Extinct microbes sought from the Lost World

The scientists in Sir Arthur Conan Doyle’s 1912 novel, *The Lost World* nearly lost their lives discovering long-extinct animals on a remote South American plateau. A similar adventure being undertaken by Prof. Peter Gogarten should not be so dangerous, but is nonetheless just as exciting. Gogarten was recently awarded a $337,287 NASA grant to find extinct families of microorganisms that contributed genes to the ancestors of living microbes. His findings could lead to the discovery of living descendants of those donor microbes, echoing the discovery in Doyle’s story.

Instead of slashing through jungles, Gogarten will compare the sequences of genes of modern microbes to find evidence of lost microbial lineages. He will use these sequence comparisons to construct evolutionary trees, diagrams like family trees of all living things. These trees can look like a Tree of Life depicting new species arising in lineages to form new branches, but trees can be deceiving. “We look at that tree and we think that this is the Tree of Life,” Gogarten said. “But it is only the

New diagnostic tool promises ultrasensitive detection

When doctors order lab tests to diagnose diseases, they want fast, reliable results using a small sample for patient comfort. This requires a highly sensitive device that processes many samples at once. A new technology being developed by Prof. Michael Lynes and his partner, Ciencia of East Hartford, promises to provide doctors with swift, sensitive detection of disease indicators in small clinical samples.

Lynes and Ciencia recently won 3 grants totaling about $600,000 from NIH Small Business Innovation Research programs to continue developing their grating coupled surface plasmon resonance (GC-SPR) devices to increase their sensitivities to toxins and pathogens. These Phase I grants allow them to develop prototype GC-SPR devices so they can apply later for Phase II funds for field-tests.

Lynes’ GC-SPR devices detect analytes (molecules, pathogens or mammalian cells) in

MCB Factoid

Over $1.75 Million in gifts have been pledged to MCB programs this year.
Lost World organisms that have the lucky ancestors that have living descendants ... most lineages went extinct."

Those extinct organisms may still have contributed to successful lineages by transferring some genes to them by a process called horizontal gene transfer. Organisms normally transmit their traits to descendants vertically through their offspring, but bacteria and archaea also transmit genes to other species, sometimes to species distantly related to the gene donor. Gogarten plans to find the sources of horizontally transferred genes that appear to have come from extinct lineages.

To do so, he and his team will compare gene trees to a tree thought to be most like the "true" Tree of Life. The gene trees will be made by comparing sequences of the same gene found in many microbes. If the test gene was passed on only by vertical transmission, then its tree would have identical branching patterns to the Tree of Life. If it has a branch unlike that of the Tree of Life, then horizontal transfer of that gene to the organisms on that branch would be indicated.

If he finds several horizontally inherited genes seem to have come from a branching point on the "true" tree, he will have found evidence of an extinct lineage as the source of those genes. The functions of those genes will give clues to the nature of that extinct gene donor. "The hope is we can learn what these organisms were doing because of what kind of enzymes they were using," Gogarten explained.

Once he discovers genes that were inherited from extinct lineages, he can hunt for living descendants of supposedly extinct lineages. Scientists have been collecting DNA from waters and soils around the world for many years to sequence the genes in microbes living there and putting those sequences in databases. If Gogarten finds his genes in those databases, then he may have discovered a place where these "extinct" organisms still live.

Diagnostic tool fluids by passing those fluids over a surface coated with antibodies that bind them. Analytes can be toxins or even whole cells with molecules on their surfaces that are recognized by the antibodies. A major challenge is to improve the GC-SPR devices' sensitivity. "When you get down to those levels of detection, the signal to noise ratio can be improved by fixing noise," Lynes said. To remove the noise, the team employs small gold beads called nanobeads. The nanobeads are coated with the desired analyte and enhance its binding to the antibodies (the signal) while inhibiting binding by non-analytes (the noise).

Pathogens that infect mice are a major problem in colonies kept for research. Detecting pathogens living with other microbes in "polymicrobial" infections is an important application of GC-SPR. Lynes is working in this area with long-time collaborators at The Jackson Laboratory, recent partners with UConn on the Center for Genomic Medicine now under construction in Farmington. "There are polymicrobial infections in research collections that are very difficult to identify," Lynes said. "It is hard to know which mice to test." Lynes' method promises to detect as few as 30 bacterial cells in a milliliter of sample. A rapid test using small samples would allow caretakers to identify and remove only infected mice and not eliminate the entire colony as is often necessary now. Once developed, this technology may be used for human diagnoses where its lower cost per assay will make routine surveillance commonplace.

One grant allows Lynes and his collaborators to devise a GC-SPR method to detect the earliest development of Type 1 diabetes. Type 1 diabetes, sometimes called juvenile diabetes, continued on page 3
results when the T cells in a person’s immune system incorrectly create an immune response to the islet cells needed to make insulin and in so doing destroy them. Current methods to identify these “autoreactive” T cells are slow and require large clinical samples, a drawback when testing children.

Lynes’ GC-SPR device will attempt to detect these autoreactive T cells in clinical samples and test them to see if they are active in beginning to elicit the destructive immune response. Lynes asks, "Is the reason that a non-diabetic doesn’t develop symptoms, yet has those cells, because the cells have somehow been turned off or is it because they have not yet encountered the right environmental stimulus to turn them on?" GC-SPR analysis might provide an answer and allow early detection of the disorder. Thus a doctor might "get in early enough to do a little bit of manipulation rather than give life-long injections of insulin or stem cells," Lynes said.

Lynes’ GC-SPR technologies resulted from a decade collaboration with Ciencia and David Lawrence at the Wadsworth Center. Much of this work is covered under a broad patent awarded to Lynes and Dr. Salvador Fernandez, the late founder, President and CEO of Ciencia. Advances in GC-SPR clinical devices continue and promise to provide sensitive, high-throughput diagnostic tools.

MORE NOTES

Genetics PhD student Biswas wins South Asian student scholarship. Genetics and Genomics PhD student Arpita Biswas was selected as the 2012 Hira Jain Scholar, an annual award made to UConn South Asian students. Ms. Biswas works in the lab of Prof. David Goldhamer on skeletal muscle regeneration investigating the cells responsible for heterotopic ossification, the abnormal appearance of bone cells in muscle tissues.

Rumpho lab hosts high school students. Asst. Res. Prof. Karen Pelletreau hosted several high school students in the lab of Prof. Mary Rumpho during their participation in the CT Regional Junior Science and Humanities Symposium. Karen directed students to design experiments with sea slugs migrating toward food sources or different light conditions.

Biology undergrad Phansalkar named Goldwater Scholar. Ragini Phansalkar, a Nutmeg Scholar and senior in Biology, was recently named a prestigious Goldwater Scholar, one of 272 national scholarships. Ms. Phansalkar conducts Honors research studying the evolution of centromere-specific histone chaperones in the lab of Prof. Barbara Mellone.

Gut microbes featured on radio show. Prof. Joerg Graf appeared on WNPR radio’s Where We Live on June 4. Graf spoke with the host, John Dankosky, about the human microbiome, the collection of microorganisms that inhabit the human body. He explained how important microbes are to human health. The subject of human fecal transplants was raised as was the role that microbes play in allergy prevention.

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