Synthesis, Antibacterial and Anti-Biofilm Potential of Human Autophagy 16 Polypeptide and Analogues

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With bacteria gaining resistance over conventional antibiotics, novel antibiotics need to be developed. Peptides, due to their wide range of activity and potency can be excellent platforms as novel antibiotics.[1] In this study we report a novel family of AMPs derived from the human Atg16.[2] The rationale for our study was to determine whether Atg16, the human autophagy polypeptide, similar to other cationic peptides would be antibacterial and, if so, to determine its spectrum of activity, potency, mechanism of action and engineer more potent analogues. The results of our assays demonstrate that the human autophagy 16 polypeptide (Atg16) has antibacterial and antibiofilm potential, perturbs both Gram positive and negative bacterial membranes and subsequently also produces ROS in compromised bacteria. Engineered Atg 16 analogues containing 1- and 2-naphthyl alanines showed significant enhancement of antibacterial activity and eradicated biofilms while also possessing negligible hemolysis of mouse erythrocytes. This new family of antibacterial peptides are promising candidates in the fight against bacterial biofilms, responsible for several thousand deaths annually which are predicted to rise into the millions.

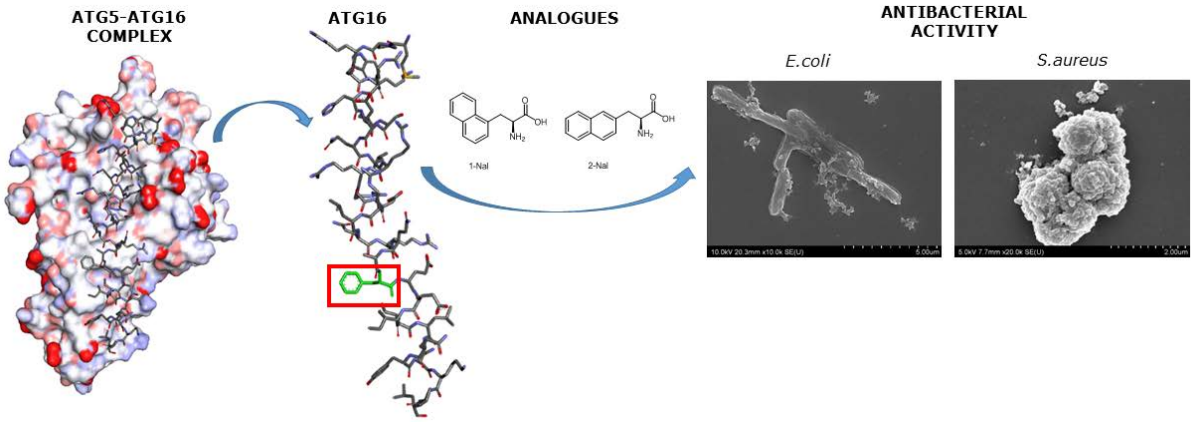

Figure 1. Engineered Atg 16 analogues containing 1- and 2-naphthyl alanines showed significant enhancement of antibacterial activity

1. De Zoysa, G. H.; Cameron, A. J.; Hegde, V. V.; Raghothama, S.; Sarojini, V. *Journal of Medicinal Chemistry* **2015,** *58*, 625-639.
2. Otomo, C.; Metlagel, Z.; Takaesu, G.; Otomo, T. *Nat Struct Mol Biol* **2013,** *20*, 59-66.