

Discovery Medicine

Medicine on the Leading Edge

Volume 4, Number 24

December 2004

Content Highlights

Inheritance of Cancer

Page 396

New Therapeutic Approaches for Alzheimer's Disease

Page 384

Echoes of the Past: Human Development, Health, and Disease

Page 401

Bipolar Disorder: Current Treatment Options

Page 415

New Drugs for Asthma

Page 421

Drug Targets in Immunological Diseases: Focus on Rheumatoid Arthritis

Page 433

And 13 additional discovery topics

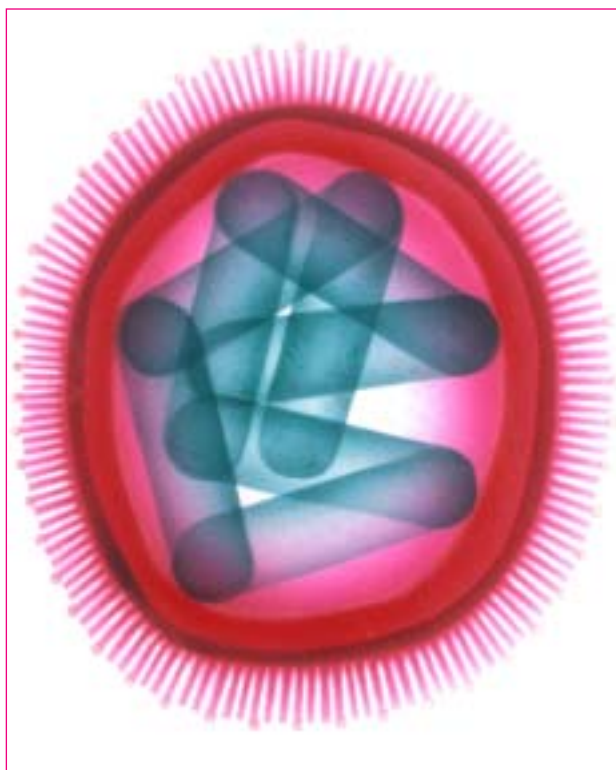


Photo Researchers

Influenza Virus: A Time Bomb?

Pages 371, 378, 482

Editor's Note

An influenza pandemic of the magnitude seen in 1918 could happen again. In recent years there has been an escalating frequency of outbreaks of poultry flu that has also infected humans.

Citing these alarming events, Klaus Stohr, head of flu surveillance at the World Health Organization, declared recently that a global influenza pandemic is closer than in previous generations. Center for Disease Control and Prevention Director Julie Gerberding has pointed out the unprecedented increase in air travel in recent decades – a sharp contrast with the early 20th Century when the influenza was carried by only a small number of world travelers who reached their destinations by ship.

However, modern technology, the knowledge and experience so far accumulated, and the speed with which we may produce an effective vaccine, all should limit the magnitude of devastation from a pandemic compared with that seen by humanity in 1918.

Currently, to produce the majority of flu vaccines, virus is grown in chicken eggs, a slow approach that takes months and is prone to contamination. This would not be a practical way to produce a vaccine from a new virus that is raging in an epidemic or pandemic. Researchers are looking for methods to safely and rapidly produce the virus in cell cultures in large quantity.

By the way it mutates, influenza virus is a time bomb. There is a race to develop a new technology for speedy vaccine production before the next pandemic. Winning the race could greatly limit future carnage.

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Discovery Medicine (ISSN 1539-6509) is published bi-monthly by Peter H. Rheinstein, M.D., J.D., 57 W. Timonium Rd., Ste. 207, Timonium, MD 21093-3105. Application to mail at Periodicals postage rates is pending at Timonium, MD 21093 and additional mailing offices. POSTMASTER: Send address changes to Peter H. Rheinstein, 57 W. Timonium Rd., Ste. 207, Timonium, MD 21093-3105.

Annual subscription rates: Personal print or digital edition, \$39.95; institutional print plus digital edition, \$349. Group bulk subscriptions are available at a reduced rate schedule which is provided upon request.

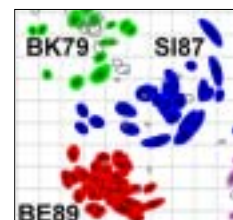
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364 **Editor's Note**371 **Mutations, Drift, and the Influenza Archipelago**

Derek J. Smith et al.

The influenza virus genome has an uncanny ability to mutate. Changes in the genome will bring about random changes in structures of viral proteins (antigens) and hence the "antigenic drift." Physicians and scientists have been chasing them following the traces they left behind – the antibodies in the blood serum. By mapping the drift course, we may know where the antigens are headed next.

