MEDBULLETIN

NEUROSCIENCE

TEACHING AN OLD BEE NEW TRICKS: REVERSING BRAIN AGING

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Dementia in the elderly is rapidly becoming a major issue. In Canada alone, a new case of dementia develops every 5 minutes.[1] Although current research on age-related dementia is primarily concerned with creating new drug treatments, a recent study has shown that social interventions may be just as promising.

A study by Baker et al.[2] has demonstrated the power of social interventions in a colony of honeybees. Young bee workers begin their lives as "nurse" bees that care for the nest and larvae. They then grow to become "foragers" that hunt for food. It has been shown that brain function rapidly declines with age in foragers while staying relatively intact in nurse bees who remain sheltered within the nest. The study's aim was to see what would happen if these foragers reverted back to performing the activities of nurse bees and if neural plasticity could be rescued.

The investigators first removed the younger nurse bees from the nest, leaving only the older foragers, larvae, and queen behind. Some foragers reverted to nurse bees to make up for this loss, caring for the nest and brood, while others remained as foragers. After ten days, the reverted nurse bees significantly improved their learning abilities, effectively reversing the brain aging process. This behavioural finding was supported by data obtained through mass spectrometry of brain tissue. Specifically, it was found that proteins involved in cellular maintenance and protection against dementia were increased.[2]

These results suggest that modifying behaviour based on one's social environment can reverse brain aging. Since social intervention programs are less costly than drug development,[3] such programs may be key to treating and preventing dementia.

1. Alzheimer Society of Canada. Facts about dementia [Internet]. 2012 [updated 2012 Sept 11; cited 2013 Sept 10]. Available from: http://www.alzheimer.ca/en/on/About-dementia/Dementias/What-is-dementia/Facts-about-dementia
2. Baker N, Wolschin F, Amdam GV. Age-related learning deficits can be reversible in honeybees Apis mellifera. Exp Geron 2012 May;47(10):764-772.
3. ScienceDaily. Bees can 'turn back time,' reverse brain aging [Internet]. 2012 [updated 2012 Jul 3; cited 2013 Sept 10]. Available from: http://www.sciencedaily.com/releases/2012/07/120703172547.htm
4. Honey Bee Takes Nectar [Image from the internet]. Available from http://en.wikipedia.org/wiki/File:Honey_Bee_takes_Nectar.JPG [accessed 27 Oct 2013]

SUPERBACTERIA

THE SILVER LINING TO ANTIBIOTIC RESISTANCE

ABRAHAM REDDA

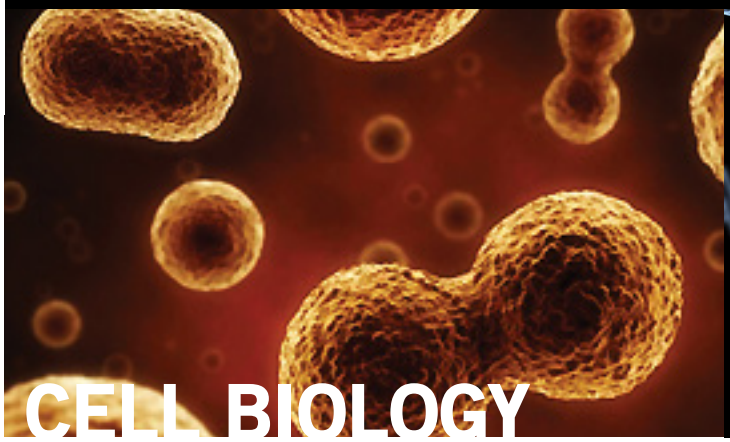
The rising incidence of antibiotic resistance and the emergence of new pathogens have highlighted the need for improving the effectiveness of current antibiotics instead of exclusively expanding our antibacterial arsenal. This issue has become increasingly important in the case of Gram-negative bacteria, which display considerably more antibiotic resistance than Gram-positive bacteria. The enhanced resistance results from the additional lipopolysaccharide membrane of Gram-negative bacteria. However, new research conducted at Boston University has shown that silver ions may hold the key to making Gram-negative bacteria susceptible to antimicrobial treatments.[1]

Jose Morones-Ramirez and colleagues reported the ability of silver ions to react with hydrogen peroxide to produce hydroxyl radicals, which readily react to disrupt disulfide bond formation, metabolism, and iron homeostasis in Gram-negative bacteria.[1] The disruption of these cellular processes increases membrane permeability and enhances the activity of antibiotics against Gram-negative bacteria.

