Summary

Since its inception in 2006, the *Zentrum für Innovationskompetenz* (ZIK) **HALOmem** has served as a nucleus for biochemical, biophysical and structural analyses of integral membrane proteins, consolidating and expanding the strong protein biochemical focus in Halle. A technology platform has been developed that combines the two defining features of membrane proteins: the active protein component itself and the equally important surrounding membrane. This inherent complexity represents a major stumbling block to pharmaceutical drug design and provides the underlying rationale for **HALOmem**. Uniting the expertise of the new groups of the first funding period (junior group I "Membrane Protein Biochemistry" and junior group II "Biophysical Chemistry of Membranes" led by Dr. Mikio Tanabe and Prof. Kirsten Bacia, respectively) with that of the initiators (NMR, Prof. Balbach and X-ray crystallography, Prof. Stubbs) has resulted in a strong partnership that has attracted further collaboration partners in and beyond Halle. The ZIK **HALOmem** is optimally integrated within Central Germany as witnessed by its participation in a variety of recent joint research projects. ZIK **HALOmem** has attained international visibility, stimulated interest from industry, and attracted young independent researchers seeking association with **HALOmem**.

Already within the first five years, the proofs of principle aspired to in the initial *Strategiekonzept* have been achieved, paving the way for contributions to commercial applications. Following a tenure track system especially conceived for **HALOmem**, the appointment of Jun. Prof. Bacia to a W2-Professorship in December 2014 guarantees the existence of **HALOmem** beyond the BMBF funding period. Furthermore, **HALOmem** will be an integral fixture of the new building "Proteinzentrum Charles Tanford" for protein research at the Martin- Luther-University Halle-Wittenberg. Thus the foundations for the continuance and expansion of ZIK **HALOmem** have been laid.

Frequently, membrane proteins are found as part of much larger macromolecular complexes. This fact is not only of academic relevance – the interaction of a potential therapeutic will depend strongly on whether the target protein is found in isolation or in association with other partners. Thus the characterisation of membrane protein complexes on the nanometer and subnanometer scale will be a major focus of the forthcoming ZIK **HALOmem** II. In order to achieve this, we plan to establish a junior group working on the structural analysis of membrane protein complexes (group III "Cryo-Electron Microscopy of Membrane Protein Complexes"). As a result of previous developments within **HALOmem**, a high resolution cryo-electron microscope for the structural analysis of biological macromolecules could recently be acquired. In addition to this BMBF-funded strategic investment, substantial support could be obtained from Saxony Anhalt for peripheral equipment as well as the necessary operative personnel. The hereby established state-of-the-art cryo-EM facility therefore provides a strong incentive for recruitment of excellent candidates.

Parallel to this, a second group is planned that will focus on structure biological studies of membrane proteins in a diagnostic and/or therapeutic context (group IV "Biophysical Characterisation of Medically Relevant Membrane Proteins"). Valuable insights into the targeting of medically relevant membrane proteins are to be gained from the investigation and correlation

of biochemical and biophysical properties (including thermodynamics, kinetics and ligand binding) with structural and dynamic data. Through cultivation of the promising industry contacts established during the first period, we expect joint projects with applications in industry to bear fruit in the forthcoming period.

Synergies between the proposed new (applied and analytical) and existing (biochemical and physicochemical) groups promise a rewarding unification of *in vivo* (medically relevant) and *in vitro* (experimentally accessible) approaches. In turn, research will become increasingly focused on the understanding and treatment of diseases in which membrane proteins are involved. The proposals detailed in this *Strategiekonzept II* serve to guarantee the continuity of ZIK **HALOmem** as an effective instrument for studies of the structure and dynamics of membrane proteins and their complexes at the Martin-Luther-University Halle-Wittenberg.