



TESTING THE EFFICACY OF ANTIMICROBIAL PEPTIDES AGAINST COVID-19

Antimicrobial peptides (AMPs) are a diverse group of short defense proteins sculpted over evolutionary time scales, produced by all classes of life as a defense against bacterial [1], yeast [2] and viral [3, 4] infections, including the coronavirus responsible for the 2002-2003 outbreak of severe acute respiratory syndrome (SARS) [5]. AMPs often play multiple roles against infections, acting directly on the infectious agents (for example by destroying bacterial membranes and viral envelopes) or modulating the innate or adaptive immune systems [3], as illustrated in the figure above.

Using a high throughput bioinformatics pipeline, we have discovered over 100 novel candidate AMPs in our labs. Although our focus and motivation so far has been on testing these candidates against World Health Organization’s Priority 1 bacterial pathogens and their multidrug resistant strains, we note that they may also be active against enveloped virus particles as indicated in the figure and in [5]. *In vitro* studies to date have validated the efficacy of our peptides against multiple bacterial species, and their safety as measured by lack of hemolytic activity against mammalian red blood cells. SARS-CoV-2, the novel coronavirus responsible for COVID-19, is an enveloped RNA virus, against which our lead peptides may also be active. We are proposing a 26-week \$955,000 rapid response project to screen our AMPs for their efficacy against SARS-CoV-2, and for their effects on human immune cell models. We aim to develop our lead targets ready for Phase I clinical trials. Our work breakdown, and project plan are described in the Gantt chart below. Some of our activities have already started, as indicated.

Currently, working with the BC Centre for Disease Control, we are developing approaches to screen AMPs for their effects on human immune cell models. We are seeking additional co-development partners to explore how we can collaborate to test our lead candidates against the COVID-19 coronavirus. We are looking for funding to support our assays, and will share our results and materials with our partner(s) for further testing. Some of the funding support for this work will be leveraged to bring in matching funding from federal and/or provincial governments.

TASK	PROGRESS	START	END	W1	W2	W3	W4	W5	W6	W7	W8	W9	W10	W11	W12	W13	W14	W15	W16	W17	W18	W19	W20	W21	W22	W23	W24	W25	W26		
Activity 1 PREPARATION																															
Agreement & Receipt of Project Grant	0%	W1	W1	█																											
Experimental Design	20%	W1	W2	█	█																										
Reagent Acquisition	20%	W1	W4	█	█	█	█																								
Candidate AMP Selection	50%	W1	W2	█	█																										
AMP Optimization I	0%	W4	W7																												
AMP Optimization II	0%	W8	W11																												
Activity 2 SYNTHESIS, IN VITRO TEST & ANALYSIS																															
AMP Synthesis I	33%	W1	W9	█	█	█																									
Toxicity Tests	25%	W1	W20	█	█	█	█	█																							
AMP Synthesis II	0%	W6	W14																												
AMP Synthesis III	0%	W11	W19																												
Efficacy Tests	0%	W5	W21																												
Activity 3 ANIMAL EXPERIMENTS																															
Toxicity Tests	0%	W3	W23																												
Efficacy Tests	0%	W5	W25																												
Select Candidates for Drug Design	0%	W25	W26																												

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4. Cole, A.M., et al., *Retrocyclin: a primate peptide that protects cells from infection by T- and M-tropic strains of HIV-1*. *Proc Natl Acad Sci U S A*, 2002. **99**(4): p. 1813-8.
5. Wohlford-Lenane, C.L., et al., *Rhesus theta-defensin prevents death in a mouse model of severe acute respiratory syndrome coronavirus pulmonary disease*. *J Virol*, 2009. **83**(21): p. 11385-90.