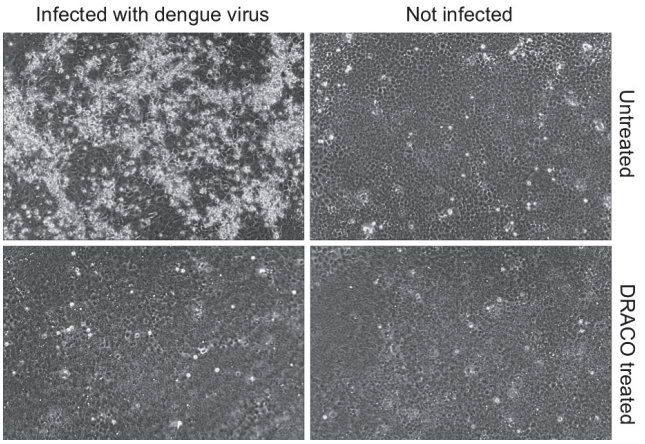
DRACO: A POTENTIAL CURE FOR ALL VIRAL INFECTIONS

Ilia Ostrovski



Upon diagnosing a patient with a bacterial infection, a physician usually follows the standard protocol of prescribing an antibiotic. However, in the case of a viral infection, much less can be done to intervene. In fact, most modern viral treatments are highly specific, prone to viral resistance and can cause adverse effects.

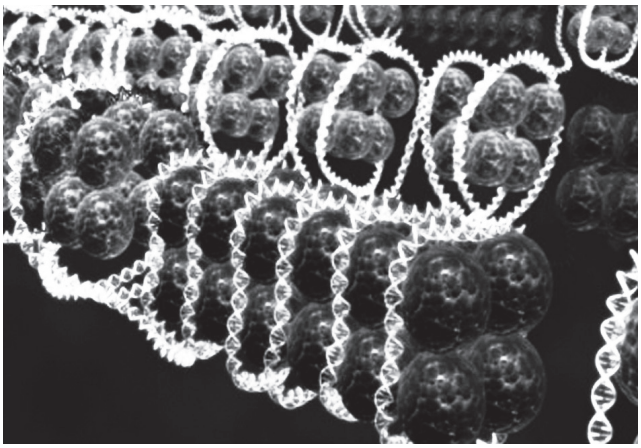
Recently, a team of researchers at MIT Lincoln Laboratory led by Todd Rider described the development and effectiveness of a drug that is capable of treating any viral infection. Double-stranded RNA Activated Caspase Oligomerizer (DRACO) has already been proven effective against fifteen different viruses, including H1N1 influenza, West Nile virus, and rhinovirus (the culprit behind the common cold). In addition to treating these viruses post-infection, this broad-spectrum drug is prophylactic and thus has the potential to also revolutionize preventative medicine.

DRACO selectively targets infected cells by detecting viral double stranded RNA (dsRNA), a marker of a virus's attempt to replicate itself inside the infected cell. Upon detection, DRACO initiates a cascade that induces apoptosis (cell death), without harming healthy cells. Isolating infected cells as targets for intervention by recognizing dsRNA was an idea inspired by the natural defense mechanism that our body utilizes to combat viral infection. By coupling this identification process with the induction of apoptosis, Dr. Rider and his team have achieved unprecedented success in combating viral infections. Rider's laboratory is now working on optimizing the efficiency of dsRNA detection and apoptosis-induction processes by DRACO, and they hope to begin human trials as soon as possible.

Rider TH, Zook CE, Boettcher TL, Wick ST, Pancoast JS, Zusman BD. Broad-Spectrum Antiviral Therapeutics. Plos One 2011 Jul 27;6(7):e22572.
Image adapted from: http://web.mit.edu/

EPIGENETIC CHANGES IN STEELWORKERS

Andrew Webster



Throughout the world, steel mill workers are exposed to airborne particulate matter (APM) containing high concentrations of toxic metals such as nickel, chromium, and arsenic.[1] While epidemiological studies have linked the APM of steel plants with an increased risk of lung cancer, the mechanism of action is unclear.[2]