378 **Highly Lethal H5N1 Influenza Virus in Asia: Genesis and Options for Control**

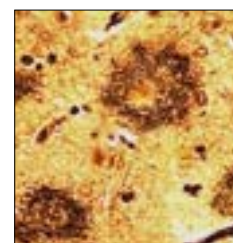
Aleksandr S. Lipatov and Robert G. Webster

There have been violent influenza outbreaks in poultry in recent years, mostly in Asia. A small number of humans were infected, but the virus was apparently not able to be transmitted from human to human. The worry is that as the viruses keep changing their chances improve.

384 **New Therapeutic Approaches for Alzheimer's Disease**

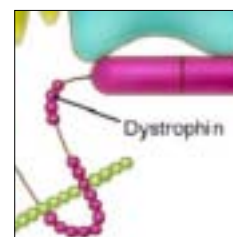
Kevin A. DaSilva and JoAnne McLaurin

Worldwide, an estimated 12 million people have Alzheimer's disease at a cost of about \$100 billion annually for their treatment and care. Current drugs help patients cope with their symptoms but are not designed to treat the underlying pathology. Despite a recent setback in a clinical trial, vaccination may still be the best bet.

390 **Novel Treatments Under Development for Muscular Dystrophy**

Giulio Cossu and Maurilio Sampaolesi

Muscular dystrophy is a "big" disease in that the affected muscle fiber protein called dystrophin is a big molecule and the disease afflicts a very large portion of the body cells. Effective treatments are scarce. The promises and challenges of gene- and cell-based therapies currently under development are discussed.

396 **Inheritance of Cancer**

Steven A. Frank

On a population level, the impact of a cancer risk gene is dependent on the severity and the age at which the cancer occurs. Some genes may have a smaller contribution to the disease, but their impact is still large if they occur frequently in the population. An accompanying article about a gene linked to the risk of type 2 diabetes (by Dr. Bowden on page 427) illustrates this point.



401 Echoes of the Past: Evolution, Development, Health and Disease

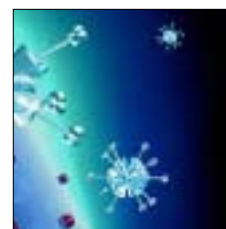
Peter Gluckman and Mark Hanson

Humans have been struggling with food and survival throughout a very large portion of *Homo sapiens*'s long history. Genes are customarily programmed to prepare the fetus for harsh conditions and deprivation outside the womb of comfort. Today's affluence in certain parts of the world would surpass the wildest dreams of hunter-gatherers. The human genome might not have had enough time to adjust to the quantity of proteins and sugars ingested each day and the result may be an increase in disease.

**408 Gene Therapy: A Possible Aid to Cancer Radiotherapy**

Dalla S. Gridley and James M. Slater

Radiotherapy and gene therapy seem far apart. Nevertheless, they can form a formidable partnership in killing cancer cells. Gene delivery technology can make cancer cells more vulnerable to radiation therapy and make surrounding normal cells more resistant to it.

**415 Bipolar Disorder: Treatment**

R.H. Belmaker and Yuly Bersudsky

Dr. Belmaker's highly readable series of articles on bipolar disorder continues in this issue with a focus on treatment. He discusses how to treat bipolar patients in a manic phase without driving them into their depression phase. Can psychoeducation help?

**421 New Drugs for Asthma**

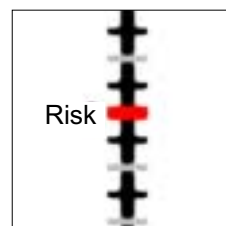
Peter J. Barnes

Inhaled corticosteroids work quickly and effectively in about 95% of patients with acute asthma. While it is challenging to beat the efficacy of inhaled steroids, new drugs should better them on their side effects profiles, especially when used frequently in a long-term fashion, which patients often do.

**427 Association of the *PTPNI* Gene with Type 2 Diabetes and Insulin Resistance**

Donald W. Bowden

The *PTPNI* gene (protein tyrosine phosphatase N1) increases the risk of type 2 diabetes by only 30%, but 35% of the population carries it. Through a complex calculation of genetic epidemiology, this translates to adding 3.6 million new cases to the total cases, a sizable number.



433 **Drug Targets in Immunological Diseases: Focus on Rheumatoid Arthritis**

Andrew D. Cook and Kumar Visvanathan

Non-steroidal anti-inflammatory drugs (NSAIDs) such as aspirin and disease-modifying anti-rheumatic drugs (DMARDs) such as methotrexate have been the mainstay treatments for rheumatoid arthritis for decades. In the past few years, anti-TNF- α (tumor necrosis factor- α) biopharmaceuticals have sparked a revolution. More drugs targeting the inflammation pathway are in the works.



