Prof. Dr. Carlo Unverzagt

Universität Bayreuth

"Glycoproteins: highly effective natural products as new synthetic targets"

Freie Universität, SFB 765 am 24. November 2009, 16 Uhr s.t.

Abstract:

The use of recombinant therapeutic glycoproteins is one of the fast growing applications in human therapy. Typical for these secretory and cell surface proteins is the attachment of oligosaccharides to asparagine residues (N-glycosylation). Despite many efforts in this field the function of N-glycosyation is poorly understood, which is mainly caused by the lack of pure glycoproteins. Since purification of natural glycoproteins is quite tedious due to heterogeneity in the sugar part, the total synthesis of homogeneous glycoproteins has become an attractive target. Native chemical ligation has enabled the synthesis of entire proteins including those carrying posttranslational modifications. We have chosen this approach using bovine ribonuclease and human interleukin 6 as model glycoproteins.

Ribonuclease (RNase) is an established model system for protein synthesis and refolding. RNase C is containing a single complex type N-glycan at Asn 34. Ligations were planned in a sequential manner by using a combination of recombinant and chemically synthesized protein segments. In order to expand this approach to the synthesis of libraries of glycoforms several new challenges need to be met. This includes the synthesis of the desired N-glycans and the convenient coupling of these oligosaccharides to the peptide chains.