

MIT Science News in Review

[Biological Sciences]

Microwave Radiation Treatment Enters Final Stage of Clinical Trials

The U.S. Food and Drug Administration (FDA) has given MIT researchers approval to begin the final stage of clinical trials for testing an innovative breast cancer treatment using microwave radiation. The randomized clinical trials will include the participation of nearly 220 women with early-stage breast cancer, and began on October 1, 2002, the first day of Breast Cancer Awareness Month.

The technology is based on radar research invented by Dr. Alan J. Fenn, a senior staff member at the Sensor Systems Division of the MIT Lincoln Laboratory. Fenn determined that the focused microwave technology previously studied for missile detection could possibly treat cancer cells. The clinical trials, based on Fenn's research, are being conducted by focusing microwave radiation externally on the breast, heating and killing internal tumor cells, prior to lumpectomy and radiation therapy.

The randomized clinical testing is expected to finish by February 2004 and will be conducted at various hospitals including the Columbia Hospital at the University of Oklahoma (OU), Harbor-UCLA Medical Center at the Martin Luther University in Halle, Germany, and the Comprehensive Breast Center in Coral Springs, Fla. Additional sites have applied for Institutional Review Board Approval. Past studies of microwave heat therapy have been promising. Early results from a prior phase II clinical trial showed significant tumor cell death in a majority of the patients prior to lumpectomy, which resulted in the FDA approval to begin the final phase of clinical testing. Dr. Robert A. Gardner, a breast surgeon at Columbia Hospital's Center for Breast Care in West Palm Beach, Fla., and Dr. Hernan I. Vargas of Harbor-UCLA Medical Center presented the results of the phase II clinical trials at the 2002 American Society of Breast Surgeons Meeting in April and in the May 2002 issue of the *Annals of Surgical Oncology*.

The study is funded and led by Celsion Corporation, who has developed the clinical thermotherapy system and exclusively licenses the focused microwave thermotherapy technology from MIT.

MIT Computational Biology Researchers Predict RNA Slicing Patterns

Four MIT researchers, led by assistant professor Christopher B. Burge, have invented a model that predicts which

genomic sequences are transcribed to proteins and which sequences get spliced or cut out.

Messenger RNA (mRNA) is a template for all human proteins. It contains exons, genetic material that codes for proteins, and introns, which do not code for proteins. A splicing mechanism then cuts out the introns, leaving the exons that signal protein formation. Sometimes, if the exons are spliced out, the protein product lacks specific functions, which can lead to several diseases. This study at MIT identified several exon-splicing enhancers (ESEs), which promote the splicing of the exons and increase the amount of mRNA containing these exons' particular genetic information.

To better understand RNA and to thus prevent diseases caused by faulty mechanisms, the researchers want to determine a set of rules, perhaps an algorithm, that will predict the splicing pattern of RNA.

This work was a collaboration between the laboratories of Christopher Burge and Phillip A. Sharp, with William G. Fairbrother and Ru-Fang Yeh, funded by the Burroughs Wellcome Fund and the National Institutes of Health.

Human Variation

Researchers from the Whitehead Institute/MIT Center for Genome Research reported in the May 24, 2002, issue of *Science* that nearly all genetic variation in the human genome is arranged into large yet tidy units called haplotype blocks. These blocks are strikingly alike in human populations from Africa, Asia, and Europe, and may be useful in tracking disease-causing genes.

Eric Lander, a biology professor at MIT, and other scientists discovered that each hereditary unit includes a set of single-letter DNA variations known as single nucleotide polymorphisms, or SNPs. Researchers have observed only three to five common haplotypes in the human population. Contrary to long-held belief, the pattern of genetic variation in a fruit fly, which has acted as a prototype for human biology, is more complex than that of humans.

With the knowledge from this study, scientists can simplify the task of combing through 10 million SNPs for disease genes to searching through 10,000 to 50,000 haplotypes. The next step might be the charting of a haplotype map of the human genome. Such a HapMap would facilitate the identification of genetic variations that may place a person at higher risk to develop illnesses such as diabetes and cancer.

