Antimicrobial Peptide Derivatives as Potential Drug Candidates for Ebola Virus Disease

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Purpose: Ebola virus (EBOV) can cause severe and fatal hemorrhagic fever in humans. Being capable of causing large-scale epidemics, EBOV also emerges as a global security threat. Therefore, it is critical to develop preventive and therapeutic drugs for Ebola virus disease (EVD) so we can be better prepared for future incidents. Currently, there are only a handful of experimental drugs in clinical trials for EVD. The goal of this study is to determine if cathelicidin antimicrobial peptide (AMP) LL-37 and its derivatives can inhibit EBOV infection. Methods: Ebola virus-like particles (eVLPs) were used as an experimental "surrogate" for EBOV. Vero (a money cell line) and 293 T (a human cell line) were used as the host cells for eVLP infection. LL-37 and its derivatives were tested for their effects on eVLP infection. Results: Two LL-37 derivatives efficiently blocked eVLP infection in both monkey and human cell lines at concentrations that do not induce cytotoxicity. Interestingly, these derivatives can synergize with an Ebola-neutralizing antibody to further block eVLP infection. Using serum samples from EBOV survivors as the source of neutralizing antibodies, LL-37 derivatives also demonstrated synergistic effects in blocking eVLP infection. Conclusions: We identified two AMP derivatives that can effectively inhibit EBOV pseudovirus infection when used alone and in combination with virus-neutralizing antibodies. Our observations need to be further validated using live EBOV and in animal models. Because of the associated low-cost, AMP derivative peptides may represent an appealing new class of drug candidates for treating EVD.

Awards Won:

Fourth Award of $500