Previous in vitro studies with lung epithelial cell lines have suggested that the metals in APM may bind to histones—the proteins around which DNA is coiled. By oxidative stress, they induce *activating histone modifications*, including H3K9 acetylation and H3K4 methylation. These modifications cause a slight uncoiling of the DNA strand, exposing specific gene sequences for transcription. It is thought that these modifications may contribute to carcinogenesis by enabling the expression of cancer-promoting genes.[3]

A recent study by the University of Milano investigated whether these carcinogenic histone modifications seen in the in vitro experiments are also produced in the peripheral *blood leukocytes* of steel plant workers exposed to a variety of airborne metal particulates.[3] The three-year study employed *enzyme-linked immunosorbent assays* (ELISAs) to analyze the state of H3K9s and H3K4s in the blood of 63 healthy males working in the same steel plant. The results of the study confirmed that long-term exposure to inhalable nickel and arsenic (but not chromium) particulates is correlated with significant increases in the concentration of modified H3K9s and H3K4s in the blood.

While further study is still required to confirm whether there is a definite link between diagnosed lung cancer and epigenetic changes caused by certain metals, this research highlights that even contemporary industrial environments may pose significant risks to worker health.[3]

[1]Cantone L, Nordio F, Hou L, Apostoli P, Bonzini M, Tarantini L, et al. Inhalable Metal-Rich Air Particles and Histone H3K4 Dimethylation and H3K9 Acetylation in a Cross-sectional Study of Steel Workers. Environ Health Perspect 2011 Jul 2011;119(7):964-969.
[2]Wild P, Bourgkard E, Paris C. Lung Cancer and Exposure to Metals: The Epidemiological Evidence. Methods in Molecular Biology 2009;472:139-167.
[3]Alley DE, Langley-Turnbaugh S, Gordon NR, Wise JP, Van Epps G, Jalbert A. The effect of PM10 on human lung fibroblasts. Toxicol Ind Health 2009 Mar;25(2):111-120.
Image adapted from: http://www.pbs.org/

TREATING DIABETES WITH NUTS

Khizer Amin

A few nuts a day can go a long way in the control of diabetes. Low in carbohydrates but high in fibre, protein, and omega-3 fatty acids, the nutritional composition of nuts has garnered fascination and interest from the scientific community for years. Previous studies have shown that the consumption of nuts significantly reduces the chance of heart disease.[1]

Recently, researchers at the University of Toronto established the value of unsalted and unroasted mixed nuts—including almonds, pistachios, walnuts, pecans, hazelnuts, peanuts, cashews, and macadamias—in the management of Type II diabetes.[2] In the study, 117 type II diabetics were randomly assigned to one of three treatment groups: a full portion of nuts, a whole muffin, or a half portion of nuts and half a muffin. This supplement to daily diet was maintained for three months. All treatments helped to significantly increase levels of good cholesterol. However, it was found that the nut-only treatment reduced baseline blood-glucose level significantly more than the other two treatments. Furthermore, individuals on the nut-only diet experienced significantly greater reductions in "bad" cholesterol levels than did those on the whole muffin treatment.

This research has positive implications for people without diabetes as well. Nuts were found to be a suitable replacement for carbohydrate intake, and the daily diet was not associated with weight gain.[2] In summary, an increase in the daily consumption of nuts could prove valuable in the maintenance of good health and a satisfactory body weight.

[1]Kendall C, Esfahani A, Truan J, Srichaikul K, Jenkins D. Health benefits of nuts in prevention and management of diabetes. Asia Pac J Clin Nutr 2010; 19(1):110-116
[2]Jenkins D, Kendall C, Banach MS, Srichaikul K, Vidgen E, Mitchell S, et al. Nuts as a Replacement for Carbohydrates in the Diabetic Diet. Diabetes Care 2011; 34(8):1706-1711.
Image adapted from: http://foodfortorte.blogspot.com/

BIOMEDICAL RESEARCH AS A WEAPON

Yasmeen Mansoor

Scientific publications openly present revolutionary findings with an aim to share knowledge for the progress of human society. Publications involving healthcare and medicine hold an area of high interest in the scientific community due to the common goal of overcoming disease and improving human health. What is often overlooked, however, is the potential threat that such information can pose if placed in the hands of terrorists seeking to develop catastrophic bioweaponry.[1]

