

## Glow in the dark fish

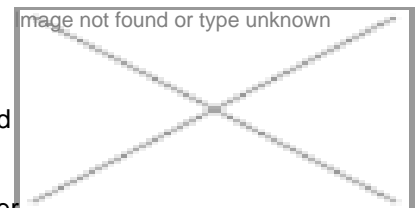
08 January 2004 | News

image not found or type unknown



We can soon have a bit of biotechnology gracing our living rooms—genetically modified fluorescent aquarium fishes. "GloFish", as these GM fishes are called, are fluorescent zebra fishes, which contain a gene from a sea coral that makes the fish bright red under normal light and fluorescent under ultraviolet light. Normally zebra fishes are silver and black in color. In other features, GloFish are the same as other zebra fishes from general care and temperature preferences to growth rate and life expectancy.

These fishes were developed at the National University of Singapore for use in environmental monitoring. The scientists wanted to develop indicator fishes that would glow on encountering certain pollutants. The first step in developing the contaminant detecting fishes was to create fishes that would fluoresce all the time. These were licensed by Yorktown Technologies, a Texan company.



Fluorescent zebra fish has been a reliable model for scientists worldwide to better understand important questions in genetics, molecular biology, and vertebrate development. These have been particularly helpful in understanding cellular disease and development, as well as cancer and gene therapy. And till date most animals have been genetically modified for scientific or medical research but manipulating them for ornamental purpose has raised ethical questions and fears of setting an unhealthy precedent. Environmentalists are also worried about the fish entering the natural waters and disturbing the natural ecosystem. Although the pros and cons of commercializing the GloFish are still being debated, Yorktown Technologies plans to start selling them from January next year.

## First artificial protein created

Scientists are one step closer in understanding the intricacies of protein dynamics. Researchers at the Howard Hughes Medical Institute have successfully designed and built the first artificial protein called Top7. This novel 93 amino acid functional protein was created using sophisticated computer algorithms running on standard desktop computers. On analyzing the three-dimensional shape of the protein it was found to be very close to what the scientists had conceptualized. Protein synthesis per se is a complicated process. Proteins are initially synthesized as long chains of amino acids, which cannot function properly until they fold into intricate globular structures. Understanding and predicting the rules that govern this complex folding process—“involving the folding of the main backbone and the packing of the molecular side chains of the amino acids is considered as one of the central problems of biology.

The researchers said that the integration of protein design algorithms (to identify low energy amino acid sequences for a fixed protein structure) with protein structure-prediction algorithms (which identify low energy protein structures for a fixed amino acid sequence) was a key ingredient in their success. This achievement will give a further impetus to research on engineering artificial protein enzymes for use as medicines or industrial catalysts. It will also help the scientific community in answering how proteins evolved and why are certain protein folds preferred over others in nature. The details of the study have been published in the November issue of the journal Science.

## And now a synthetic virus

Synthetic life on earth has arrived! A synthetic virus has been created and that too in a record time of 14 days. It took Craig Venter, the scientist who pioneered the mapping of the human genome, and his team just this much of time right from arranging the DNA to build a complete virus capable of invasion and replication.

But unlike the polio virus created last year, which set the alarm bells ringing across the scientific community, the synthetic virus created by Dr Venter's team, known as phi X174, infects only bacteria. The scientists zeroed on synthesizing phi X174 because its genome is small (5,386 nucleotides) and total integrity of its structure is required for the virus to replicate. The virus was made by joining together ready-made overlapping DNA fragments called oligonucleotides, each built from 40 chemical building blocks, or bases as per its published genetic sequence. To ensure correct and orderly sequence of bases the team filtered out common oligonucleotides that harbor genetic mutations and used enzymes to paste the oligonucleotides together accurately. When the completed viral genome was inserted into bacteria, it was able to replicate like a natural virus. Genetically, some of the resulting virus strains were found to be 100 percent identical to the natural virus.

But this was just the trial round, the scientists ultimately aim to create novel life forms (microbes) which can clean the earth or provide alternate fuel sources like hydrogen or methane gas. That designer bacterium will be 100 to 1,000 times larger than phi X174's genome, containing the minimal number of genes to support independent life. Once created, this minimal microbe could be assigned special functions like degrading pollutants or producing fuel by modifying it with some extra genes.

This landmark achievement has brought the scientists one step closer to their final goal but has renewed the debate of misuse of scientific knowledge for creating bioterror weapons and the impact of these synthetic organisms on the environment. The virus was created at the Institute for Biological Energy Alternatives in Rockville, Maryland and this work will be published in an upcoming issue of the Proceedings of the National Academy of Sciences.

## Novel gene therapy for cancer

Researchers at the University of Texas MD Anderson Cancer Center have developed a new treatment system for cancer. It consists of genetically engineering stem cells and injecting them in the body, where the modified cells can find tumors and then produce biological killing agents right at the cancer site. It offers probably the first gene therapy "delivery system" capable of targeting and then attacking cancer that has spread in a patient's body. The researchers have performed a number of successful experiments in mice in support of their claim. Notably the stem cells will not be rejected, even if they are not derived from the patient.

The researchers have tested the system in mice with a variety of human cancers, including solid ones such as ovarian, brain and breast cancer, melanoma and even blood-based cancer as leukemia. The drug delivery system is attracted to cancer cells no matter what form they are in or where they are.

The therapy uses human mesenchymal progenitor cells (MSC), the body's natural tissue regenerators. These unspecialized cells can migrate to an injury by responding to signals from the area. There they develop the kind of connective tissue that is

needed to repair the wound and can become any kind of tissue required. Tumors are "never-healing wounds" which use mesenchymal stem cells to help build up the normal tissue that is needed to support the cancer, thus there is constant remodeling of tissue in tumors. Researchers have taken advantage of this ability of the tumor to attract the stem cells.

In their novel delivery system, researchers isolate a small quantity of MSC from bone marrow, and greatly expand the quantity of those cells in the lab. They then use a virus to deliver a particular gene into the stem cells. When turned on, this gene will produce an anti-cancer effect. When given back to the patient through an intravenous injection, the millions of engineered mesenchymal progenitor cells will engraft where the tumor environment is signaling them, and will activate the therapeutic gene.

During the experiments the researchers found that when mice having metastatic tumors in the lungs were treated with just four weekly injections, their lifespan doubled, on average. They also discovered that when treated cells were placed under the skin of the mice, there was no effect. The cells are required in the immediate environment of the tumor to work, which suggests that normal tissue will not be adversely affected. Though it may be required to further fine-tune the genes that are delivered, but the very fact that these cells are capable of migrating from the bone marrow or blood circulation into tumors suggests its potential. M D Anderson has filed patent applications on the system.