UNIVERSITÀ DEGLI STUDI FIRENZE

DIPARTIMENTO DI CHIMICA "UGO SCHIFF"

PeptLab UNIFI

Prof. Dr. APHRODITE KAPURNIOTU

Technische Universität München
Division of Peptide Biochemistry
85354-Freising (Germany)

Venerdí 5 LUGLIO 2019

Ore 10:00

Aula 43

Dipartimento di Scienze Farmaceutiche

Polo Scientifico dell'Università di Firenze
Via Ugo Schiff 6 – 50019 Sesto Fiorentino

Terrà una conferenza dal titolo:

EXPLOITING CROSS-AMYLOID PEPTIDE INTERACTIONS TO DESIGN INHIBITORS OF AMYLOID SELF-ASSEMBLY

la S. V. è invitata a partecipare.

Prof. Piero Baglioni
(Coordinatore del Dottorato)

Prof. Anna Maria Papini
(Coordinatore di PeptLab)

Exploiting cross-amyloid peptide interactions to design inhibitors of amyloid self-assembly

Aphrodite Kapurniotu,
Technische Universität München, Division of Peptide Biochemistry, 85354-Freising, Germany

Amyloid self-assembly is linked to more than 30 devastating cell-degenerative diseases. Increasing evidence suggests that "cross-amyloid" interactions modulate amyloidogenesis; such interactions might thus link pathogenesis of different amyloid diseases to each other. For instance, Alzheimer's disease (AD) and type 2 diabetes (T2D) appear to be linked to each other. A possible molecular link between the two diseases could be the interaction between their key amyloid polypeptides Aβ (AD) and islet amyloid polypeptide (IAPP).[1]

However, cross-amyloid interactions can be also used to generate potent peptide-based inhibitors of amyloid self-assembly. In fact, we earlier designed conformationally constrained, non-amyloidogenic and bioactive analogs of full length IAPP, a glucose regulatory neuropeptide, as potent inhibitors of amyloid self-assembly of both IAPP and Aβ.[1-3] More recently we designed a series of IAPP-derived peptides as mimics of putative IAPP interaction surfaces with Aβ.[4] These so-called "interaction surface mimics" (ISMs) are linear peptides designed by linking "hot segments" of the IAPP interaction surface to each other via tripeptide linkers. ISMs are able to block amyloid self-assembly of Aβ, IAPP or both peptides; thereby, the nature of the linker determines both inhibitory potency and target selectivity. Most recently, we designed macrocyclic peptides as a novel class of nanomolar inhibitors of amyloid self-assembly of Aβ or both Aβ and IAPP.[5] These peptides, termed MCIPs (macrocyclic inhibitory peptides), were designed to mimic IAPP interaction surfaces by maintaining only minimal IAPP-derived self-/cross-recognition elements. Systematic sequence optimization yielded an Aβ-selective MCIP exhibiting high resistance toward human plasma proteases and the ability to cross human BBB in a cell model.

Here I will present our studies on ISMs and MCIPs. Due to their favorable properties, some of these peptides are promising leads for anti-amyloid drugs and templates for peptidomimetics for targeting pathogenic amyloid self-assembly in AD, T2D or both as yet incurable diseases.

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2. L. M. Yan, M. Tatarek-Nossol, A. Velkova, A. Kazantzis, A. Kapurniotu Proc Natl Acad Sci U S A (2006), 103, 2046.
3. L. M. Yan, A. Velkova, M. Tatarek-Nossol, G. Rammes, A. Sibaev, E. Andreetto, M. Kracklauer, M. Bakou, E. Malideli, B. Goeke, J. Schirra, M. Storr, A. Kapurniotu Angew Chem Int Ed Engl (2013), 52, 10378.
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5. A. Spanopoulou, L. Heidrich L, H. R. Chen, C. Frost, D. Hrle, E. Malideli, K. Hille, A. Grammatikopoulos, J. Bernhagen, M. Zacharias, G. Rammes, A. Kapurniotu, Angew Chem Int Ed Engl. (2018), 57, 14503.

Prof. Dr. Aphrodite Kapurniotu

Professor Kapurniotu performs research in the field of peptide biochemistry. A major aim of her research is to develop novel peptide-based molecules as leads for therapeutics and tools for understanding the molecular mechanism of amyloid diseases, in particular Alzheimer's disease (AD) and type 2 diabetes (T2D). In addition, her research aims at characterizing interactions of inflammatory chemokines in atherosclerosis and the development of peptide-based inhibitors. She uses chemical, biochemical and biophysical methods. Professor Kapurniotu studied Chemistry in Athens and obtained her PhD degree in Tübingen in 1990. She performed postdoctoral studies at Rutgers University with Prof. J. W. Taylor and the Picower Institute for Medical Research (1992-95) in the US with Professors Richard Bucala and Anthony Cerami. She was group leader at the University of Tübingen between 1995-2002 and completed her "Habilitation" in Biochemistry in 2001. She moved to the RWTH Aachen (2002) where she headed a biomedical research group (2002-2007). In 2007, she was appointed as a Professor for Peptide Biochemistry at the Technical University of Munich (TUM).

Selected Publications

Spanopoulou A., Heidrich L., Chen H.R., Frost C., Hrle D., Malideli E., Hille K., Grammatikopoulos A., Bernhagen J., Zacharias M., Rammes G., Kapurniotu A. (2018). Designed macrocyclic peptides as nanomolar amyloid inhibitors based on minimal recognition elements. Angew Chem Int Ed Engl. 57; 14503-14508.

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