ADD TITLE

Dear Dr. Bob Hancock and Dr. Evan Haney,

My name is Alex Sanchez. I am a biotechnologist with a passion for bioinformatics and antimicrobial peptides. I would like to propose a research topic that fits the Cationic Antimicrobial Peptides project. This research can be done in a six-month internship as an extension of my undergraduate thesis where I obtained exciting results.

I studied the potential antimicrobial activity of spider silk *in sillico*. Using a bioinformatic pipeline, I found AMPs from Expressed Sequence Tag data in the GenBank/EST database. I got known and novel sequences using Blast and Hidden Markov Model approaches. This study produced a preprint next to this letter for a complete explanation procedure. I discovered three novel peptides with putative antimicrobial activity. These sequences were analyzed in several antimicrobial predictors, and their structural models were determined. Results highlight the potential of spider silk as an AMP source and the potential activity of novel sequences.

Previously, spider silk was tested *in vitro* against several microorganisms showing inhibitory activity. However, no mechanisms have been described until now. I would like to continue the analysis of these peptides at the Hancock lab under the Cationic Antimicrobial Peptides project and the Bioinformatic team.

I propose to use both *In sillico* and in vitro approaches to continue this research. I was reading your articles and found that you had published studies that perform peptides synthesis and several bioinformatic analyses such as neural networks and molecular dynamics which are the same that I would like to learn and perform on above mention peptides. We can perform molecular docking and molecular dynamics studies against a simulated bacteria membrane. This study can reveal how the peptide’s structure changes during the membrane interaction, how this is affected, and the affinity of these structural models to the membrane. *In vitro* approaches can be used to prove in-sillico results. We can perform different assays to test its antimicrobial activity and safety by synthesizing and purifying at least one of three peptides. I propose to perform susceptibility assays against resistant strains of *E. coli*, *P. aeruginosa*, *C. albicans*, and more bacterial species of public health importance that you have available. Together with the results of these exploratory assays, we can perform several analyses such as MIC and IC50, hemolytic, and genotoxicity activity.

Expected results will be published in a public health and biomaterials journal. To my knowledge. This is the first approach to antimicrobial mechanisms of spider silk, and could expand the broad application of this biomaterial. With this study, we can find novel AMP to face pathogen resistance and understand spider's immune mechanisms. I consider that working and publishing with you will benefit both my professional and personal life. I aim to join the Bioinformatics post-grade program, and I would love to join your lab for this purpose. Attach this proposal; you can find my CV to know my current background. I would like to request a meeting to expand this proposal and my bioinformatic pipeline. If you have any questions, do not hesitate to contact me at sanyumale@gmail.com

I look for hearing you forward,

Alex Sanchez