Brown's new lab aims to decode body's protein

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Editor's note: Students in an advanced feature writing class at Brown University were assigned to write a feature story about a street that conveys a sense of place. The project, in its seventh year, presents aspects of city life from the perspective of college journalism students.

PROVIDENCE -- Light shines long past midnight from the large industrial sash windows of 70 Ship St., Brown University's new biomedical research facility located in the heart of the Jewelry District.

Between the slats of half-open shades, rows of graduated cylinders gleam on spacious lab benches. A bleary-eyed researcher dozes in front of her computer. Beyond her, rows of white lab coats and dry erase boards adorn the walls.

And somewhere within the five-story concrete structure, an $80,000 mass spectrometer is smashing proteins into peptides, genetically modified mice are glowing under ultraviolet light, and the DNA of deactivated HIV is undergoing a computerized dissection.

Brown's new Laboratories for Molecular Medicine are located on a key cross street between Eddy and Chestnut streets in the Jewelry District, a triangular neighborhood just south of downtown and bounded by Route 195 to the west and the Providence River to the east.

Once a thriving center of jewelry manufacturing, the area today is dominated by sprawling brick and reinforced concrete factories that have been converted to other uses.

The biomedical research building's facilities include a state-of-the-art X-ray diffraction facility able to map the structure of large molecules, a facility that generates mutant mice for scientific research, and a new spectrometer capable of making measurements with unparalleled accuracy. All of the research relates to understanding and curing disease. Projects range from efforts to understand how the shapes of cells relate to disease, to how asbestos promotes cancer, and how certain chemicals damage DNA.

While much of the scientific research is cutting edge, the work of Arthur Salomon, a 31-year-old biochemist who works with the mass spectrometer, stands out. His custom-built instrument is helping put the Jewelry District on the map as a hot spot for a booming new arm of biology called proteomics.

Proteomics, an outgrowth of genomics, aims to catalog the identity and function of every protein found in living organisms. Generally, DNA and genes get all the glory from the media, but proteomics researchers such as Salomon say that proteins are the real workhorses of a cell. Proteins have a flexible structure, which allows them to participate in a spectrum of cellular tasks, while the rigid structure of DNA permits it to participate only in protein production.

While the field of genomics -- the systematic study of organisms' genetic information -- offers a look at the blueprint of life, proteomics reveals the nuts and bolts of cellular functioning. This nuts and bolts understanding could lead to a better understanding of disease and for this reason, researchers such as Salomon are so interested in understanding how proteins work.

Salomon's first-floor lab feels like a combination of a kitchen, an industrial assembly line, and an appliance showroom. Fans hum loudly in the background. The air is laced with the smell of chemicals. Wrenches, wire cutters and pliers are scattered about.

Chris Kowalczyk, the soft-spoken lab manager with a distinctive English accent, shuffles between the lab's three benches, poring one moment over a spike-filled graph at his double-screened computer and the next at the tiny beads he is packing into glass tubes that are thinner than human hair.

Since Salomon came to Brown last summer from the Genomics Institute of the Novartis Research Foundation in San Diego, much of his time and energy has gone to working with his beast of a mass spectrometer, which serves as the focal point of his lab. It's about the size of a small car and alive with little green lights and a series of tiny protein-filled tubes that loop in and out of its mechanical innards.

Salomon, 31, who favors polo shirts over lab jackets, is gregarious. He has the easy-going confidence of a perpetual overachiever and seems to thrive in the chaos involved with starting up a lab. He's spent countless hours tweaking his spectrometer and is the sort of person who will launch, with little prompting, into a detailed description of how the bulky piece of machinery works.

Salomon has rigged up a small video camera so he can monitor and control the spectrometer's progress from his home in East Providence, and when he goes overseas, using the Internet.

The mass spectrometer, he explains, uses collisions with helium atoms to smash pieces of proteins called peptides into even smaller pieces, which in his setup, are weighed, sorted and sequenced with the help of computers.

Salomon says the process is akin to slicing open a cell to see what's inside. Specifically, he's looking for proteins joined to phosphate groups -- a widespread biological phenomenon called phosphorylation.

When proteins get worn out, their patterns of phosphorylation often change and, in fact, abnormal phosphorylation is associated with many diseases related to aging. By sequencing -- and in a sense mapping these patterns -- Salomon is taking the first step toward a cure. Recently, advances in his field have led to better treatments for leukemia and breast cancer.

"It takes the mass spectrometer 1.2 seconds to do what used to take a year. We can look at thousands of these phosphorylations in an hour," said Salomon, whose methodology has revolutionized his field. In fact, he's collecting such massive amounts of data on proteins that the problem is actually what to do with it all.

Part of his lab's focus, then, is to develop tools that will sort through the deluge of data more efficiently.

