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CANCER, OLD CELLS AND MOLES: HINTS AT A COMPLEX WEB

by Daniel Auld

Aging and cancer are certainly related. Counter-intuitively, however, some new research suggests that certain aspects of aging might make some types of cancer less likely.

To understand this, it helps to recognize that cancer results from volatile cellular division following genetic mutations that accumulate over years. On the other hand, some features of aging - such as poor tissue regeneration - are related to cellular senescence, a state where cell division is impaired. A kind of molecular cap that sits astride our genes at the ends of chromosomes determines when senescence hits a cell. The system works by telomere length shortening every time a cell divides, so that when no telomere is left, a cell cannot divide and is said to become senescent. Thus, as we age and cells accumulate cancer-causing mutations, they have also

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TELOMERES AND TELOMERASE: A MATTER OF LIFE OR DEATH FOR CELLS

An interview with Chantal Autexier, Bloomfield Center for Research in Aging, Lady Davis Institute for Medical Research, Sir Mortimer B. Davis - Jewish General Hospital

by Elaine Waddington Lamont

Basic mechanisms of cell survival and cell death are the focus of the work of Dr. Chantal Autexier and, in her view, fundamental to the understanding of aging and age related diseases. She became excited about science while doing a Bachelors degree at Concordia University's Science College. The Science College is a unique program that allows students to get a well-rounded science education by doing projects in several different laboratories. Dr. Autexier really enjoyed this hands-on approach to science and took full advantage of the opportunity to explore the fields of

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"BRAINY BOOMERS" LECTURE SERIES DRAWS CROWDS

A big "thank you!" to the Jewish General Hospital, l'Institut universitaire de gériatrie de Montréal and Janssen-Ortho for their generosity in supporting "Brainy Boomers" / *"Baby-boomers Brillants"*.

In conjunction with the Montreal Alzheimer Society, the Education Committee of the MCSA organized a six-part public lecture series in October 2007 with the goal of suggesting healthy lifestyle choices based on the latest research findings, to help maintain brain health and to prevent age-related diseases. Close to three hundred people registered for the event.

The topics presented were "Memory and Aging" / *"Un esprit sain dans un corps sain"* with physicians Lorraine Mazzella and Josée Filion; "Nutrition for a Healthy Brain" / *"Bien manger pour un cerveau en santé"* with nutritionists Risa Segal and Pascale Fournier, and "Brain Gym"/ *"La gymnastique du cerveau"* with neuropsychologists Nora Kelner, Lennie Babins, and Nicole Caza. The extensive question periods following the lectures proved to be one of the most stimulating aspects of the series. We walked away with new knowledge, techniques and enthusiasm to engage the challenges of the latter half of life.

An interview with Chantal Autexier, Bloomfield Center for Research in Aging, Lady Davis Institute for Medical Research, Sir Mortimer B. Davis - Jewish General Hospital

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ecology, microbiology, and molecular biology. After getting her feet wet at Concordia, Dr. Autexier did her Ph.D. at McGill University. She joined the Department of Microbiology and Immunology, where she worked on the ways that proteins interact with and regulate DNA, the molecule that contains all of the genetic information needed for organisms to develop, function and reproduce.

Her interest in aging began at a large genetics conference in Toronto, where Dr. Autexier saw a lecture by renowned researcher Dr. Elizabeth Blackburn, famous for her work on telomeres. Telomeres are the "protective caps" on the ends of chromosomes. They help to keep the DNA on one chromosome from getting re-arranged with the DNA on other chromosomes and so keep the cells "blueprints" from becoming scrambled. Each time a cell divides, the telomeres get shorter. The shortening of telomeres is a factor that contributes to the aging of a cell by limiting the number of times it can divide. However, this process is reversible. Telomeres are lengthened by an enzyme called telomerase, which was discovered by Dr. Blackburn and her student, Carol Greider. Theoretically, the presence of telomerase could allow a cell to divide an unlimited number of times. Thus, there is a delicate balance between the shortening of telomeres and aging, and the run-away cell replication that can occur in a disease like cancer.