Ramirez and colleagues also showed that silver ions are able to restore antibiotic susceptibility to previously resistant bacterial strains. Using mice whose urinary tracts were infected with a resistant strain of *E.coli*, experimenters found that neither silver nor antibiotics on their own were effective. However, when mice were treated with antibiotics in conjunction with silver ions, the researchers found that the combination proved lethal to the *E.coli* bacteria.[1]

Ramirez highlighted the ability of silver ions to increase the membrane permeability of Gram-negative bacteria, thereby sensitizing the bacteria to vancomycin, a Gram-positive-specific antibiotic. The finding is especially intriguing because it suggests the potential to increase the applicability of existing antibacterial drugs by coupling them with silver ions.

1. Morones-Ramirez J. Silver enhances antibiotic activity against Gram-negative bacteria. Science Translational Medicine. 2013 Jun 19; 5 (190): 1-11
2. Bacteria [Image from the internet]. Available from http://images.sciencedaily.com/2008/09/080918192836-large.jpg [accessed 27 Oct 2013]



CELL BIOLOGY

INDUCING STEM CELLS IN VIVO OVER IN VITRO

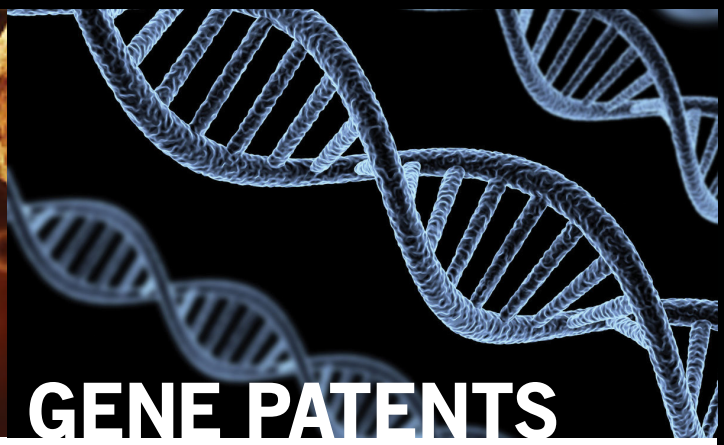
AVRILYNN DING

Over the past 50 years, stem cell therapy has aimed to use the regenerating and differentiating abilities of stem cells to grow new tissues and replace diseased or damaged ones.[1] While scientists have developed many techniques to generate and culture stem cells *in vitro*, challenges remain when introducing them into mammalian models for clinical treatments. However, recent research led by Manuel Serrano at the Spanish National Cancer Research Centre successfully reprogrammed adult mouse cells *in vivo* to become induced pluripotent stem (iPS) cells, a laboratory equivalent of embryonic stem cells.

The scientists genetically engineered mice to express the four genetic factors capable of inducing pluripotency in somatic cells: Oct4, Sox2, Klf4 and c-Myc. The gene's expression levels were controlled using varying dosages of an antibiotic, doxycycline. After treating mice with low doxycycline doses, the researchers found teratomas in many of their organs. Teratomas are tumours containing multiple cell types, which result from disorganized differentiation of pluripotent cells, and are indicative of cellular reprogramming. Researchers also found iPS cells circulating in the mice's blood. These *in vivo* generated iPS cells are genetically closer to embryonic stem cells at an early developmental stage than standard *in vitro* iPS cells. The *in vivo* iPS cells are also capable of forming embryo-like structures and trophoblast giant cells, placental cells that cannot be formed by other artificial stem cells.[1]

In vivo cellular reprogramming has great implications for regenerative medicine, bypassing the need to grow cells outside of the body and functionally integrate them back. The findings suggest not only that *in vivo* reprogramming is feasible, but that it also generates iPS cells with greater differentiation capacities than standard stem cells. Future research will focus on controlling the differentiation of *in vivo* iPS cells to regenerate specific cells without producing tumours.

