“Biophysical investigations of histidine-rich designer peptides with a wide range of biomedical applications”

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Abstract:

The synthetic LAH4 peptides were designed to investigate the interactions that determine the membrane topology of helical peptides (1). Their core consists of alanines, leucine and four histidines arranged to form an amphipathic helix, as well as two lysines at each terminus. Through protonation of its histidines (pKs between 5.4 and 6.0) the alignment of the helices is transmembrane at neutral pH and in-plane at pH <5.5 (1).

The LAH4 peptides exhibit membrane pore-formation and antimicrobial action at both neutral and at acidic pH including against clinical isolates where the low pH configuration is more active (2). The LAH4 peptides have been found to also exhibit potent DNA and siRNA transfection activities (3). Therefore, they can act as a non-viral vectors and have indeed been used for the delivery of quantum dots or protein-based vaccines. Furthermore, transduction by adeno-associated viruses or lentiviruses is enhanced by LAH4 (4). Furthermore, non-peptidic mimetics of this family of peptides have been developed for transfection (5). Recent and ongoing biophysical, NMR structural and cell biological investigations will be reported which aim to understand these activities at atomic resolution (3, 6-8).

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