She was intrigued and so in 1991, Dr. Autexier began a postdoctoral fellowship with Dr. Greider, who had been recruited to work at Cold Spring Harbor Laboratory in New York, at that time home of the legendary Dr. James D. Watson, Nobel Prize winner and co-discoverer of the structure of the DNA molecule. In this exciting environment, Dr. Autexier began working on basic questions related to the way that telomeres are lengthened by telomerase.

In 1997 she brought this work to McGill when she joined the Departments of Anatomy and Cell Biology, and Medicine, and the Bloomfield Center for Research in Aging, at the Lady Davis Institute for Medical Research, Sir Mortimer B. Davis - Jewish General Hospital.

According to Dr. Autexier, one way of studying aging is by studying the diseases of aging. Aging is not a single process, and there is no one cause of aging. She has been fascinated by two questions concerning the role of telomeres and telomerase in aging. One is the treatment of cancer, while the other is preventing age-related cell death. She says: "One way that you can prevent cancer or prevent it from progressing is to direct cells toward either death or senescence." In other words, if you could prevent telomerase from doing its job, the telomeres would get shorter and the cell would begin to age and die. This would either prevent the cell from becoming cancerous or stop the spread of the tumor.

Beyond diseases like cancer, she is also interested in looking at a role for telomerase in the prevention of stress-related cell death in neurons. She says, "If you could overexpress telomerase or get it to become more active, you might prevent cells from dying." Evidence suggests that telomerase, and other mechanisms that protect chromosomes, might make good targets for therapies aimed at improving the survival of brain cells in the case of neurodegenerative diseases like Alzheimer's disease (Jain *et al.*, 2007). Animal models are valuable in this process, but there are also important differences between human and rodent telomeres and telomerase. For this reason, Dr. Autexier is developing techniques to meet the challenge of finding a source of human neurons. She has been doing exciting work to generate cell cultures that are similar to neuronal cells. Once this technique has been perfected, they will have an excellent model for understanding diseases and testing therapies that could protect neurons from cell death.

In the future, Dr. Autexier sees the potential of her research not just for treating aging cells, but for cell replacement for healing wounds or during transplantation. Although some people have raised the concern that these cells would begin to divide uncontrollably and become cancerous, there is good reason to believe that this is not the case. Telomerase may be present in cancer cells, but it is not the only step in turning a normal cell into a cancer cell. This makes telomeres and telomerase very exciting targets for future medical research. She says, "If there was some way to get cells to live, this would be helpful for diseases where cells are dying."

Dr. Autexier feels that basic research on the mechanisms of cell death and cell survival is critical for the identification and development of new molecular targets for aging and disease. For her efforts, she was recently awarded two operating grants from the Canadian Institutes of Health Research. Congratulations Dr. Autexier and best of luck in your future work to uncover the secrets of telomeres and telomerase.

For more information on Dr. Autexier, see: http://www.bloomfieldcentre.org/e/bios/c_autexier.htm

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POLICY AND POLITICS

VIOLENCE IN LONG-TERM CARE FACILITIES: RESIDENTS ON THE GIVING END OF THE BLOWS

by Tania Elaine Schramek

When our loved ones leave their homes to enter a long-term care facility one of the last things we would expect is for them to be subject to violence. What's more is that we would certainly not imagine that *they* could be the ones committing violent acts. A recent Ontario Ministry of Health and Long-term Care report[1] states that this is unfortunately a reality in many of the province's nursing homes. A CBC news investigation[2] citing official Government of Ontario documents revealed that the number of violent incidents has more than tripled over the course of the last three to four years. In 2003 for instance, 446 cases of resident violence were reported while in 2006 the number increased to 1,416.

As revealed by the Ministry's data, violence in general is on the rise in Ontarian long-term care facilities, be it in the form of residents abusing staff, residents abusing other residents, or residents being the victims of violence perpetrated by staff.

This problem is not only an issue in Ontario however; in British Columbia, the number of nursing home employees filing claims because they were attacked by residents was so on the rise that WorkSafeBC (BC's version of the CSST) recently commissioned a special report to study the issue. Approximately 1 out of every 30 adults over the age of 65 and 1 in 5 over 85 are living in long-term care facilities across Canada. Given that estimates put it at 1 in 5 residents in long-term care facilities being aggressive and could be a danger to other residents, this growing problem will likely need to be addressed by the respective governmental agencies that are in a position to do something.

