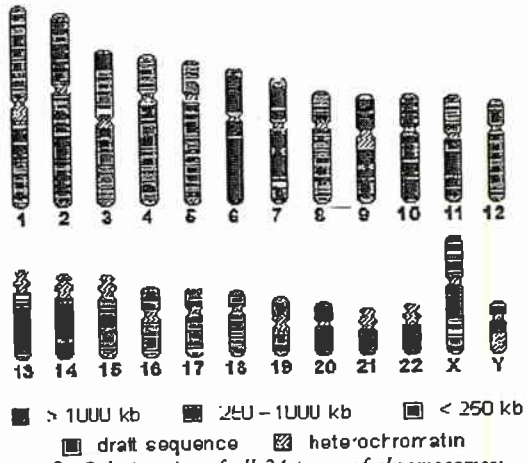


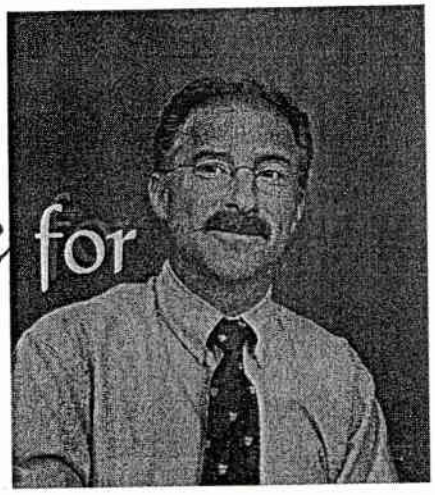
Figure 2: *Relative size of all 24 types of chromosomes; Number of bases along chromosome measured in kilobases (kb)–1000 nucleotide bases*

body. Doctors can eventually tailor doses of drugs to a person's unique genetic make-up. These novel drugs hold the promise to have fewer side effects and to be more effective than much of today's medicine (Casey, 1999).

Current drug therapy often attempts the treatment of large patient populations, disregarding the potential for individual, genetic-based differences in drug responses. In contrast, pharmacogenomics may help focus effective therapy on smaller patient subpopulations that, although demonstrate the same disease phenotype – the observable physical and biochemical characteristics of an organism (The American Heritage Dictionary of the English Language, 2002) – are characterized by distinct genetic profiles. The result of this individual-specified, genetic-based approach to medicine to provide an improved, economically feasible therapy, remains to be seen. All of the obstacles involved in developing any new medical therapy apply to pharmacogenomics as well. To exploit these opportunities in genetic medicine, novel technologies will be needed, health care professionals must be educated, and the public must be informed about the implications of genetic testing in drug therapy and disease management (Mancinelli et al., 2000).

The Human Genome Project is of great scientific importance and has already shown great promise. The discovery of two genes involved in the origins of breast cancer in 1994 is one such example of a vital breakthrough (Miki, 1994; Wooster et al., 1994). In lieu of such advances, the Department of Energy (DOE) and the National Institute of Health (NIH) expect to complete 100% of the high-quality sequenced – only a single error in every 10,000 bases – human genome by the year 2003 (HGMIS, 2001). Although gene tests and gene therapy have yet to demonstrate their full potential in preventive-based medicine, the next step to be taken in genome research – functional genomics: study of gene function – will enable scientists to predict the formation of any disease and to offer a therapeutic gene that replaces or corrects the defected gene(s) (HGMIS, 2001). In addition, pharmaceutical companies will be racing to develop customized drugs that will be tailored to specific gene sites. As amazing as the prospects of the HGP's effects on society may be, according to Daniel Drell (DOE) and Anne Adamson (HGMIS), "We need to be alert to challenges and misuses of the knowledge about ourselves. Society as a whole, not just genome scientists, must address these considerations. It has to be all of us." (Drell and Adamson, 2001).

A Vaccine for HIV



BY JEFFREY LI AND JONATHAN NG

McMaster University professor of pathology and molecular medicine, Dr. Ken Rosenthal, is leading breakthrough research into the development of a vaccine against HIV (Human Immunodeficiency Virus), the world-wide killer virus responsible for AIDS (Acquired Immunodeficiency Syndrome). He has successfully developed a mucosal vaccine for an HIV equivalent in mice that may be applicable to humans in the coming years. As the disease responsible for the death of 3 million last year and about 21.8 million since the beginning of the epidemic (AVERT, 2002), AIDS has established itself as a formidable opponent. Through these findings, Rosenthal and his colleagues are providing a glimmer of hope for ending the epidemic. Join us as we delve into the immunology behind the potential AIDS vaccine of the future.

