

**First author:**

Title : Prof.

Firstname: Alesia A.

Last name: Tietze

Institutions: University of Gothenburg  
Department of Chemistry & Molecular Biology,  
Division of Organic and Medicinal Chemistry  
Address: Kemigården 4, 412 96 Göteborg,  
Sweden

Email: alesia.a.tietze@gu.se

Phone: +46 31 786 6248

**Co-authors (with their institutions) :**

**Andreas C. Baumruck, Lena K. Müller,**  
Darmstadt University of Technology, Clemens-  
Schöpf Institute of Organic Chemistry  
and Biochemistry

**Daniel Tietze,** University of Gothenburg  
Department of Chemistry & Molecular Biology

**Biography**

Assistant Professor in Medicinal Chemistry with focus on **total synthesis of bioactive peptides**, i.e. cysteine-rich peptides, which are derived from biologically-active natural sources (i.e. cone snails, spiders, snakes), their targets (**membrane proteins**) and their structural analogues as well as engineering of bioinspired materials based on functional peptides/proteins and artificial carriers (i.e. nanopores, polymers). Alesia A. Tietze received her M.Sc. in Chemistry in 2008 and her PhD in Biochemistry in 2011 from the Friedrich-Schiller University of Jena, Germany. She did her post-doctoral studies at the Iowa State University in Ames/Iowa, USA and came back to Germany in 2013 to start her independent career as junior research group leader at the Technische Universität (TU) Darmstadt. In 2014 she received Liebig Fellowship from the Fonds of the Chemical Industry which was two times positively evaluated and prolonged. In 2017 she was also selected and appointed as Athene Young Investigator from the TU Darmstadt. In 2018 she was recruited as Assistant Professor in Medicinal Chemistry to the University of Gothenburg within the Wallenberg Centre of Molecular and Translational Medicine

**Abstract title: Chemical synthesis of membrane-associated peptides: studies on influenza virus B protein BM2**

Membrane-associated proteins play a key role in the disease's progression, such as multiple sclerosis, cancer, due to their special role as gateways between the cell interior and its environment. <sup>[1-3]</sup> The unique 3D-structure of each membrane protein enables functional studies and development of new drugs. However, providing enough material represents a challenging step. The chemical synthesis of membrane proteins or their functional fragments could solve this problem, moreover, offering the basis for modifying and customizing these class of proteins. Design of SPPS conditions and especially of native chemical ligation (NCL) is one of the limiting steps in membrane protein synthesis.

In two associated studies we developed NCL approaches for hydrophobic, poor soluble peptides. An influenza B virus proton channel BM2 represent possible drug target side for the treatment of the seasonal flu and its molecular structure has not been determined yet.<sup>[4]</sup> Therefore, we developed our synthetic strategies using this protein.

In a first study we developed a removable solubilizing unit attached to a thioester-forming rearrangement Hmp-group. By attaching polylysine sequence (Lys<sub>5</sub>) to Hmp we increased the solubility during peptide purification and NCL yielding > 90% of desired product.<sup>[5-6]</sup>

In a second study we used ionic liquid as an alternative media for NCL. By a detailed investigation with small organic, sulfur-containing model compounds and cystine-containing peptides we were able to understand the nature of possible interactions with ionic liquids.<sup>[7]</sup> Finally, we found conditions where ionic liquid can be used as a solvent only and is not involved in chemical transformations as a reactant. Applying these findings, we developed an efficient approach and applied it successfully for BM2(1-51) synthesis.

#### Literature:

- [1] L. Raibaut, et al. *Chem. Soc. Rev.*, **2012**, 41, 7001–7015.
- [2] G.G. Kochendoerfer, et al. *Biochemistry* **1999**, 38, 11905-11913.
- [3] J. Tailhades, et al. *J. Pept. Sci.* **2015**, 21: 139–147.
- [4] J Wang et al. *Nature Structural & Molecular Biology*, **2009**, 16, 1267–1271.
- [5] F. Liu, et al. *J. Org. Chem.* **2013**, 78, 9848–9856.
- [6] A. Baumruck, D. Tietze, L. Steinacker, A. Tietze, *Chem. Sci.*, **2018**, 9, 2365-2375.
- [7] Baumruck, A.C., Tietze, D., Stark, A., Tietze, A.A.\*, **2017** *J. Org. Chem.*, 82 (14), 7538–7545.