1. Bathesda MD. Stem Cell Basics. National Institutes of Health, U.S. Department of Health and Human Services, 2009 [cited 2013 Sept 15] Available from: http://stemcells.nih.gov/info/basics/Pages/Default.aspx
2. Abad M, Mosteiro L, Pantoja C, Canamero M, Rayon T, Ors I, et al. Reprogramming in vivo produces teratomas and iPS cells with totipotency features. Nature. 2013[cited 2013 Sept 11]. doi: 10.1038/nature12586
3. Cells Web [Image from the internet]. Available from: http://wid.wisc.edu/content/uploads/2012/09/cells-web-550x367.jpg [accessed 27 Oct 2013]



GENE PATENTS

IS OUTLAWING NATURAL GENE PATENTS HARMFUL?

KACPER NIBURSKI

Two fundamental bases often decide one's lot in life: wealth and genetics. Recently, the two came together when the Supreme Court of America ruled, in a 9-0 unanimous decision, that natural genes could not be patented.[1]

Siding with the American Civil Liberties Union (ACLU) against the Utah-based Myriad Genetics Corporation, the legal decision was heralded as a step forward by civil liberty groups and as a disincentive to research by disgruntled biotech corporations.

The legal ruling centered around two genes, $BRCA_1$ and $BRCA_2$, which are paramount in the diagnosis of breast and ovarian cancers.[1,2] Carriers with mutations to these genes are approximately 80% more likely to develop some form of aggressive cancer. Preliminary clinical tests, previously and exclusively owned by Myriad Genetics, were necessary to detect these mutations. Due to a previous patent that ensured sole rights to Myriad Genetics, however, these medical tests were inaccessible to some patients as a result of their increased costs.[3]

The decision sought to reverse this exclusivity by ensuring that isolated DNA from natural sources, no matter the extensive research, localization, and purification techniques, could not be legally "invented".[1] Synthetic DNA, however, could very well be patented, the decision stated, as it is a "human-made invention."

This verdict has far-reaching ramifications beyond human DNA as it leads into questions involving the inventorship of microbial, plant, and other animal genes.[2] Furthermore, it may have an adverse effect on biotechnology companies as the investment of human genetic research may be compromised by the inability to patent a final product.

1. Liptak, A. Justices, 9-0, Bar Patenting Human Genes. The New York Times. 2013 Jun 13.
2. Than, K. 7 Takeaways From Supreme Court's Gene Patent Decision. National Geographic Daily News. 2013 Jun 14.
3. Ellis, J. Opinion: On Patenting Genes. The Scientist. 2013 Jun 18.
4. Genome [Image from the internet]. Available from http://i.huffpost.com/gen/968322/thumbs/o-GENOME-facebook.jpg [accessed 27 Oct 2013]

LIFESTYLE

THE ROLE OF EXERCISE IN OBESITY

ISHAN ADITYA

Obesity has become so prevalent in the world that it is now classified as a disease due to its multiple complications.[1,2] In fact, this condition is now known to affect the entire body, including the immune system. When the body is in a state of obesity, it tends to secrete inflammatory mediators called chemokines, which are produced by immune cells in the body.

Dr. Samaan and colleagues from McMaster University decided to study Chemokine (C-C motif) Ligand 2 (CCL2) because very little is known about the immune response of this factor.[3] The initiation and propagation stages of the inflammatory responses in obesity occur when these chemokines are secreted into muscle and adipose tissue. The study aimed to determine whether CCL2 levels are higher in obese children when compared to lean controls and if fitness plays a role in reducing the concentration of CCL2 levels in the body. The study involved a group of 18 obese and 18 lean children in which half of each group was placed into a "high" fitness group while the other half was placed into a "low" fitness group. An aerobics fitness test was performed using a cycle ergometer in which the resistance was gradually increased every two minutes. Serum insulin and CCL2 variables were measured using an enzyme-linked immunosorbent assay (ELISA) technique. The results of the experiment confirmed the hypothesis that CCL2 levels were higher in obese children and children of the "low" fitness group, thus supporting the link between exercise and inflammation.