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Calorie Restriction Can Lead to Longevity

Through his experiments with yeast, MIT biologist Leonard Guarente has discovered that calorie restriction causes higher respiration rate, and therefore might promote longevity.

A previous theory suggests that calorie restriction functions by slowing metabolism, thereby slowing the generation of toxic free radicals, the molecular by-products from respiration that damage DNA and other cells. However, Guarente says that oxygen-free radicals do not limit the reproductive life span of yeast. Instead, restricting calories in yeast led to a higher respiration rate, which stimulates NAD, a coenzyme that then activates SIR2, an information regulator gene that slows aging by making a protein called Sir2, which promotes longevity. Guarente aims to create a “miracle pill” that enables people to lose weight and live longer. He found that, in yeast, scarcity of food led to a metabolic shift toward respiration, increasing SIR2’s activity and the organism’s life span. In mammals, excess carbon is converted to fatty acids and stored carbohydrate energy. The miracle pill would cause the body to use up these energy stores throughout the respiration process, and less food would be converted to fat. People could live to be very thin and very old.

Guarente’s research was supported by the National Institutes of Health, the Ellison Medical Foundation, the Seaver Institute, and the Howard and Linda Stern Fund.

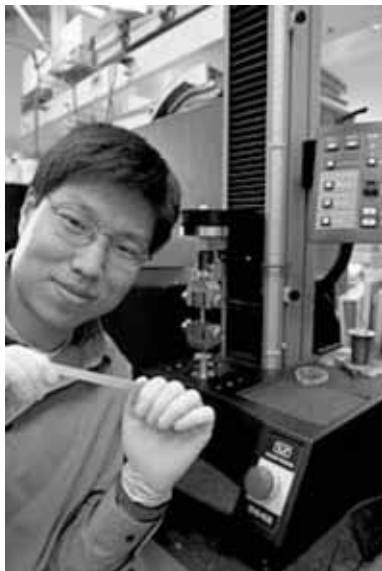
[Bioengineering]

Biorubber Predicted to Change the Face of Tissue Engineering

Researchers from around the globe have been contacting the MIT Langer Laboratory of Chemical and Biomedical Engineering for samples of “biorubber.” This is a new material with many anticipated applications including engineered lungs, heart valves, and other elastic tissues.

Biorubber is unique because of its superior elasticity. Tissue elasticity can often be essential to the function of a particle body tissue. For instance, researchers note that the air sacs in the lungs expand more than seven-fold during inhalation.

The other biodegradable polymers currently



being used in the human body for drug delivery and tissue engineering are relatively hard and brittle. These products are in use either as the vessels for medication or as the scaffold for growing cells. Biorubber has an additional advantage versatility because its properties can easily be adjusted to a variety of specifications such as its rate of degradation. In addition, biorubber is strong, biocompatible, and inexpensive (it can be made in large batches of 400 grams per batch).

Constructed of two principal building blocks that are non-toxic, biorubber is expected to be approved by the Food and Drug Administration (FDA) for use in human beings. Although the process could take years, researchers are optimistic. In the meantime, they have turned their attention to exploring the applications of biorubber in engineering blood vessels, heart valves, the liver, and cartilage.

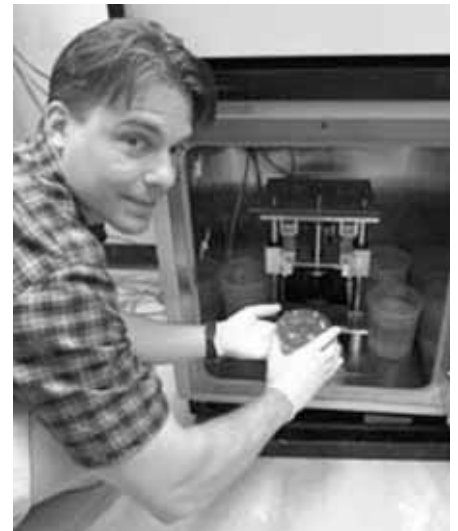
Cartilage in Hydrogel Implants Could Repair Joints

Professor Alan Grodzinsky and Ph.D. student John Kisiday from MIT’s Biological Engineering Division have grown cartilage cells in a peptide hydrogel. When this cartilage is inserted into a damaged joint, the new cells merge with the patient’s original cartilage, repairing the joint as the gel slowly disintegrates.

