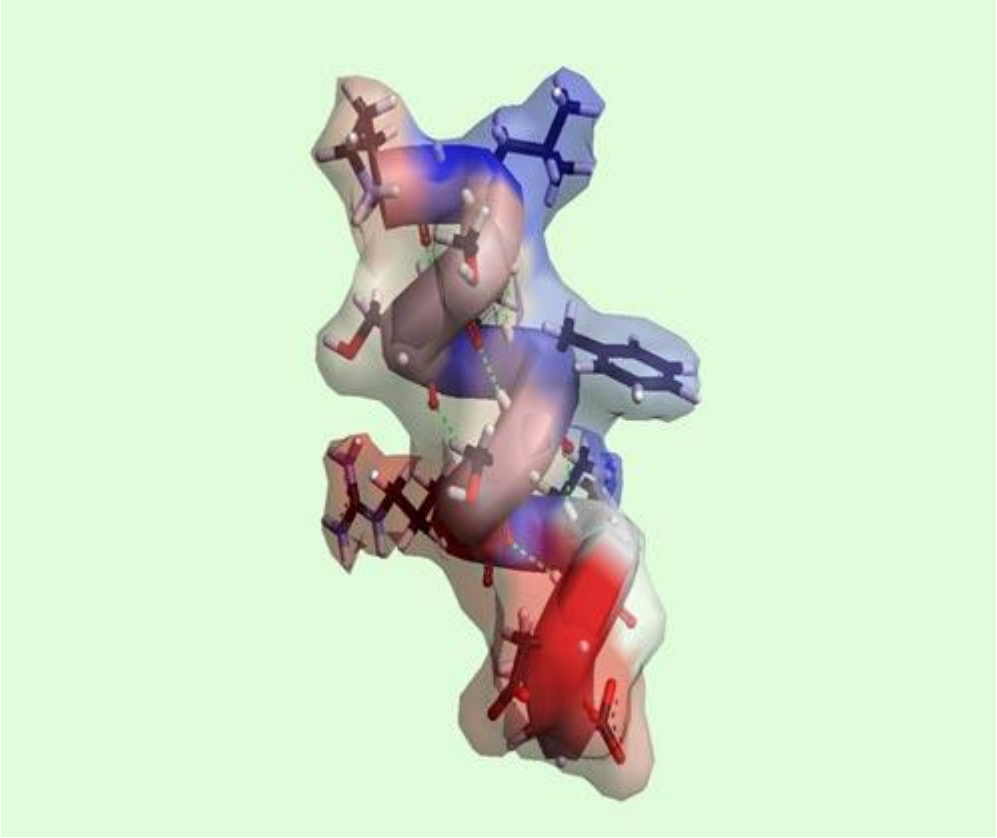
Development of novel strategies for gene and protein transfer into cells and tissues

Recently, we identified a novel membrane-permeable peptide within the surface protein of HBV that plays a crucial role for viral entry into the cell. Fusion of this peptide designated TLM (translocation motif) with other peptides or proteins results in the formation of membrane-permeable molecules. This technology represents a novel approach for the delivery of molecules across cellular membranes into cells and tissues and opens novel routes for drug delivery.



Structure of the HBsAg-derived TLM peptide: The TLM peptide encompasses 12 amino acids that form an amphipathic alpha helix. Source: PEI

We are using this approach to interfere with multiple signal transduction cascades by producing cell-permeable dominant-negative mutants of specific key regulators of these pathways. Moreover, we are designing cell-permeable, TLM-fused peptides with the goal of dissociating protein/protein interactions, eventually aiming at interfering with viral morphogenesis.

By fusion of TLM-peptides to virus-like particles (vlps) we generated membrane permeable particles that serve as a novel efficient tool for gene transfer (Brandenburg et al., 2005) combining the advantages of viral and non viral gene transfer. At present, we are using these membrane-permeable vlps as a carrier for HCV-specific antigens in order to improve their antigenicity thus leading to the induction of a robust B- and T-cell response.