Further study of the inflammatory pathways of these chemokines will establish new avenues for drug development and lifestyle plans that will help combat the aptly-named epidemic of "globesity".[3]

1. Thomson, A. Obesity now recognized as a disease. CBC News. 2013 Jun [cited 2013 Sept. 14]; Available from: http://www.cbc.ca/news/health/obesity-now-recognized-as-a-disease-1.1320011
2 Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of obesity and trends in body mass index among US children and adolescents, 1999-2010.~Journal of the American Medical Association 2012;307(5):483-490.
3 Samaan MC, Obeid J, Nguyen T, Thabane L, Timmons BW. Chemokine (C-C motif) Ligand 2 is a potential biomarker of inflammation & physical fitness in obese children: a cross-sectional study
4. Obesity [Image from the internet]. Available from http://thinkprogress.org/wp-content/uploads/2012/05/obesity4.jpg [accessed 27 Oct 2013]

SOCIETY

THIRD HAND SMOKE: A GROWING CONCERN

MAYLYNN DING

In 2009, the term "third-hand smoke" (THS) was coined by Dr. Jonathan Winickoff's team at the Dana-Farber/Harvard Cancer Center to describe toxic tobacco smoke contaminants that accumulate on surfaces.[1] A critical property of THS is its tendency to undergo chemical transformations to produce secondary toxicants. A 2010 study demonstrated residual nicotine's ability to react with common indoor air pollutants, specifically ozone and nitrous acid, to produce a class of potent carcinogens called tobacco-specific nitrosamines (TSNAs).[2]

Recently, a research team led by Dr. Bo Hang at the Lawrence Berkeley National Laboratory established a direct link between THS and damage in a cell's genetic material, or genotoxicity.[3] To simulate acute and chronic THS, researchers exposed chromatography paper strips to tobacco smoke in a closed chamber for varying lengths of time. The compounds on the paper strips were extracted and then used to treat human liver cell lines. Cultured cells were then probed for DNA breaks and oxidation – both strong indicators of genotoxicity. Cells treated with acute or chronic THS extracts had notably more DNA breaks than untreated cells. Cells treated with chronic THS extract exhibited the highest levels of DNA oxidation and TSNA concentration. This suggests that THS becomes more toxic over time. THS extracts reacted with nitrous acid contained more NNA, a THS-specific carcinogen, than unreacted extracts – further evidence of the dangers of THS chemical transformation.[3]

The study is the first to show the genotoxicity of THS to human cells and to compare acute THS exposure with chronic THS exposure. Future research will focus on understanding the chemistry of THS reaction with DNA and testing the genotoxic effects of THS *in vivo*.

1. Winickoff JP, Friebely J, Tanski SE, Sherrod C, Matt GE, Hovell MF, McMillen RC. Beliefs About the Health Effects of "Thirdhand" Smoke and Home Smoking Bans. Pediatrics. 2009 Jan 1; 123(1):e74-e79.
2. Sleiman M, Gundel LA, Pankow JF, Jacob P, Singer BC, Destaillats H. Formation of carcinogens indoors by surface-mediated reactions of nicotine with nitrous acid, leading to potential thirdhand smoke hazards. Proceedings of the National Academy of Sciences. 2010 Feb 8; 107(15):6576-6581.
3. Hang B, Sarker AH, Havel C, Saha S, Hazra T, Schick S, Jacob P, Rehan V, Chenna A, Sharan D, Sleiman M, Destaillats H, Gundel LA. Thirdhand smoke causes DNA damage in human cells. Mutagenesis. 2013 Jul; 28(4):381-391.
4. Smoke and Fish Desktop [Image from the internet]. Available from http://www.wallpopr.com/wallpaper/2013/02/01/smoke-and-fish-hd-desktop-high-definition.jpg [accessed 27 Oct 2013]