At the Heart of the Matter

Why would the incidence of violence be so on the rise? Nursing associations and senior advocate groups argue that long-term care facilities are short-staffed and that the low-paid personnel left to work with residents are ill-prepared by their training to deal with the portion of the residential population that requires constant care.

It is well known that some individuals suffering from dementia, Alzheimer's disease in particular, can be aggressive. Experts explain that this aggression often arises from individuals feeling frightened or humiliated, being frustrated because they are unable to understand others or making themselves understood, and/or because the dementia has affected brain areas involved in judgment and impulse control. This aggression can take the form of being verbally abusive or threatening, physically threatening (e.g. kicking and pinching) or simply lashing out rather violently at people or property.

In most instances, steps can be taken to avert these outbursts[3]. However to do this a caregiver has to first receive the training that teaches how to prevent or deal with aggression (e.g. learning to recognize the common triggers of aggression). But a caregiver has to spend enough time with an individual to understand what the triggers are for this person, find ways to decrease the occurrence of these triggers, and very importantly, take time for themselves to deal with their own feelings. Although most long-term care facility workers who have received such training would gladly take these steps, shortages in personnel and increases in the number of residents simply do not allow for them to do so.

This raises another important issue facing caregivers and older adults in need of specialized care. For the Government, nursing home beds come much cheaper than do beds in specialized facilities or psychiatric hospitals. In addition, deinstitutionalization has made it such that there are few beds in these facilities to begin with. Here is the thing, better health care, diet, and lifestyles have made it so that life expectancy has increased. We now have more individuals living well into their eighties and nineties. But, one in four adults over the age of 85 lives with Alzheimer's. As such, the need for specialized care is increasing while our resources are decreasing.

This may in part explain why the Ontario Government has not implemented any of the recommendations made by the province's Chief Coroner's Office in the wake of an inquest looking into the deaths of two residents of a Toronto nursing home[4]. The victims died of blunt-force trauma to the head after having been attacked by another resident suffering from dementia. One of the most salient recommendations made states “The Ministry of Health and Long-Term Care should fund specialized facilities, as an alternative to long-term facilities, to care for demented or cognitively impaired residents exhibiting aggressive behaviour”. This jury and its members were not the only ones to make recommendations to the Ontario Government, in fact, every year, the Ontario Geriatric and Long-Term Care Review Committee sends out its annual report, with reports going back several years warning the Ministry that violence was on the rise.

For instance, the 1999 report states the following: "Given that the projected number of demented patients requiring institutional care is expected to increase dramatically in the coming years, it is recommended that the Ministry of Health, in consultation with representatives from the long-term care industry and the health-care professions, develop both a short-term and a long-term strategy to manage physically aggressive, demented patients. Inherent in this recommendation is the recognition of the principle that the safety of other vulnerable residents within long-term care institutions must be maximized."

When asked to comment on these recommendations by CBC news the Health Minister replied “the government does not want to build jails for the elderly”. The Honourable George Smitherman further states “I do understand, of course, the necessity of protecting individuals from one another, we can take appropriate steps to do that, but within an environment of long-term care instead of creating some segregated model where we've got all those individuals in newly built facilities."

To be sure, this important issue is one added to the long list of critical concerns the Provincial (residential care facilities are not governed by the Canada Health Act; individual provinces and territories set spending levels) and Federal governments have regarding the state of our health care system. In the interim, individuals can make some headway by becoming informed about issues surrounding older adults and especially finding tips on how to deal with Alzheimer's and its consequences. A good place to start is at the Alzheimer's society website and of course Geronto-McGill!

Sources

1 http://www.health.gov.on.ca/

2 http://www.cbc.ca/news/background/nursing-homes/

3 See the Alzheimer's Society website for tips on dealing with aggression in dementia http://www.alzheimers.org.uk/site/scripts/documents_info.php?documentID=96