Many top tier journals have gained the attention of organizations such as the World Health Organization (WHO) and the US National Science Advisory Board for Biosecurity (NSABB) due to the potential misuse of the information that they present.[1] This information is referred to as "dual use research" (DUR), and can facilitate terrorism depending on the detail of the information presented. Some examples of research topics that have been categorized as DUR are findings that show certain vaccines as ineffective, research about microbial virulence, and the need for biodefense (e.g. quarantine of infected patients) against antibiotic resistant bacteria.[1]

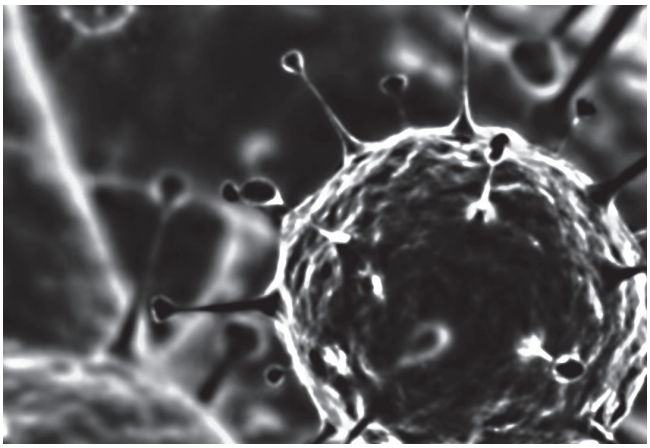
Bioterrorism is a relatively simple task to accomplish once the necessary information and the tools required are made available to a terrorist.[2] The area of biotechnology itself has become so advanced that simple genetic engineering techniques can be used to synthesize deadly viruses and pathogens.[2] Not only is bioterrorism geared as a threat to public health, but it can also harm agriculture, animals, or the environment.

In terms of reducing the threat of future bioterrorism, journal editors are in the process of developing policies to communicate research in ways that "maximize public benefits and minimize risks of misuse."[1] Current strategies are targeted towards all members of the scientific community in an effort to raise awareness about the implications of their published research.[1]

[1]Nightingale SL. Scientific Publication and Global Security. JAMA-Journal of the American Medical Association Aug 3 2011;306(5):545-546.
[2]Marietta, D. Terror in a vial. Sci Am 2010 2010-Jun;302(6):28.
Image adapted from: http://www.vvallpaper.net/

THE WORLD'S FIRST TRIAL IN VIRAL CANCER THERAPY

Humna Amjad



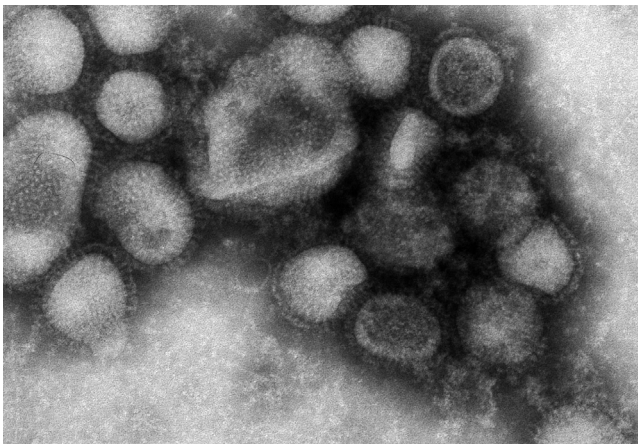
Researchers at the Ottawa Hospital Research Institute (OHRI) and Pusan National University in Korea have recently reported the results of promising trial on intravenous virus therapy to combat cancer. This is the first trial of its kind to show expression of transgene in selective tumours after intravenous delivery using a specially engineered virus. The trial consisted of 23 patients, all of whom had cancers that spread (metastasized) to multiple organs and failed to respond to standard cancer treatment. The patients were given one of five doses of the engineered virus, and biopsies were obtained ten days later. Seven of eight (87%) patients that were given the two highest dosages presented increased viral replication in *only* their cancerous tissue, with normal tissue remaining unharmed.

