

ISN CAEN Lab Visit Report (CAEN Award Category 1A (April 2018 Round))

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Report

Project title: Anticonvulsant activity of cryptolepine and its solid-lipid nanoparticles in management of drug-resistant epilepsy.

Host laboratory: Isom Laboratory, University of Michigan Medical School, Ann Arbor, Michigan, United States of America.

Host laboratory PI: Lori L. Isom, PhD.

I was awarded the ISN CAEN Award Category 1A in June 2018 to visit the laboratory of Dr. Lori Isom, University of Michigan Medical School, Ann Arbor, Michigan, United States of America, from June 01 to August 30, 2018. Dr. Isom was very welcoming and supportive of my project. She granted me full access to her laboratory, reagents and equipment available. For experiments where equipment was not available in the Isom Lab, I was connected to laboratories that Dr. Isom frequently collaborated with. All other researchers in the lab were very supportive with my project as well. I took part in bi-weekly electrophysiology and weekly laboratory meetings/journal clubs where I could freely discuss results and problems with experiments with other researchers.

The objectives of my stay were to assess

- 1) central pharmacological actions using genetic animal models of resistant epilepsy.
- 2) comparative blood-brain barrier permeability between the two formulations.
- 3) potential voltage-gated sodium channel activity using whole-cell/ slice electrophysiology.
- 4) ligand-channel interactions using 3H-saxitoxin binding.
- 5) potential P-glycoprotein blocking activity.

During the visit, I was able to achieve objectives 1, 2, 3 and 4 with slight modifications to the methods. Slight modifications were made to some of the proposed methods as a result of unavailability of cells, animals or reagents needed to perform assays as stated in my proposal. Another reason for some of modifications was the identification of more modern methods for such investigations.

For Objective 1, compounds were tested in wild as well as Scn1a zebrafish mutants (zebrafish model of Dravet Syndrome) rather than in Scn1a knockout mice as proposed. This approach represents a newer direction in modelling pediatric drug-resistant epilepsy and is useful in identifying novel therapeutic agents for this epilepsy disorder. Even though I have had previous experience with Zebrafish, it was my first experience handling mutant zebrafish.

For Objective 2, blood-brain barrier permeability between the compounds was tested using co-cultures of endothelial cells, pericytes and astrocytes. This test gave me the opportunity to learn how to work with primary cultures.

For Objective 3, compounds were tested potential voltage-gated sodium channel blockade activity (Nav 1.1) using patch-clamp technique. Compounds were tested for their effect on channel activation, inactivation, use-dependent blockage and recovery from inactivation.

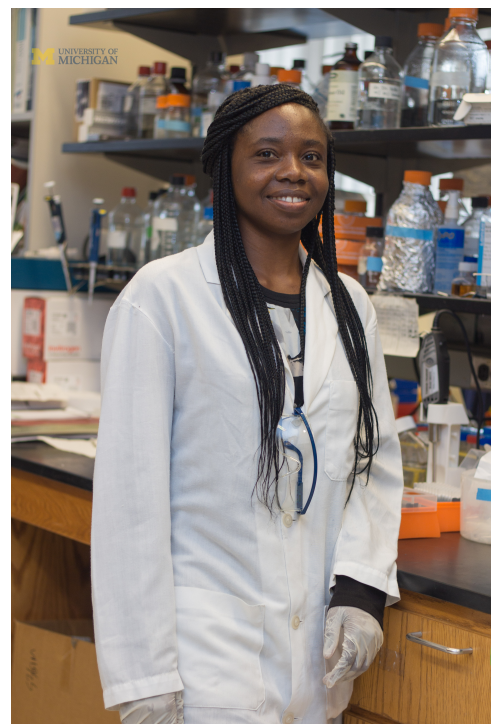
For Objective 4, compounds were tested for potential VGSC blockade of Nav1.1 channels using 3H-saxitoxin binding method in comparison to tetrodotoxin.

Objective 5 was however not achieved due to insufficient time.

Results obtained are still undergoing processing and approval in collaboration with Dr. Isom.

Visiting Dr. Isom's laboratory has undeniably been beneficial to achieving the aim of my project. I am still working with Dr. Isom to bring this project to completion.

I am very grateful to ISN CAEN for this opportunity.





Brief Statement of Accounts

Total amount received by wire transfer from ISN = \$3,875

Roundtrip Airfare (Accra-Detroit) = \$1887.91

Accommodation: \$2070

Total Expenditure: \$3957.91