptides and sets of di- and tetravalent carbohydrate templates, were prepared. Their folding was studied by CD-spectroscopy, confirming previous template effects; SEC indicated the expected dimerization of ‘half 4-helix’ carboproteins.

Thus, we believe we have demonstrated that carbohydrates are useful not only in peptide design, as shown by several groups, but also as distance-geometry directing templates in protein design.

[1] DeGrado, et al.. *Annu. Rev. Biochem.*, 68 (1999) 779.

[2] Brask et al. *J. Am. Chem. Soc.*, 125 (2003) 94, and references herein.