Bioengineering at USC

What if …

We could identify the specific genetic profile of a viral pathogen faster, decreasing the time from infection to detection?

What if *we could find ways to repair DNA, inhibiting the growth of dangerous mutations like cancer?*

What if *we collaborated with other universities to design and engineer materials for medical implant devices that could withstand sterilization requirements while retaining the capability to reduce irritation and/or infection?*

What if *we could sterilize pharmaceutical implants and invasive devices with environmentally safe carbon dioxide instead of more toxic and/or destructive substances?*

At the University of South Carolina Research and Health Sciences division, we are making "what if?" what is!

Cancer. It is a word that fills anyone who knows the disease with dread. A leading cause of death in the United States and around the world, it's also a horrifying example of how the body's defense mechanisms can be overridden. The process can create dangerous, malignant growths that interfere with normal functions, hijack resources needed by healthy cells, and—if untreated—eventually kill the host.

Although cancer is a common malady, many of its triggers remain unknown to scientists. The mechanisms by which normal genes can be corrupted into dangerous mutations are only partially understood.

USC researcher John Rose and his colleagues in both the School of Medicine and the Department of Basic Pharmaceutical Science and at the S.C. Cancer Center are working to unravel this mutation mystery using mathematical modeling and computer analysis—bioinformatics. This discipline studies the representation and transformation of information in organisms. USC research in this area is likely to offer some significant advances in understanding the functional role of the approximately 30,000 genes comprising the human genome, particularly in the way cancers are formed and can be recognized.

To accomplish this, Rose and his colleagues are specifically focusing on those genes that are expressed differently in cancer cells compared with normal cells—the analysis of differential gene expression data as they present themselves in cancers.

"Cancer cells have a different gene expression profile than do normal cells of the same type," Rose said. "By finding those differences in gene expression, conclusions can be drawn that a patient has cancer, and with such early detection, the prospect of successfully treating the cancer, in most cases, goes up."

Newly funded research and equipment at the S.C. Cancer Center will supply the researchers with significant opportunities for finding correlations between gene expression in sample populations and the clinical nature of the cancer common to the different populations.

Rose noted that this is an area ripe for increased computational power and improved statistical and analytical algorithms, which must be combined with the knowledge and intuition of the medical research specialists to understand and interpret patterns found in the data.

"If we can find out what the genetics are behind a specific cancer, we can then use that information to more quickly identify the presence of that cancer in other individuals and perhaps also learn what turns that gene on in a body and, even better, how to turn it off. The cell has built-in error-correcting mechanisms for dealing with potentially harmful mutations. We need to know why this 'self-correcting' mechanism fails in the case of cancer," he said.

In addition to his recent cancer work, Rose has undertaken significant research projects of computational biology during his several years at USC. In collaboration with Wallace Dawson and Michael Dewey in the Department of Biological Sciences, and with the support of the National Science Foundation, Rose is developing a comprehensive database of

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information on the biology and evolution of Peromyscus (deer mice) and other related species. (Peromyscus is the mouse associated through the deer tick with Lyme disease, and also the primary carrier of the virus responsible for hantaviral pulmonary syndrome. As the most populous mammal in North America, Peromyscus plays a significant ecological role.)

Currently, Rose is working with the USDA to analyze viral genomes because "by analyzing and modeling the genomes of different viruses, we may be able to more quickly detect their presence and someday also discover how to prevent them from establishing themselves in the body." Genetic classification of viruses also offers security against terrorist threats, he noted.

"The Office of Homeland Security and other researchers are constantly looking for ways to detect pathogens at very early stages. With some of our methods, the presence of the pathogen can be detected quickly based on genetic fragments present in the patient. If we can jumpstart the analysis of a pathogen before isolating and culturing it, we may be able to quickly determine its origin. And, if we find something unusual, we can also offer advice on whether it is a naturally occurring outbreak or possibly an engineered pathogen being deployed in biological warfare," he said.

The control of viruses and the implications of that capability for national security also are of the focus of USC researcher and bioengineer Dr. Mike Matthews. He and colleagues from Clemson and MUSC are currently studying ways to sterilize materials from viruses and bacteria in a way that is reliable and practical and does not damage the material. And their answer appears to have come out of thin air—literally.

Carbon dioxide is one of the most prevalent gases in the world today. It is used to extinguish fires, and in some novel approaches by Matthews it might also be used to sterilize medical devices and implants.

As Matthews wrote in a recent abstract, "Cleaning, particulate removal, and sterilization are currently separate steps crucial to the viability of medical devices. As medical implants grow more complex and as new biomaterials are developed for advance applications, there is a crucial need to develop new techniques and processes that can clean and sterilize a wide variety of materials and devices at moderate to low temperatures, without introducing potential contamination and without damaging the surfaces or otherwise compromising the bioacceptability or functionality of the device."

Current sterilization practices using radiation, toxic gases, or steam to destroy bacteria, along with even the more primitive treatments of alcohol or ethylene dioxide, can damage or otherwise alter the surface of different implants. Even worse, these approaches can inhibit the safety, functionality, or longevity of the device.

For example, if an improvement in biocompatibility in hip replacements could be found (by cleaning the implants in a way that did not cause premature deterioration of the materials), the time between total hip replacements could stretch from 10 years to 20 years.

Based on some proprietary research and collaborations among USC, MUSC, and Clemson, Matthews expects to deliver a method for sterilization that uses CO_2 under acceptable temperatures and pressures to create a device that can "wash" and sterilize implants with no damage to the outside of the devices and no reduction in functionality or bioacceptability.

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> **Dr. Mike Matthews**

"We are doing the research on how to model the amount and pressures and temperatures of CO_2 to kill any contaminants. Clemson is devising materials that can stand up under this kind of treatment, and MUSC will be designing the implants and conducting some clinical trials for biocompatability with our methods and materials," Matthews said.

To test the effectiveness of the CO_2 sterilization, USC also is working with several strains of bacteria and spores to study what provides the best solution for all types of contaminants.

Matthews' research also has an application for homeland security. Anthrax spores distributed via mail caused considerable reworking of the U.S. mail system, and there are new requirements for sterilizing documents. Meanwhile, traditional ways of sterilizing paper have been found impractical—steam destroys paper, radiation affects many heat-sensitive inks and papers, and chemical treatments can damage documents. However, by using CO_2 it is possible that mail and other things could be rapidly decontaminated safely with no damage to the goods.

"When it comes to CO_2 sterilization, a lot remains to be done," Matthews said, "but we feel this is a good solution, this is good chemistry. Now we just have to make it work."