Cartilage, the soft tissue that cushions bone movement at the joints, is damaged or worn away in sport-related injuries, accidents, old age, and diseases like osteoarthritis. At present, the FDA has approved only one method of cartilage repair: Doctors extract some cartilage from a patient, culture these cells, and then implant this tissue into the patient’s damaged area, a procedure that costs \$30,000. The new “cartilage gel” could be inserted through a small incision, reducing both recovery time and price of operation.

In 1993, Shuguang Zhang, the associate director at MIT’s Center for Biomedical Engineering (CBE), discovered that various peptides from human proteins can be modified to self-assemble into completely different natural materials. Peptides can lead to “nanosoaps” and biomedical devices, or they can be used to support nerve, bone, liver, and cartilage cells.

This particular peptide scaffold consists of interwoven fibers that are 10 to 20 nanometers in diameter. The small structure enables growth factors to attach to peptides and directly stimulate



cell growth. The gel can degrade over time. It also provides less risk of disease because the peptide is not from animal tissues and so does not pass along animal viruses. The peptide scaffold, coupled with a mechanical “exercise regimen,” has resulted in a cartilage-like tissue, which provides hope for a cheaper and more efficient joint repair method.

This work was a collaborative effort among John Kisiday, Alan Grodzinsky, Moonsoo Jin, Bodo Kurz, Han-Hwa Hung, Carlos Semino, and Shuguang Zhang, and funded by the NIH and the DuPont-MIT Alliance.

[Physical Sciences]

New Design for Quantum Computer

Scientists at MIT, the National Institute of Standards and Technology (NIST), and the University of Michigan have proposed a design for a quantum computer based on a large number of interconnected ion traps using experimentally proven techniques.

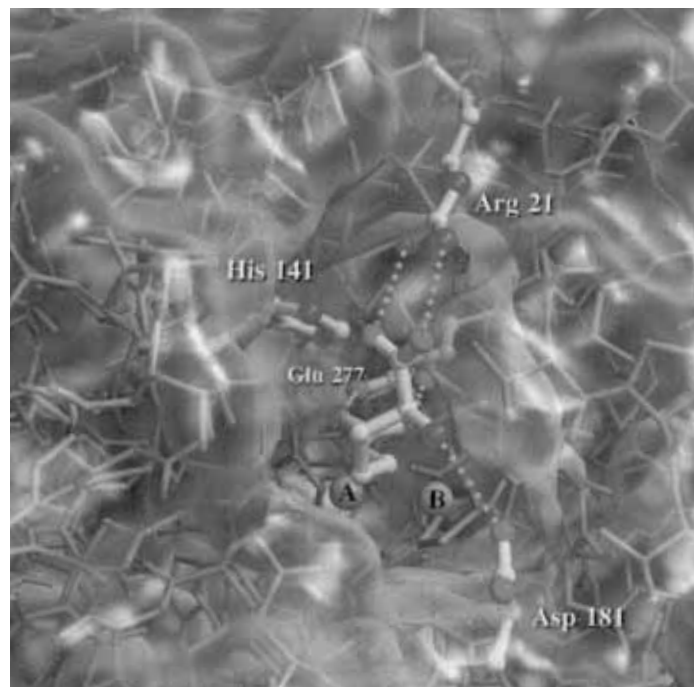
Transistor computers common today can be in only one of two states at one time, either on or off, symbolized by a 1 or a 0. By manipulating atoms or molecules to different states, a quantum computer can be in several states simultaneously, and so can process much more data than a traditional computer, performing tasks like factoring large numbers, deciphering cryptograms, or modeling weather patterns.

