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BENCHSMART

A Newsletter for the UMDNJ Laboratory Community

In the News

Patient Death Prompts NIH Investigation

An "unusual and deadly immune system response" to an adenovirus vector used in a gene therapy protocol took the life of 18-year-old Jesse Gelsinger this past September 17. Researchers at the University of Pennsylvania's Institute for Human Gene Therapy were testing the efficacy of a recombinant containing the ornithine transcarbamylase (OTC) gene. Half of those born with no OTC activity die within a month; Mr. Gelsinger had a milder form of the disease allowing him to control it through diet and medication. The OTC gene product is a liver enzyme critical for the removal of metabolically produced ammonia from the bloodstream.

Within hours of receiving treatment, Mr. Gelsinger ran a high fever and had an upset stomach, anticipated effects noted in previous administrations of adenovirus recombinants to humans and animals. However, a blood clotting disorder developed the next day, followed by lung and kidney failure. He died four days after initiation of the protocol. A blood clotting disorder was the cause of death in three monkeys treated with a similar construct in an earlier experiment. Consequently, researchers lowered the dose of the recombinant and developed a "safer" vector, one in which additional viral genes were deleted. Subsequent human and animal tests using the lower dose of the re-engineered vector showed a level of safety satisfactory to the NIH, leading to their approval of the protocol in which Mr. Gelsinger participated

On December 8, the NIH's Recombinant DNA Advisory Committee convened a three-day meeting to discuss the results of an investigation into Mr. Gelsinger's death. The committee further analyzed the safety of adenovirus vectors used in approximately 25% of gene-therapy clinical trials.

At the meeting, FDA officials stated that Mr. Gelsinger should never have been included in the protocol because of his sub-optimal liver function, a condition that was known before the experiment. The FDA also criticized the researchers for not reporting immediately serious side effects seen in two patients in earlier experiments and for omitting information about the previous monkey deaths on the "informed consent" forms used in the protocol. Autopsy findings presented December 9 suggested that a bone marrow abnormality, in conjunction with an undetected parvovirus infection, might have contributed to the immune response that killed Mr. Gelsinger.

While apologizing for the cited lapses, the lead scientist in the gene transfer study, Dr. James Wilson, maintains that there was no prior evidence from either animal or human testing that could have predicted the fatal outcome. Regardless of the investigation's outcome, additional requirements for disclosure of safety data and information about side effects are likely to be added to governmental oversight procedures for gene therapy activities.

Chips Are Not Just Silicon

Biochips are silicon or glass wafers the size of a microscope slide embedded with biological molecules (DNA fragments, antibodies) that react in a substrate-specific manner with test materials allowing for their identification. They have potential for use in rapid DNA sequencing and in pharmaceutical development.

The technology's first critical test will come next year in an attempt to

identify drug resistant strains of tuberculosis. The project is a joint venture of the federally funded Argonne National Laboratory and Affymetrix, a biotechnology company.

TB was selected because the emergence of drug resistant strains over the past twenty years is one of the world's most serious Public Health problems. Untreated, TB kills about 5% of those infected, a staggering number considering that 15% of the world's population is infected. TB claims about 3 million lives a year. If successful, identification will be possible in minutes, not days, allowing for administration of the most effective treatment. In turn, the time that a patient remains infectious and capable of spreading the disease to others is greatly reduced.

Source: http://real.snap.com

Recent Incidents

Flame Sterilizing Fire

A University of California at San Diego laboratory worker narrowly escaped injury when an ethanol container ignited while he was flame sterilizing microscope slides. He had been taking ethanol-soaked slides from the container and passing them through a Bunsen burner flame. A drop of flaming alcohol ignited the container.

When attempts to extinguish the fire by covering the container failed, the employee went for a fire extinguisher. When he returned to the lab, the door was locked. The employee then activated the building fire alarm system and telephoned the emergency number.

Damage was minimal, limited to the interior of the biosafety cabinet.

While the employee's actions in response to this incident were admirable, UMDNJ's fire safety policy states that the fire alarm should be activated before any other actions are taken. Attempts to put out a small fire should commence only after notification is made to the local fire department. The lessons to be learned for anyone doing similar work are:

1. Position the work area to minimize the chances of igniting any flammable materials.

2. Eliminate ethanol in flame sterilizing procedures.

3. Keep biosafety cabinet clear of excess supplies.

4. Be sure to carry a key at all times or disable the automatic door-lock.

Adapted from UCSD EH&S Dept. Lab Notes http://www-ehs.ucsd.edu/NEWS/LABNOTES/ln-nd99.htm

Water Bath Fire

Malfunctioning water level and temperature controls on water baths are a major cause of laboratory fires. Recently a Columbia University laboratory experienced a fire due to such a malfunction. Check water baths periodically to ensure that the water is at the required level. If possible, turn the water bath off prior to going home for the weekend and turn it back on Monday morning.

Adapted from Columbia University EHS Newsletterhttp://cpmcnet.columbia.edu/dept/ehs/newsletter.html

It Happened at UMD

EOHSS and Physical Plant staff spent parts of three days investigating a lingering odor, variously described as natural gas, a sewer smell, and beta mercaptoethanol. The common feature of these materials is the presence of sulfhydryl groups. (In the case of natural gas, these compounds are added to aid in the detection in leaks of natural gas, which is odorless.)

The cause was ultimately traced to ethanethiol (also a sulfhydryl compound) stored in a laboratory refrigerator. The investigator had transferred it to a plastic container because the original glass bottle had broken. The vapors of this highly volatile material were capable, as is sometimes the case, of passing through the plastic. Because the laboratory's air flow was not properly balanced, the vapors escaped into the surrounding corridors. The typical pattern is for the air to move from the corridors into the laboratories. (The ventilation problem was corrected shortly after it was detected.) Materials such as ethanethiol should be stored in an impermeable leak-tight container and used in the chemical hood.

Contact EOHSS if you have any question about the storage of hazardous and/or odiferous chemicals

Metal-Cased Cylindrical Dewar Flasks

The metal casings of some Dewar flasks do not cover the cylinder's bottom, making it subject to shattering when liquid nitrogen is added too rapidly. Such an accident recently occurred at the University of California, San Diego (UCSD) involving Fisher product # 10-196-9, "Metal-Cased Cylindrical Dewar Flask". This should not be regarded as an isolated incident due to a rare material defect because UCSD personnel have noted a number of similar occurrences was the past several years. Always wear a face shield and protective gloves for operations involving liquid nitrogen and never store it a poorly ventilated area such as a cold room.