This is the first time in medical history that an intravenously-delivered viral therapy was able to selectively target cancerous tissue. Dr. John Bell, a Senior Scientist at OHRI, explains that intravenous delivery is vital for the treatment of metastatic cancer because it allows all tumours in the body to be targeted. Furthermore, in moderate doses, viral therapy has only mild side effects—somewhat similar to flu symptoms. Enthusiastic about the results, Dr. Bell states that, "[they] are promising, especially for an early-stage trial, with only one dosage of therapy. However, we are working to advance our understanding of these viruses and figure out how best to use them." Indeed, in the future, engineered viruses may become the gold-standard treatment for combating cancer.

Breitbach CJ, Burke J, Jonker D, Stephenson J, Haas AR, Chow LQM, et al. Intravenous delivery of a multi-mechanistic cancer-targeted oncolytic poxvirus in humans. Nature 2011 Sep 1;477(7362):99-102.
Image adapted from: http://www.health-healths.com

H1N1: BLOWN OUT OF PROPORTION

Kimia Sorouri



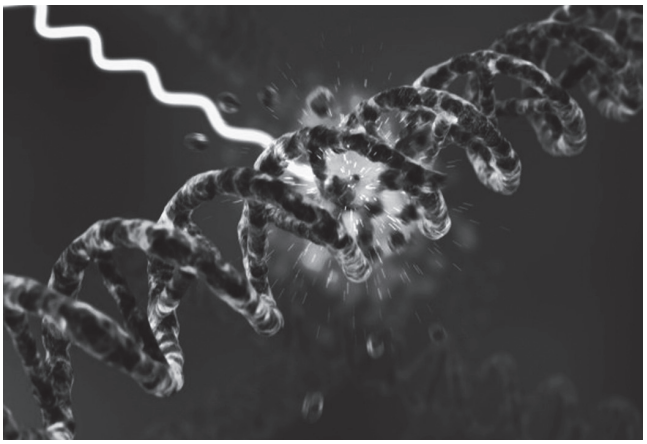
During the H1N1 (swine flu) outbreak, there was a clash between the global health system, the World Health Organization (WHO) and the pharmaceutical industry. It has been speculated that pharmaceutical companies encouraged WHO advisors to label the H1N1 outbreak a pandemic in order to boost vaccine sales. This notion of misinformation is echoed by external organizations that claim that the WHO exaggerated the dangers of H1N1 to the general public, resulting in a costly disruption to healthcare. The names of the members on committees involved in the WHO decision-making process have yet to be disclosed. Without this transparency, it is only natural to doubt the intentions and reliability of the decisions. Regardless of the level of authority, effective decisions arise from controlled communication among the decision-makers and timely disclosure of information to everyone else affected. This level of clarity among public health organizations was arguably not present during the H1N1 outbreak and may have contributed to the disease being amplified as a pandemic.

The WHO's handling of the H1N1 pandemic prompted the American College of Chest Physicians to establish guidelines to avoid the undue influences of 'big pharma' in global health policy. Each guideline chapter was assigned initially to an individual free of such conflicts of interest. Furthermore, any information gathered from experts with conflicts of interest is vetted through a panel of members without such conflicts. The US National Academies and the European Medicines Agency have also followed in stride, all in an effort to regain public confidence.

Evans MR. The Swine Flu Scam? Journal of Public Health 2010 August 4; 32(3):296-297.
Image adapted from: http://www.cdc.gov/

DEFICIENT DNA REPAIR AND NEURODEGENERATION

Keith Lee



Despite the high prevalence of age-related cognitive decline and neurodegenerative diseases, little is known about the mechanisms by which these conditions progress. Some research suggests that accumulation of DNA damage is associated with neurodegeneration, but until recently little evidence has demonstrated direct causality in this association.