HIV Basics

One of the most common modes of HIV transmission occurs through sexual contact. Infected semen or vaginal fluid containing the virus may enter the system of an uninfected person through the mucous membrane, the protective tissue layer lining the mouth, vagina, and rectum (The Body: New Mexico AIDS InfoNet Fact Sheet, 2002). After gaining access to the bloodstream and lymphatic system, HIV binds to cells that are recognized by its outer glycoprotein complex, gp120. The deadliness of the virus is a result of gp120's high affinity for the cell-surface protein, CD4, found on immune system cells (leukocytes) that help defend the body against pathogens and other foreign agents. Of the several targets, CD4 T cells are one of prime importance. These cells are responsible for helping B cells of the immune system to produce antibodies and activating macrophages that defend the body against intracellular bacteria and other pathogens (Janeway, 1999).

How the Vaccine Works

Under normal circumstances, the immune system responds to HIV infection by increasing production of HIV antibodies and cytotoxic T lymphocytes that target and destroy infected cells. Despite this response, however, the defense is usually unable to eliminate HIV. The aim of Dr. Rosenthal's vaccine is to boost the immune system so that it is capable of a powerful initial response to infection that will control the virus at manageable levels. Following the same principles of vaccines of the past, the vaccine introduces an antigen into the body that mimics natural disease exposure, in this particular case it is a whole killed envelope-deprived virus. Following antigen exposure, the body responds by producing antibodies that fight against the infection and stores this defensive ability in immunological memory. This allows the immune system to respond rapidly and effectively to the real disease when it strikes (Janeway, 1999).

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Evaluating the Effectiveness of Complementary and Alternative Medicine

BY SEAN PARK

The dramatic increase in the use of complementary and alternative medicine (CAM) in the Western health care setting has caused much debate. Critics of CAM therapies view research in this field to be scientifically unverified, and as such, not effective or safe to administer to patient populations. Proponents of CAM, however, argue that the evidence-based medicine model that conventional medicine uses focuses to heavily on the randomized controlled trial (RCT) as a source of evidence.

In recent years, much debate and frustration has arisen over the basis, development and delivery of health care, particularly in the Western hemisphere. Key to this debate is the relationship between conventional and unconventional medicine. Unconventional medicine, commonly referred to in many journals as Complementary and Alternative Medicine (CAM), is a very general term given to wide array of therapies. Some have defined these therapies as "medical practices that are not in conformity with the standards of the medical community" or as interventions that are not generally available in hospitals or not usually taught at medical schools (Eisenberg et al., 1993).

The authors that formulated this definition for a study on unconventional medicine in the US analyzed the prevalence of some of the following therapies in the US population (Eisenberg et al., 1993):

UNCONVENTIONAL THERAPIES

Relaxation techniques	Prayer
Massage	Imagery
Spiritual healing	Herbal Medicine
Megavitamin therapy	Self-help groups
Energy healing	Biofeedback
Hypnosis	Homeopathy
Acupuncture	

While a number of these therapies have been in existence for much longer than conventional medicine, their increased use in developed nations has sparked great debate. The issue of CAM use is particularly prominent in the US as conservative estimates of 1997 out-of-pocket spending on CAM therapies reached $27 billion with annual visits to CAM therapists exceeding visits to US primary care physicians (Beyerstein, 2001). Assailants of CAM are now arguing that many, and in some cases all, CAM therapies are scientifically unfounded and carry false promises about safety and efficacy (Beyerstein, 2001). What is the basis for this argument and how will it affect the future of CAM?

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Dr. Ken Rosenthal and the immunological science behind his innovative new AIDS vaccine.

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The Key Component of Rosenthal's Vaccine

Where AIDS vaccines in the past using whole killed virus approaches have been unsuccessful, Dr. Rosenthal's approach champions to success. The key element lies the clever use of an additional substance added to the vaccine, an adjuvant called CpG DNA. In the immunological community, vaccine adjuvants are agents used to boost immune response against foreign invaders. As CpG DNA has a structure resembling that of bacterial DNA, it is believed that the human immune system has evolved to respond potently to it. In specific, the adjuvant boosts the immune system by directly activating B-cells and antigen presenting cells. Activation of B-cells increases antibody production whereas activation of antigen presenting cells such as macrophages, monocytes and dendritic cells increases the number of antigens processed for adaptive immunity. In addition, by causing antigen presenting cells to secrete interferon and cytokines, the adjuvant is capable of activating natural killer (Nk) cells, cells capable of spontaneously recognizing and killing virus infected cells. The combination of these immunostimulatory effects induced by CpG DNA allows the body to respond to the whole killed virus introduced with the vaccine to produce long lasting immunity (Rosenthal, 2002).

Beyond the HIV Vaccine

Beyond the mouse model, the concept of using CpG DNA as an adjuvant holds a candle of hope to victory over the AIDS epidemic. Furthermore, the uses of CpG DNA are not limited to HIV vaccines, the adjuvant may help strengthen other vaccines as well. Currently, Dr. Rosenthal is using a similar concept to develop a vaccine for the herpes simplex virus. At this continued rate, the future of disease control looks very optimistic - it is clear that McMaster is at the forefront of a healthy tomorrow.