4 http://www.cbc.ca/news/background/nursing-homes/pdf/casa-verde-inquest.pdf

OLD DOGS REALLY CAN LEARN NEW TRICKS: TRAINING THE PERCEPTUAL SKILLS OF SENIOR TENNIS PLAYERS

by Elaine Waddington Lamont

That old cliché that you can't teach an old dog new tricks just isn't true. According to a recent article by Ryan J. Caserta, Jessica Young, and Christopher M. Janelle published in the *Journal of Sport and Exercise Psychology*, training your brain helps your tennis game even more than training your body. They compared three groups of older intermediate level competitive tennis players. One group got no training. A second group got physical training, which included work on their swing and footwork development. A third group received what they called "multidimensional perceptual-cognitive skills training". This training was originally developed for fighter pilots and consists of situational awareness - responding to only relevant cues, comprehension of the current situation, and prediction of future situations, as well as anticipation and decision-making. A tennis professional played 4 singles games against each of the subjects before and after training, both to evaluate their play, and to force them to play a "smart" game that challenged them both physically and mentally. Both types of training were one-on-one and lasted for 40 minutes per day for 5 days. Subjects who received the cognitive training played a more accurate and much faster game - almost half a second faster. They also made smart decisions that forced their opponent to work harder. This was true even for those players suffering from mild cognitive impairment. The footwork training group and control group showed no improvement. This is exciting news for anyone who wants to improve their skills in tennis, or any sport, and brings to mind another old cliché: "Keep your head in the game."

Source:

Ryan J. Caserta, Jessica Young, and Christopher M. Janelle. 2007. Old dogs, new tricks: training the perceptual skills of senior tennis players. Journal of Sport and Exercise Psychology, 29(4), 479-97.

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undergone many divisions, pushing them towards senescence, which makes cell division unlikely. In one sense, shrinking telomeres might be a kind of last rung defense against cancer.

Veronique Bataille and her colleagues have recently addressed the cancer / senescence hypothesis in an interesting fashion. Her team compared the number of moles on women volunteers - though most moles are benign, a high count is a risk factor for skin cancer, specifically melanoma - with the length of telomeres in white blood cells. While white blood cells are unrelated to skin cancer, the research team considered them to be a general indicator of the state of telomeres throughout the body as a whole. Interestingly, they found that the more moles present, the longer the telomeres were. This is somewhat counterintuitive when one reflects that longer telomere length is typically a measure of youth, biologically speaking. Thus, even though these women were biologically younger than their counterparts, they had more moles - and their moles were larger and more irregularly shaped - than their biologically older counterparts, and were therefore more at risk to develop skin cancer.

This study illustrates the complex nature of cancer and aging. In a strange fashion, it is telling us that while some forms of cancer are usually diseases of aging (mutations that cause cancer accumulate over time), they may be more likely to strike when the cells are biologically younger (that is to say they are not senescent, have longer telomeres and are still capable of division). In an analogy, a drunk driver cannot do damage if their car won't start in the first place. As we continue to study aging, we are sure to continue to discover that the inner world of our bodies is a more mysterious place that we ever imagined.

Bataille V, Kato BS, Falchi M, Gardner J, Kimura M, Lens M, Perks U, Valdes AM, Bennett DC, Aviv A, Spector TD. Nevus size and number are associated with telomere length and represent potential markers of a decreased senescence in vivo. Cancer Epidemiol Biomarkers Prev. 2007 Jul;16(7):1499-502.

TO BE TREATED OR NOT TO BE TREATED: THAT IS THE *NEW* QUESTION…

by Tania Elaine Schramek

Prostate cancer is the most common form of cancer in men, with 22,000 new cases diagnosed last year in Canada, which, according to the Canadian Cancer Society estimates, will unfortunately result in over 4000 deaths. A new debate amongst physicians and urologists in particular centers on whether we are over-diagnosing the disease and whether some men with prostate cancer are being treated too aggressively.

It's hard to imagine any form of cancer being treated too aggressively because we tend to think the worst the moment the word 'cancer' enters the picture but specialists explain that there is more than one form of prostate cancer and that over 40% of men diagnosed have what is considered a low-risk form of the disease. As such, many doctors would argue that they are best served by being followed closely over years until some are reclassified as being intermediate or high risk at which time the more aggressive forms of treatment would definitely be called for.

These treatments include prostatectomy (complete removal of the prostate) and radiation therapy. Unfortunately, treatment also comes with a high incidence of erectile dysfunction, bladder control problems, and in some cases, rectal bleeding. This is why doctors and researchers like Dr. Laurence Klotz, a urological oncologist at Toronto's Sunnybrook Hospital, prone a more conservative approach to the detection and treatment of prostate cancer.