In order to elucidate the nature of this relationship, Dr. Nils Zuiderveen Borgesius and his team examined whether defects in DNA repair were sufficient to induce age-related neurodegeneration. For this purpose, the researchers mutated ERCC1, a gene in mice that is required for three different DNA-repair mechanisms. The mutant protein is not as effective at DNA repair, causing an accumulation of damaged DNA in the brain.

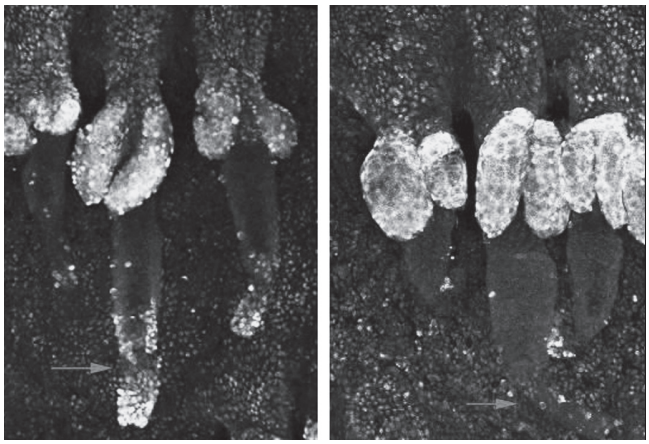
By examining biological markers for neuronal injury, degeneration and cell death, it was established that defective DNA repair causes a brain phenotype that is representative of aging and neurodegeneration. Adult mice with the defective protein developed learning and memory problems and had impaired cognitive function compared to mice without the ERCC1 mutation.

The results of this study demonstrate that an impaired DNA-repair system in mice is sufficient to reproduce the pathology and symptoms typical of neurodegenerative diseases. The discovery of this relationship provides insight into the development of new therapeutic and prevention strategies for age-related cognitive decline and neurodegenerative diseases.

Borgesius NZ, de Waard MC, van der Pluijm I, Omrani A, Zondag GC, van der Horst GT, et al. Accelerated age-related cognitive decline and neurodegeneration, caused by deficient DNA repair. J Neurosci 2011 Aug 31;31(35):12543-12553.
Image adapted from: http://www.e-nox.net/

"MOLECULAR CLOCK": CLUES IN SKIN STEM CELLS

Matthew Chong



Circadian rhythms are defined as "a physiological timing mechanism that allows organisms to anticipate and adapt to the day-night cycle".[1] For instance, the rise and fall of the hormone melatonin is intricately tied to our sleep-wake cycle. The programmable nature of this cycle explains why one feels particularly groggy after oversleeping or so-called all-nighters.[2] Circadian rhythms are not exclusive to the sleep-wake cycle and are found in a variety of organisms, large and small.

Writing in *Nature*, Spanish scientists show that stem cells possess signaling proteins that regulate gene expression in a circadian-like manner. Differential, time-dependent gene expression within stem cells is important to maintain an active population of stem cells to respond to any alterations in homeostasis, while at the same time keeping some cells in reserve. Interestingly, when the main core protein of the clock was knocked out, there was an accumulation of dormant stem cells, which led to premature aging of the cell line and reduced tumorigenesis. Given the association of aging with cancer, the findings may be paradoxical, but nonetheless shed light on the molecular machinery that keeps our gene expression in sync with the world. Further research into the role of circadian rhythms within stem cells, which are important for tissue repair and regeneration, can give us a better understanding of the aging process and neoplasia.[3]

[1]*Cavallari N, Frigato E, Vallone D, Frohlich N, Lopez-Olmeda JF, Foa A, et al. A blind circadian clock in cavefish reveals that opsins mediate peripheral clock photoreception. PLoS biology. 2011;9(9):e1001142. Epub 2011/09/13.*
[2]*Barion A. Circadian rhythm sleep disorders. Disease-a-month : DM. 2011;57(8):423-37. Epub 2011/09/21.*
[3]*Janich P, Pascual G, Merlos-Suarez A, Batlle E, Ripperger J, Albrecht U, et al. The circadian molecular clock creates epidermal stem cell heterogeneity. Nature. 2011. Epub 2011/11/15.*
Image adapted from: http://www.sciencedaily.com/