What's the molecular meaning of MIC when working with AMPs? Lessons from the peptides Omiganan and BP100

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Antimicrobial peptides (AMPs) omiganan (H-ILRWPWWPWRRK-NH_2) and BP100 (H-KKLFKKILKYL-NH_2) were studied and their interaction with model bilayers was characterized. Marked differences in interaction patterns and in functional properties of the peptides were observed when high peptide:lipid ratios in the membrane were reached. These occurred for both peptides, despite their being unrelated in sequence and in occurrence in nature. Such events at high membrane coverage could represent the molecular scale equivalent of the conditions at which the antimicrobial activity of the peptides is triggered. The physiological plausibility of the low lipid:peptide ratios at these transitions (less than 10 phospholipids per peptide molecule) was demonstrated by a simple model that takes into account an estimate of the amount of lipid per bacterium and the bacterial concentration in minimum inhibitory concentration (MIC) assays. The results of this analysis, together with the partition constants obtained towards bacterial membrane models, indicate that these peptides are expected to reach, at the MIC, precisely those high concentrations in the membrane. In addition, surface charge neutralization was shown to occur in these conditions. Activity triggered at high membrane coverages is thus a possible and likely characteristic not only of these peptides but also of any displaying high enough membrane affinity and micromolar MICs, which is common amongst AMPs. Additionally, insight was gained regarding the mechaninsms of cytotoxicity towards mamallian cells, indicating that cell membrane disruption might not be the lethal process.

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