Dr. Klotz explains that "A guy who is diagnosed at 45 and observed for 15 to 20 years and is treated curatively is better off than being treated up front and having potential side effects for 15 to 20 years. I'm inundated with patients who are told they have cancer but are low risk. A lot of them see me as a lifeline to rationality." Dr. Klotz is conducting a 15-year study involving researchers in Canada, the United States and England, comparing radical treatment to the close surveillance approach. He stated that "in 500 patients at Sunnybrook managed that way there is a 99 per cent prostate cancer survival rate." Despite these numbers Dr. Klotz explains that 90% of men with low-risk cancer opt for radical treatment most likely because the idea of living with untreated cancer is too unnerving.

Advances in screening for prostate cancer are likely at the root of the issue. A healthy prostate normally produces a substance known as Prostate-Specific Antigen (PSA). It is when PSA levels in the blood become elevated that something is up and could indicate cancer but not always. Given this capacity for early detection we now are seeing prostate cancer diagnoses in much younger men than before. In fact, these days, PSA screening is common place in men over the age of 45. Men that are considered high risk like those with a family history of the disease or that are of African descent often begin screening at the age of 40.

Dr. Klotz told the CBC news network that "Many of my colleagues think prostate cancer equals removal. As well, the cancer societies, the research organizations and the media all hype this anxiety about cancer, which is justified in some cancers". Indeed "Patients who have high or intermediate risk of prostate cancer - which is determined by PSA level, the grade of the cancer and how extensive it is - need more aggressive treatment. However, with most of them nothing will happen and they will die of some unrelated cause."

It appears as though with low-risk forms of prostate cancer we are at a point where one has to balance the piece of mind that comes with radical treatment with the better quality of life close surveillance offers. For this, no one knows best but the person involved, their doctor, and their loved ones.

Source:

1. Klotz, L (2007) Low-risk prostate cancer can and should often be managed with active surveillance and selective delayed intervention. Nature, Clinical Practice Urology, Nov 27, PMID: 18091507

2. CBC news reports: http://www.cbc.ca/news/background/cancer/prostatecancer-toomuch.html

SCIENCE HERE AND NOW
DR. HÉLÈNE PAYETTE: LOOKING AT NUTRITION IN SENIORS

by Daniel Auld

Dr. Hélène Payette is a key figure in geriatric research in Quebec. Working out of the Research Center on Aging at the Sherbrooke Geriatric University Institute, she is involved in a number of important projects in aging research, ranging from nutrition to quality of life to depression, all the while maintaining a wide network of collaborations. Much of her work concerns nutrition in seniors. In fact, she and her colleagues have recently made several contributions to the field. In one study, Dr. Payette concludes that good nutrition 'can promote healthy aging,' which is associated with less sickness, more autonomy and more limited use of the health care system. The second study concerns a large-scale, long-term, longitudinal study playfully termed NuAge. In it, Dr. Payette helps to address the influence of nutrition on cognitive and physical status, as well as social support and functional autonomy in older adults aged from 62-82 (split into 3 different age groups) who have been followed since 2003. One feature that distinguishes this work is its multidisciplinary approach, spanning multiple research disciplines. When all is said and done, Dr. Payette and her collaborators will have amassed an impressive body of information on nutritional (diet, body type, appetite, etc.), health (physical and mental), social support (participation in social activities, support network, etc.) and function (physical capabilities, exercise habits, etc.) characteristics of older adults. Moreover, in this study, Dr. Payette and colleagues have looked at biological markers, including antioxidant levels and various hormones and other markers. Their goal is to understand how nutrition might impact multiple aspects of aging. Dr. Payette and her collaborators hope that by better understanding these relationships, recommendations can be made to guide food intake for healthy aging. On the more practical side of things, her group has also investigated the influence that the popular 'Meals on Wheels' program - where food is delivered to seniors' homes - has on community living seniors who are at risk for nutritional inadequacy. They found that the program helped improve the diet of these at risk elders, but it did not completely eliminate the risk for these seniors, suggesting that the program could be improved or augmented in order to achieve better results. Surely, Dr. Payette will continue her efforts to improve our understanding of nutrition in seniors and hopefully her recommendations will lead to improved lives.

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