

Glycostructures and sphingolipids in Infectious diseases

Prof. Dr. Jürgen Seibel

Institut für Organische Chemie,, Julius-Maximilians-Universität Würzburg

E-Mail : seibel@chemie.uni-wuerzburg.de

In spite of the availability of preventive strategies, infectious diseases continue to be a major threat worldwide. Therefore, there is a demand for continuous development of anti-infective or immuno-therapeutic strategies, in particular for conditions where conventional interventive means are not available, prohibited or fail. Because sphingolipids are major components of membranes, sphingolipid biosynthesis and metabolism and availability of their signaling inert or bioactive species substantially affects the biophysical properties of membranes and the subcellular redistribution of receptors and signaling complexes. Targeted intervention of sphingolipid turnover has proven to be a successful strategy in inflammation, but its potential as a target in controlling infectious diseases at the level of metabolism and immune controls requires further definition.

The lecture will show how we identify and validate targets for novel anti-infective strategies targeting infectious diseases at the level of modulation of the sphingolipid metabolism. As a long-term perspective, rationally defined synthetic sphingolipid analogues will be evaluated for therapeutic options in the respective different models of infectious diseases models.

Literature

- 1) M. Zimniak, L. Kirschner, H. Hilpert, N. Geiger, O. Danov, H. Oberwinkler, M. Steinke, K. Sewald, J. Seibel & J. Bodem. The serotonin reuptake inhibitor Fluoxetine inhibits SARS-CoV-2 in human lung tissue. *Sci Rep* **2021**, 11, 5890. <https://doi.org/10.1038/s41598-021-85049-0>; M. Zimniak, L. Kirschner, H. Hilpert, J. Seibel, J. Bodem. The serotonin reuptake inhibitor Fluoxetine inhibits SARS-CoV-2. bioRxiv, doi: <https://doi.org/10.1101/2020.06.14.150490>, **2020**.
- 2) Julian Fink, Fabian Schumacher, Jan Schlegel, Philipp Stenzel, Dominik Wigger, Markus Sauer, Burkhard Kleuser, and Jürgen Seibel. Azidosphinganine enables metabolic labeling and detection of sphingolipid de novo synthesis, *Org. Biomol. Chem.* **2021**, 19, 2203-2212.
- 3) R. Götz, T. Kunz, J. Fink, F. Solger, J. Schlegel, J. Seibel, V. Kozjak-Pavlovic, T. Rudel, M. Sauer. Nanoscale imaging of bacterial infections by sphingolipid expansion microscopy. *Nat. Commun.* **2020**, 11, 6173.
- 4) N. Wolf, L. Kersting, C. Herok, C. Mihm, J. Seibel. High Yielding Water-Soluble Asymmetric Cyanine Dyes for Labeling Applications. *J. Org. Chem.* **2020**, 85, 9751–9760.
- 5) K. Rajeeve, N. Vollmuth, S. Janaki-Raman, T. Wulff, M. Schmalhofer, W. Schmitz, A. Baluapuri, C. Huber, J. Fink, F. R. Dejure, E. Wolf, W. Eisenreich, A. Schulze, J. Seibel, T. Rudel. Reprogramming of host glutamine metabolism during Chlamydia trachomatis infection and its key role in peptidoglycan synthesis. *Nat. Microbiol.* **2020**, 5, 1390–1402.
- 6) J. Lang et al. Acid ceramidase of macrophages traps herpes simplex virus in multivesicular bodies and protects from severe disease. *Nat. Commun.* **2020**, 11, 1338. doi:10.1038/s41467-020-15072-8