Unravelling the mode of action of membrane-active drugs

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Background

A wide variety of drugs interact with membranes. Antimicrobial drugs, viral fusion inhibitors and analgesic compounds are among them. At the molecular biophysics lab (Faculty of Sciences, University of Lisbon, Portugal), we use optical spectroscopies to unravel the mechanism of action of membrane-active drugs, mainly peptides. The knowledge on the mechanism of action of these drugs helps developing second-generation drugs, which are more effective.

Outcomes

- New antimicrobial molecules
- New analgesic drugs

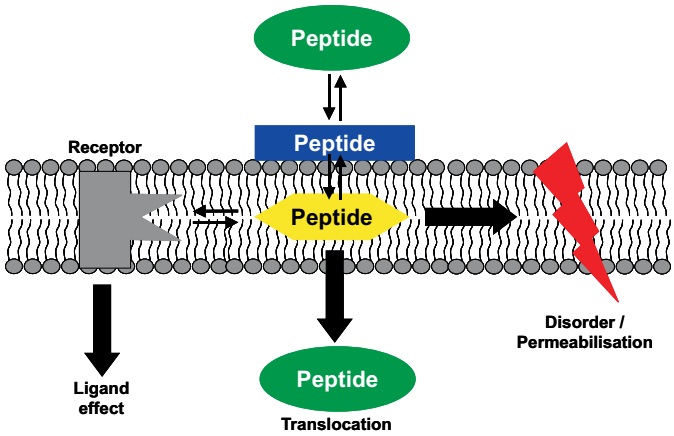

Figure 1 - Outline of peptide-membrane interactions. Peptides in contact with membranes may change conformation, which may facilitate proper binding to a receptor, a physiological effect resulting there from Peptides may also exert local specific effects like disorder and permeabilisation (e.g. AMPs – Antimicrobial peptides). Other peptides have the ability to translocate through the membrane, having no apparent effect in the lipid bilayer. (Eur Biophys J (2006) 35: 92–103)

Progress to date

Proof of concept only (for new drugs).
The role of membranes in the mode of action of some commercial drugs has been elucidated (e.g. *Biochem. J*. (2004) **377**, 1-4; *J. Am. Chem. Soc*. (2004) **126**, 14758-14763).

Things still to do

Animal tests for the new analgesic drug

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