"For proteomics, scientific papers are becoming obsolete," he said. This is because researchers can report only some 10,000 sequences in a traditional paper, while his equipment collects many times that in a few days of work. Now, he said, proteomics researchers have begun to use large public databases to warehouse the information on the Internet. The development of tools to sort and organize the biological data he collects is a major focus of Salomon's lab.

Salomon and his colleagues have their work cut out for them. His work treads in uncharted territory and unlike other fields of science, there is hardly a precedent that explains how to conduct the type of experiments he's interested in running. In fact, Salomon's lab manager, Kowalczyk, quit after a few weeks because he was overwhelmed by the absence of a methodology for running the mass spectrometer.

"There is no manual," the frazzled scientist said as he cleaned out his desk on his last afternoon at work. "It's the sort of situation where you have to develop it yourself and at this stage of my career, I didn't want that."

In terms of complexity, proteomics makes genomics look like child's play and, though promising, Salomon's advance represents a small ray of light in a tiny corner of an enormous field.

In contrast to the body's estimated 30,000 to 40,000 genes, which took about a decade to sequence, experts think that humans have between 200,000 and 2 million proteins. Even more irksome, while genes remain essentially unchanged throughout life, proteins are constantly changing and thus considerably more difficult to understand.

Given the obstacles, Salomon is exceptionally grateful that Brown, which as part of a campus-wide academic enrichment plan, has been pouring millions of dollars into the sciences to help ambitious "young sprouts" such as himself make a mark in their fields.

When he was looking for a place to start a lab, he said some other universities recruiting him wanted to purchase the equipment on the cheap, but that Brown was willing to pay to do it right.

Brown paid $18.6 million to refurbish the Ship Street building and is constructing a $95.5-million Life Science Building on College Hill. Between the two buildings, the university's biomedical laboratory space will increase nearly 70 percent.

Once they're both up and running, experts believe the research activity from the two Brown facilities will spin off at least two start-up biotechnology companies each year. Salomon doesn't have plans to start a firm, but he's just the sort of person who might be able to cash in in a significant way if his lab does well over the next few years. "It's definitely the sort of technology that industry might find interesting," he said.

Some of Salomon's colleagues have already made the leap to biotech. In 1998, Dr. Anne De Groot, who directs Brown's HIV/TB lab and also works from 70 Ship St., founded EpiVax, a firm based in the Jewelry District that provides protein and genome analysis services.

EpiVax is developing vaccines for smallpox, HIV, and tularemia, a bacteria that could be used as a bioterrorism weapon. . The company has received grants to screen the genomes of these diseases for elements called epitopes that can code for immunity to the diseases.

"This is the future," says De Groot. "Biotech is coming to the Jewelry District. There's no doubt about it." She thinks the Jewelry District is an ideal location for biotech development because it is convenient to Brown, the hospitals, and the interstate. De Groot says that one of the Jewelry District's greatest assets is that it has an ample supply of affordable, sturdy industrial buildings capable of handling the heavy equipment required by biotech.

While the development at Ship Street is exciting to some, it raises concerns for others. Michael Hogue, the president of the Jewelry District Association, a neighborhood group devoted to promoting the development of the area , has reservations about the expansion of

biotech into the area.

The urban plan calls for 40 percent residential development and 60 percent commercial development. Although he is pleased that the research facility at 70 Ship St. brings vitality to the area, Hogue says he is worried that an expansion of biotechnology by Brown or private industry might involve labs that work with potentially dangerous infectio diseases -- something that might discourage prospective residents.

There are four levels of biosafety labs. Researchers in level 1 labs work with agents not known to cause illness in humans. Work in level 2 labs involves moderately hazardous agents, such as hepatitis B. Scientists in level 3 labs work with more hazardous agents, such as tuberculosis. Agents that are used in biosafety level 4 are the most exotic and lethal, such as Ebola.

The highest level biosafety lab at Brown is a 2. Most of the labs at Ship Street use agents that require biosafety level 1.

Recently, Boston University researchers inadvertently infected themselves with the tularemia bacteria at a level 2 lab and BU failed to publicly disclose the accident. That intensified protests over a level 4 lab, which Boston University plans to build in a busy part of Boston. The incident heightened concerns among some Providence residents about the specter of similar development.

While Brown has no plans to pursue a lab for biosafety level 3 agents, researchers such as De Groot are interested in one.

"We would be able to do certain experiments that we can't do now," De Groot said. For example, if her TB vaccine work progresses, it might be necessary to expose laboratory mice to an airborne contagion before testing the vaccine on them -- something she can't do now. She says the lack of a level 3 lab at Brown means there are some research grants that are lost.

The Jewelry District Association recently a roundtable discussion about biosafety attended by biotech and university representatives and residents. Participants agreed that the district should consider

banning level 4 research in the downtown are and that they should work with area biomed companies to establish special zoning restrictions for level 3 labs.

Salomon said the best way to deal with community concerns is with lots of communication. "We need to be very open about what we're doing," he said.