Previously, NIST had developed electromagnetic traps where ions can be stored, observed, and manipulated. The MIT/NIST/U of M team proposes to build a large number of these interconnected ion traps. By changing the operating voltages in separate traps, they can manipulate a number of ions in each trap or shuttle them between traps, allowing communication between sets of ions. At the NIST lab in Boulder, Colo., the scientists have constructed a pair of traps, which have been shown to maintain stable electronic states. This is evidence of a practical system from which to build a computer capable of quantum computation scalable to large numbers of qubits (quantum bits).

Structure of Complex Sugar Molecule Discovered

Using a newly developed analytical method, MIT researchers have determined the structure of heparan sulfate, a sugar molecule found on the surface of all cells in the body, and heparin, a commercial drug used to prevent blood clotting.

For decades, the structure of proteins and DNA has been relatively quick and cheap to analyze, while due to their greater complexity and structural variability, sugars (polysaccharides) have been very difficult to decipher. According to researchers, in the postgenome era, research is shifting toward the functional impli-



cations of proteins and carbohydrates. Therefore, developing newer methods of analysis of sugar molecules is greatly needed.

The technique was developed by MIT Professor of Biology Robert D. Rosenberg and postdoctoral associates Kuberan Balagurunathan and Zhengliang L. Wu, technical associate Mirosław Lech, research affiliate Lijuan Zhang, and research scientist David Beeler. It is unusual in that it combines liquid chromatography with mass spectrometry. By means of this method, researchers can separate out heparin and heparan sulfate oligosaccharides that are three to four times larger than what was previously possible. Different labels are used to identify the key areas on the molecule critical for biological action.

Thirty years ago, Rosenberg demonstrated that heparin inhibits blood coagulation by thinning the blood. Heparin achieves this end by binding its sugar groups to its target, antithrombin, a blood-coagulation protein. In response, antithrombin increases the rate at which it inhibits blood coagulation enzymes, thereby inhibiting blood coagulation. Heparan sulfate is of interest to researchers because it plays a role in normal physiological functions, such as tissue regeneration, as well as in disease-related functions, such as developmental disorders and tumor growth.

Caught in the Act: Pulsar Found Stealing Material from Stellar Companion

MIT scientists have spotted a pulsar in a binary star system that is in the process of whittling away its companion star. The companion star has been reduced considerably, making it only 10 times more massive than Jupiter. This system has one of the lowest-mass companions of any known stellar binary; as such, it provides further evidence that neutron stars

can slowly accrete material from their companions. During this process, the spin rate of the neutron star dramatically increases, causing it to transform into an isolated, radio wave-emitting pulsar spinning a thousand times per second. The fate of the companion, once a bright orange gem with 500 times the mass of Jupiter, is extinction, growing dimmer and dimmer until it vanishes completely.

According to researchers, this rare find will help them understand the link between slow-spinning pulsars in binary systems, which are quite common, and fast-spinning isolated pulsars. A pulsar is a neutron star that emits steady pulses of radiation with each rotation. Neutron stars are the remains of a massive star that exhausted its nuclear fuel and subsequently collapsed into a sphere about 12 miles in diameter. The theory is that the powerful gravitational field of neutron stars accretes gas from its companion. Matter spirals toward the neutron star in the form of an accretion disk, a pathway that can be observed using X-ray radiation.

Pulsars have been found scattered throughout the Milky Way galaxy, but this is only the third known accreting millisecond pulsar of its kind and the second identified with the Rossi Explorer in the past two months. The advantage of this system is that its location is less crowded and observations are not as obscured by star fields and interstellar gas and dust.

