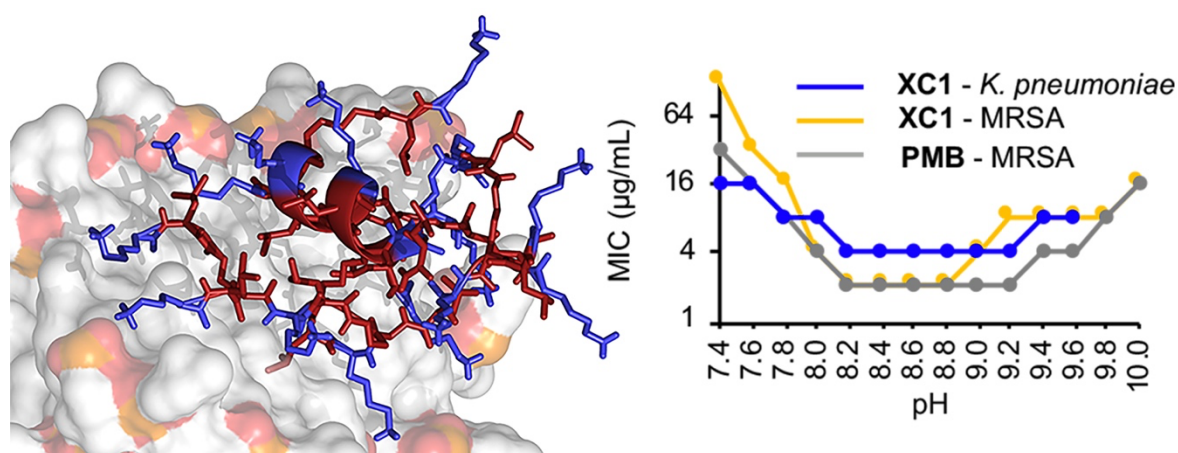


## The Antibacterial Activity of Antimicrobial Peptide Dendrimers and Polymyxin B Increases Sharply Above pH 7.4

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Recently we reported antimicrobial peptide dendrimer (AMPD) **G3KL** and **T7** with potent activities against *P. aeruginosa* and *A. baumannii*, two of the most problematic antibiotic-resistant nosocomial pathogens<sup>[1][2]</sup>. In our efforts to develop new AMPDs against Gram-negative bacteria, we investigated their activity at acidic and basic pH, which correspond to the conditions of the site of bacterial infections on skin or biofilms and chronic wounds respectively. Removing the eight low pKa amino termini by substituting the N-terminal lysine residues with aminohexanoic acid in our reference dendrimer **G3KL** provided the modified peptide dendrimer **XC1** with a broader pH-activity range. Furthermore, we discovered that raising the pH to 8.0 reveals strong activities against *Klebsiella pneumoniae* and methicillin at pH 7.4, an effect also observed with polymyxin B and tentatively assigned to stronger binding to the bacteria at higher pH as observed with a fluorescence labeled dendrimer analog. This work has been published in *Chemical Communication*.<sup>[3]</sup>



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[2] T. N. Siriwardena, A. Capecchi, B.-H. Gan, X. Jin, R. He, D. Wei, L. Ma, T. Köhler, C. van Delden, S. Javor, J.-L. Reymond, *Angew. Chem. Int. Ed.* **2018**, *57*, 8483–8487.

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