There is a growing interest in the development of novel synthetic methodology for conformational restriction of peptides in order to mimic the bioactive conformation as closely as possible. Ring-closing metathesis (RCM) has been used for this purpose, since it displays an extraordinary functional group tolerance and high yield of cyclization. Thus, RCM has been used to prepare mimics of nisin and to mimic the central ring system of the antibiotic vancomycin. Similar to the ring-closing metathesis reaction, the Sonogashira coupling reaction displays also a broad functional group tolerance as well as, more recently, the Cu(I) catalyzed Huisgen 1,3-dipolar cycloaddition ("click") reaction. Furthermore, a tremendous challenge in the design and synthesis of protein mimics is replacement of the greater part of a protein by a relatively small synthetic scaffold. This scaffold may provide the right orientation and rigidity of peptide sequences, which are crucial for the biological activity. For this purpose we have developed CycloTriVeratrylene (CTV), TriAzaCyclophane (TAC) as well as multi-arm amino acid based dendrimeric scaffolds. CTV was used for the design and synthesis of collagen mimics. The selectively addressable synthetic TAC-scaffold was used for mimicry of discontinuous epitopes present in a protease inhibitor and in whooping cough pertactin by confined presentation of several different peptide arms. This approach yielded protective antibodies. As such it will be employed to design and construct new synthetic vaccines that induce functional antibodies of for example gp120.

Universitätshauptgebäude, Hörsaal 3, Donnerstag, den 2. Dezember 2010 um 17 Uhr c.t

gez. Prof. Dr. Thomas Koop, Prof. Dr. Jochen Mattay, Prof. Norbert Sewald