

## Venom Analysis Lab

### MISSION

The Mackessy Venom Analysis Lab (MVAL) is committed to identifying compounds in snake venom that improve the health of people with debilitating diseases and disorders.

### VALUE

Purified toxins from snake venom are increasingly recognized for their life-saving properties. The use of a reptile “toxin” as a human therapeutic at first seems counterintuitive, as venoms kill and incapacitate other animals. Yet in reality, the various components of snake venom — if tamed by purifying and targeting their toxic destinations — can fight cardiovascular disease, cancer, blood diseases, and a host of other yet-to-be identified health problems. Drugs derived from venoms can also be used to diminish pain and suffering from certain conditions.

Animal venoms have been used in the search for potent pharmaceuticals to treat human conditions for millennia. One of the best-known modern examples includes a hypertension drug which was developed in the 1960s from the venom of the South American Lance-headed Viper. More recently, a treatment for type II diabetes was based on work with venom from the Gila Monster, one of only two venomous lizards; this drug, Byetta, is currently marketed by BMS-AstraZeneca Pharmaceuticals, with annual sales of \$518 million in 2011, according to Advantage Business Media.

### FOCUS

Research conducted in MVAL at UNC is focused on the biochemistry of venoms from snakes, with two major objectives:

1. Analysis of venoms for novel compounds using discovery science-based approaches, and
2. Drug discovery: analysis and evaluation for potential commercialization of a subset of compounds which shows promise toward development of human therapeutics.

### THE SCIENCE

The challenges in identifying potentially medicinal properties from hundreds of snake species are enormous. Snakes obviously must be handled with utmost caution, are not easily bred or maintained in the lab, and need to be tested over their lifespan



rather than at single intervals, as venom compounds change during the snake's lifespan. The biochemistry of isolating compounds and determining properties from different snakes — all of which have their own distinctive venom — is likewise difficult, and the next step of testing their effects with cells and living tissue samples is an art and a science of its own.

Within the framework of our objectives and goals, we maintain a large number of snakes as a source of crude venoms, which are extracted approximately every two months. This step provides the starting material for our work, and the venoms of many species maintained in MVAL are not commercially available from any sources.

Once a sufficient amount of venom is available, several lab procedures allow us to isolate crude venoms and purify specific components and stabilize them for later tests. Based on the caliber of work conducted in MVAL, scientific equipment was recently donated to UNC that will permit cutting edge analyses necessary for documenting the chemical structures of molecules in venoms. Using our approach, we are able to process small amounts of venom rapidly and screen them for potentially medicinal compounds. We are also developing new sequencing methods that allow us to determine primary structure of target molecules more cost-effectively. Obtaining this information is a critical early step in the molecular characterization of potential therapeutics.

Current drug discovery projects include purification of specific proteins from rattlesnake venoms, substances with specific effects on blood coagulation or cancer cells. To analyze these proteins, we use biochemistry techniques, cell cultures, and other methods. Our specific interest includes several distinct lines of cancers and ultimately the use of animal models to evaluate effectiveness in curbing the spread of cancerous cells. Studies in progress are yielding compounds that show potent activity toward limiting metastasis in several lines of human cancers, and we will begin animal model studies later this summer.

In addition, we have purified specific enzymes from several viper venoms, and in a paper we published last year showed that one of these (from *Daboia russelii* venom) has potential for use as an antithrombotic agent, with high activity but exceptionally low toxicity in mice. This line of work shows promise for treating clotting disorders that can cause strokes and possibly some forms of cancer.

Finally, several of these substances appear to be useful as clot-promoting agents to control bleeding, with strong emergency medical implications, and we are currently evaluating several candidate molecules.

## THE LAB

The Mackessy Venom Analysis Lab is a vibrant setting for scientific discovery in which Dr. Mackessy, visiting scholars from all around the world, and students at the University of Northern Colorado are discovering and harnessing venom compounds with promise for drug discovery research and development. Unlike many other labs, the MVAL extracts its own venom directly and has direct access to many species that have been completely unknown until recently.

## POINTS OF PRIDE

- Research in the Mackessy lab has been funded by national (NIH, NSF, CRDF) and regional (COEDIT, CPW, UNC) agencies, and we have been the recipients of major equipment (mass spectrometers) donations from industry.
- Dr. Mackessy has been an invited speaker at recent conferences in Spain, England, India and Brazil, as well as numerous conferences and universities in the United States.
- His research programs have been the subject of numerous local, national and international news articles, blogs and television news broadcasts, and his work has been featured in productions by the Discovery Channel (2012) and the BBC (2014).
- His graduate students have been successful in securing excellent positions in universities, biotech companies, and governmental agencies.
- Many undergraduate students participating in research have gone on to become successful physicians, research scientists, and other professionals.
- Dr. Mackessy has received top awards at the University of Northern Colorado for excellence in research and teaching and is a world-renowned expert in snake venom biochemistry and proteomics.

### References

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