Dr. Ron Remillard of the MIT Center for Space Research discovered the pulsar along with Drs. Jean Swank and Tod Strohmayer of NASA Goddard Space Flight Center. During a routine survey of the sky, using NASA's Rossi X-ray Timing Explorer, the X-ray source, named XTE J0929-314, was found in mid-May 2002. Dr. Duncan Galloway, a postdoctoral associate at MIT, conducted the follow-up observation that revealed the pulsar system's unique properties.

"It's exciting that we are finally discovering pulsars at all stages of their evolution, that is, some that are quite young and others that are transitioning to a final stage of isolation," reported Galloway.

[Cognitive Sciences]

Color Now Shown To Be Instrumental in Face Recognition

In contrast to previous studies, MIT researchers report that color is an important factor in face recognition. Experiments in which headshots are blurred show that the brain relies on color cues to pinpoint identity. Previously, color had been considered unessential to face recognition, because people were able to accurately identify faces that were artificially colored in such colors as hot pink and electric blue.

Pawan Sinha, assistant professor of computation neuroscience at MIT, and Andrew W. Yip, a recent MIT graduate, found that

color was heavily relied upon by subjects looking at degraded images. Subjects used color to determine hair or skin hue. Additionally, the brain probably uses color cues to locate the start and endpoint of the hairline, for instance.

More than just providing insight into the workings of the recognition process in the brain, this further research could assist in improving machine vision systems and developing better criminal identification kits for generating sketches of police suspects based on eyewitness descriptions.

Face recognition is an integral part of human beings' role as social animals. Sinha is therefore exploring several different approaches to find out what the brain looks for in a face. To this end, he is compiling and analyzing 5,000 digitized caricatures of celebrity and noncelebrity faces. His goal is to determine the top 10 or 20 key attributes used in face recognition by the brain from the hundreds of attributes. In another ongoing project named Project Prakash ("light" in Sanskrit), Sinha is working with hospitals in India that treat blind children in order to determine whether face recognition is innate or whether the brain has to learn to use visual cues for this skill. By observing children who were born blind and have since regained their eyesight, Sinha intends to answer the question of whether some visual abilities, like language, have a critical period that makes them inaccessible to those who gain sight after the "window" has passed.

MIT Neuroscientists Research Neural Mechanisms behind Counting

Through experiments involving monkeys' recognition of numbers and counting ability, MIT researchers Earl Miller, Andreas Nieder, and David Freedman have identified neural networks in primates that explain fundamental numerical competence. These discoveries might lead to understanding of how human beings learn mathematically, which will hopefully illuminate how to resolve cognitive deficits in humans.

For seven months, Miller, Nieder, and Freedman taught a 4-year-old and a 5-year-old male rhesus monkey the numbers from



one to five. Then they taught them the concept of sameness by giving them treats if they raised a lever when two pictures looked identical. Finally, the monkeys were rewarded if they responded when the images had the same number of random items (dots, triangles, etc.)

After the monkeys learned how to judge between one through five objects, the researchers identified which individual neurons reacted to each number, discovering that a neuron that responded strongly to a given number of objects would also respond less strongly to other numbers. For example, the neuron responding to “three” would respond a little less to “two” and less to “one.” This shows that neurons have “tuning curves” in which response is centered around a preferred number and also preserves the ordinal relationship among numbers; in other words, numbers are not

treated as separate categories. This way, our neurons can discern that three is larger than two and less than four.

Scientists must examine how the brain processes numerical concepts in order to better understand fundamental intelligent behavior. Animals have rudimentary mathematical abilities; a necessary aspect of survival is determining how many friends or foes exist, or how many fruits to forage. The prefrontal cortex might be the central core of numerical judgments and abstract categories. Knowing how the brain functions and which processes affect which neurons will help to resolve nervous disorders such as acalculia, impaired mathematical abilities.

The work is funded by the National Institute of Mental Health, the Human Frontiers Science Program, and the RIKEN-MIT Neuroscience Research Center. ■

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