Barnett researcher eyes changing shape, size of human proteins

Small targets, big aims

BY LAURA SHEA

This is the part of the work that I do that can best be explained through interpretive dance,” joked John R. Engen, associate professor of chemistry and chemical biology, describing how proteins in the human body change shape and size depending on whether they’re behaving normally.

Engen, a Faculty Fellow at the Barnett Institute, thinks a lot about these proteins — specifically, about how better understanding their changing shapes and what happens when they mutate could help treatment options and strategies for a number of devastating diseases, including AIDS and cancer.

Engen and his colleagues use sophisticated tools to measure the molecular weight of proteins to the Dalton (1 Dalton = 1 trillionth of a trillionth of a gram). They do this by weighing them with a mass spectrometer, an instrument that can measure the masses and relative concentrations of atoms and molecules. Labeling them with a substance called deuterium during the analysis enables the researchers to get a sense of the shape, size and other features of the proteins, even though they are thousands of times smaller than what you can see with a microscope.

Engen came to Northeastern in September from the University of New Mexico in Albuquerque. He brought along his existing strong ties to researchers at the University of Pittsburgh School of Medicine, and since being jointly appointed in Northeastern’s Department of Chemistry & Chemical Biology and the Barnett Institute, has partnered with a number of local institutions also conducting groundbreaking research in the field, including Harvard Medical School and the Dana Farber Cancer Institute.

Engen has also forged a strong relationship with the Waters Corp., the company that makes the mass spectrometers that Engen and his colleagues use in their research. Barnett has historically worked with James Waters, founder of the Waters Corp., very closely: the center’s director, Barry Karger, holds the James L. Waters Chair in analytical chemistry and the lab that Engen works in is named “The James L. Waters Mass Spectrometry Facility.” The lab has been completely refurbished and updated with Waters Corp. equipment and is reopening in a ceremony May 1. The lab is fitted with four new mass spectrometers, one of them generously donated by Waters.

“Two of the primary reasons I came to Northeastern were the Barnett Institute and Boston,” said Engen. “When it comes to the work that I do and the people and institutions on the cutting edge, many of them are in or near Boston. This is where I felt I could really advance my work.”

Engen speaks fast and with the enthusiasm of an investigator hot on the trail of a suspect when he describes the work that his lab is doing. One current project involves the investigation of a protein called Nef, which is important for HIV/AIDS.

“We’re trying to gather more information and determine why the Nef in some people is deadly but a slightly different form of Nef in other people is harmless,” said Engen. “It has to do with the shape, and we’ve got to figure this out.”

“I think of our research like this: when you’ve dropped your keys at night and you’re trying to find them on the ground in a dark parking lot, the first place you look is under the streetlight,” said Engen. “We’re just hoping to shine a light on the pavement – the proteins – to try and see what’s happening. One of our streetlights is mass spectrometry.”

“There are people all over the world working on all different aspects of this kind of research,” he said. “What I hope we’re doing in my lab is adding a piece to the puzzle that will help researchers, scientists and doctors better understand these diseases and ultimately, treat and cure them.”