439 **Systemic Lupus Erythematosus (SLE): Trials and Issues**

Ioana Moldovan and Ellen M. Ginzler

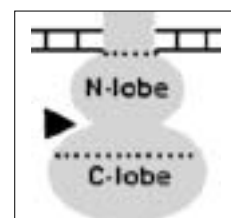
Lupus is believed to be an autoimmune disease, affecting many more women than men. Patients develop immune responses to self DNA, omnipresent in the body. Estrogen and androgen are involved in the disease. Immunosuppression and sex hormone therapeutics are two major classes of drugs in clinical trials.



444 **Mutations of EGFR in Lung Cancers and Their Implications for Targeted Therapy**

Hisayuki Shigematsu and Adi F. Gazdar

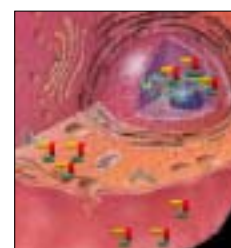
Iressa, Erbitux, and Tarceva, all targeting EGFR, have recently been approved for cancer treatment. Recent studies demonstrated that certain EGFR mutations caused structural changes of EGFR molecules so that they may bind more tightly to the drugs and predict an increased response to treatment with these drugs.



448 **Dying Dangerously: Necrotic Cell Death and Chronic Inflammation Promote Tumor Growth**

Michael T. Lotze and Richard A. DeMarco

Authors believe that cancer is primarily a disorder of cell death rather than cell growth. There is a consequence when cells don't die an apoptotic death. Cells release a bunch of hazardous molecules when they die by necrosis. A new theory describes that necrotic death and chronic inflammation may foster the onset and growth of tumors.



457 **Hepatitis B and C Treatment: New Perspectives**

Janice Main and Emma Thomson

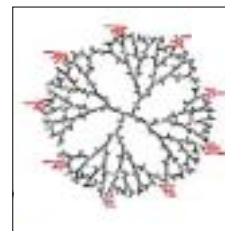
350 million people worldwide carry the hepatitis B virus and 170 million the hepatitis C virus. There has been encouraging progress in recent years in the management of both infections. The combination of pegylated interferon and ribavirin is perhaps the most effective treatment today.



464 Dendrimer Drugs Prevent Scar Tissue Formation

Sunil Shaunak

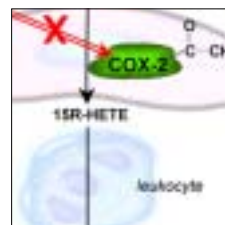
Scar formation is a dreaded consequence of eye surgery. It is invariably associated with inflammation, angiogenesis and wound healing. There is always a balance in healing the wound with the least scar formation possible. Certain dendrimers (polymers) compounds help keep this balance by reducing inflammation and thus scar formation but leaving the wound healing process largely intact.



470 Aspirin Triggers Formation of Anti-inflammatory Mediators: New Mechanism for an Old Drug

Nan Chiang and Charles N. Serhan

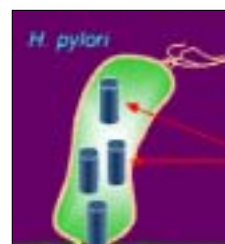
There are some fascinating studies that demonstrated aspirin's superior benefits with serious side effects. Aspirin inhibits COX-1 (cyclooxygenase-1). Its effect on COX-2 is more delicate: it "turns off" COX-2's production of prostaglandins but "switches on" the enzyme's ability to produce novel protective lipid mediators.



476 *Helicobacter pylori* Causes Gastric Cancer by Hijacking Cell Growth Signaling

Masanori Hatakeyama

Gastric cancer may not affect a lot of people in North America and Europe, but it is one of the top killer cancers in Asia. A persistent infection with the bacterium *Helicobacter pylori* in the stomach contributes greatly to the occurrence of gastric cancer in Asia. It turns out that Asian bacterial strains are more potent in transforming normal cells to cancerous ones than "Western" or African strains.



482 "The Great Influenza: The Epic Story of the Deadliest Plague in History" (Book Summary)

Book by John M. Barry, Summary by David Eve

"The Great Influenza" recounts what humanity witnessed and experienced during the 1918 influenza pandemic. Author John M. Barry also describes the remarkable transformation of U.S. medical education just prior to 1918. That transformation not only helped America cope with the pandemic but also continues to influence medical research and practice today.

