AG Molekulare Bibliotheken

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Homepage:
http://immunologie.charite.de/forschung/ag_volkmer/
http://openwetware.org/wiki/Molecular_Recognition_Laboratorium

Forschungsgebiet:

The AG Volkmer emerges from a strong training in peptide chemistry and cultivates its expertise in the synthesis and preparation of peptide/peptoide probes, either as core service or to meet the demands of our own research in cellular biology and molecular medicine.

The objectives of our research principally spread around three main topics: profiling the binding specificity of protein recognition modules, analyzing the diagnostic potential peptide-based analyte capture assays, and exploring the potential of peptide/peptoide probes to define or modulate specific therapeutic strategies.

Profiling the binding specificity of protein recognition modules
Protein recognition modules (PRM) are non-catalytic domains of protein structure dedicated to read molecular motifs of primary structure and post-translational modifications of proteins. Reading or recognition is not restricted to protein motifs, as shown by the emerging field of epigenetics. It is clear that methylation and other signatures on DNA are also recognized by modular structures of nuclear factors.

The tinkering of evolution has repeatedly duplicated and diverged different structural modules resulting in several homology families with some degree of functional conservation. This is observed as regular expressions of short linear motifs that can be recognized by a PRM family and by specific affinity traits of individual PRMs.

We aim to identify key events in cellular processes of information reading and transduction. Success in such aim translates to engineering congruent interaction networks, complementing drug efficiency and designing new therapeutic strategies, as has been shown

by our group with several domains, i.e. WW domains in X-linked intellectual disorders and mechanosensing, SH3 domains in endocytosis, as well as PDZ domains in cystic fibrosis.

Analyzing the diagnostic potential of peptide-based analyte capture assays
We intend to focus away from single biomarker for diagnosis and use either validated collections or agnostic collections of peptide probes to analyze complex biological samples. The former approach relies on the use of peptide probes known to interact with one or multiple target biomarkers for a specific pathology, the later one relies on extensive stochastic peptide probes to capture eventually unknown analytes in the sample that can be used as a diagnostic pattern of detection signals upon a multiplex binding assay.

The development of these approaches can be estimated from reports of our group and cooperation partners inside as well as outside RCIS. These reports show the difficulties and potential of the use of peptide probes to analyze blood samples and diagnose hypersensitivity, autoimmune responses, and immunological responses to infection.

Exploring the therapeutic potential of peptide/peptoid probes
The flag ship of this research venue derives from the unique expertise for generating immobilized but C-terminal exposed peptide probes and accurate experience with PDZ specificity profiles. A peptide probe has been design to selectively inhibit the CFTR–CAL interaction —relevant in cystic fibrosis— without affecting the biologically relevant PDZ competitors NHERF1 and NHERF2.

In this venue of research we also explore the potential of cell penetrating peptides to be applied as vector to transport drug probes, such as the CFTR-CAL inhibitor, across the cell membrane.

Spezialtechniken:

Analytical biochemistry (HPLC, MS), peptide chemistry (synthesis, immobilization, conjugation, and modifications), modular recognition assays (profiling peptide binding specificity of WW, SH3, PDZ, and other protein domains), diagnostic peptide binding signatures (analysis of biological samples via steady-state binding assays), cell-penetrating peptides, SPR-based real-time binding assays.

Publikationen:

Bleeke, M., Fest, S., Huebener, N., Landgraf, C., Schraven, B., Gaedicke, G., Volkmer, R., and Lode, H.N. (2009). Systematic amino acid substitutions improved efficiency of GD2-peptide mimotope vaccination against neuroblastoma. Eur. J. Cancer *45*, 2915–2921.

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Tapia, V., Bongartz, J., Schutkowski, M., Bruni, N., Weiser, A., Ay, B., Volkmer, R., and Or-Guil, M. (2007). Affinity profiling using the peptide microarray technology: a case study. Anal. Biochem. *363*, 108–118.

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Volkmer, R., Tapia, V., and Landgraf, C. (2012). Synthetic peptide arrays for investigating protein interaction domains. FEBS Lett. *586*, 2780–2786.

Drittmittelprojekte:

DFG	Ein label-freies optisches Sensorsystem in Silizium: Bestimmung der thermodynamischen und kinetischen Kenngrößen von Protein-Ligand Wechselwirkungen
	VO 885/8-1, 01.05.2014-30.4.2017
NIH	Preclinical development of CFTR stabilizers targeting the CAL PDZ domain.
	1R01DK101541-01, 01.07.2014 – 30.04.2018

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Prof. Jörg Höhfeld, Bonn, Deutschland	Hsc70-associated chaperone complex
Prof. Karola Rück-Braun, Berlin	optical biosensor
PD Dr. Jürgen Bruns	optical biosensor
Prof. Michel Steinmetz, Villingen, Schweiz	microtubule cytoskeleton regulation