BC Cancer Agency www.bccancer.bc.ca

Headlines

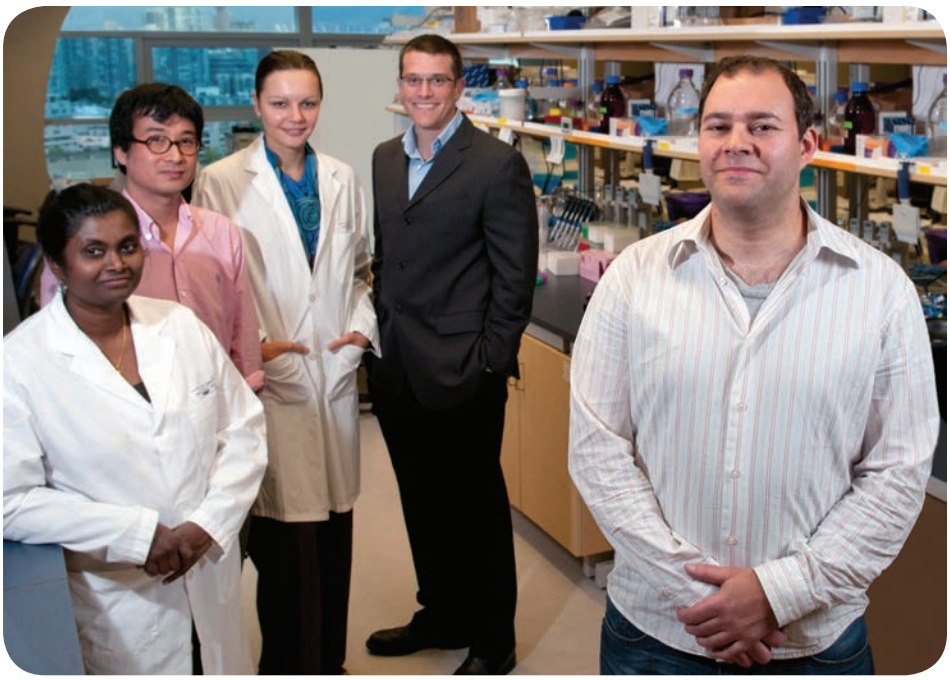
Fall 11 A newsletter for brain tumour patients and their families

MY STORY

My Cancer Journey

IN FEBRUARY 2004, my life changed forever when I collapsed in a grand mal seizure one Monday morning. My world faded into darkness. I gradually came out of a drug-induced state two days later at Vancouver General Hospital with a compressor on my legs, a tube sticking out of my chest due to a collapsed lung, another tube in my arm and my mom dabbing my dry mouth with a wet sponge. Scans indicated a mass in my brain and a biopsy was needed to determine its nature. After the excruciating pain of having a device drilled into my skull to enable a stereotactic brain biopsy, I was sedated just enough to be able to conduct a conversation, but not enough to be aware of the surgery. The anesthesiologist asked me what I do for a living. I started to talk about the work I was involved in at the Genome Sciences Centre (GSC), including sequencing the SARS coronavirus genome under Dr. Marco Marra's leadership just a few months previously.

When the biopsy was completed and the drugs wore off, the anesthesiologist thanked me for telling him all about genomics. A week later, my family and I received the devastating news: grade 4 astrocytoma (glioblastoma), a fast growing and aggressive form of brain cancer with a poor prognosis. It was hard for all of us to hear. After giving me the news about the prognosis, my surgeon, Dr. Brian Toyota, drew a survival curve explaining that although this curve represented the statistical prognosis, I was an individual, not a statistic. He said that I could be on the long-term survival end of the curve, and I wouldn't be the first person to do that. It was from this point that I made the decision to take an active role in doing whatever I could to be part of the survival end of that curve.



Yaron Butterfield, foreground, with members of his team, Suganthi Chittaranjan, Stephen Yip, Olena Morozova and Marco Marra

Treatment began a month or so after diagnosis: six weeks of radiation with concurrent temozolomide (TMZ), chemotherapy pills that looked like poison to me. I was not able to complete the chemotherapy regime because of the effects on my blood cells in the fourth week, but I thought that perhaps this was a sign that my body was very sensitive to the drug. In the fall of 2004, magnetic resonance imaging (MRI) showed that the tumour had indeed shrunk, but a year later, the tumour grew back and I enrolled in a clinical trial. The clinical trial drug I was given, lapatanib, proved to be ineffective in treating brain tumours. So I started back on TMZ treatment again for the first eight months of 2006, and thankfully, this was effective in shrinking the tumour. It has

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Making the transition to your "new normal"

ONE OF THE MOST COMMON QUESTIONS I hear from brain tumour survivors is: "How do I reconnect to my old life after I complete treatment for a brain tumour?" Although active treatment is challenging in many ways, it can also provide a focus for attention and effort and gives structure to life after the shock of diagnosis. So even though the end of a treatment can be a cause for celebration, it often also means directly confronting the need to adjust to a "new normal." Family caregivers may feel the same tension and uncertainty as they enter the period when they are not so tied to treatment, side effects and appointments at the cancer clinic and can begin to negotiate a return to their former lives.

Because the transition to a new normal is such a common challenge for the patients and families whom Braincare BC serves, I am excited to tell Headlines readers about a new program of research which is aimed at helping to make this transition easier. Through this program, the BC Cancer Agency, Vancouver centre, will offer two workshops for cancer survivors and their families. Workshops may take place at other cancer centres in the future.

The first, **Cancer Transitions**, is designed for BCCA **patients** who have finished active treatment within the last two years. The second, **Empower**, is designed for **family caregivers** of patients who have completed treatment within the last two years.

Both programs provide information about living with cancer, and will include expert advice about exercise, nutrition, goal setting, and emotional wellness. Both programs will also help participants to hone personal skills to help them feel stronger and more capable moving forward to their new normal.

Each program will include a single, full day workshop followed by four weeks of guided self-study to actively put the skills presented during the workshop into practice. A two hour "booster" session will conclude the programs and will ensure that participants' concerns are reviewed and addressed.

Participants will be asked to respond to study questionnaires and may also be asked to participate in short interviews asking about their experiences in the groups.

People who might be interested should call the number listed below. I will then call you back to tell you more about the group and to see if would be a good fit for you.

By Dr. Douglas Ozier, Braincare BC Researcher/Clinician

When:
Cancer Transitions: Monday, October 31, 2011
Empower: Monday, October 31, 2011

Where:
BC Cancer Agency, Vancouver Centre, John Jambor Room

For more information:
Call Patient and Family Counselling 604 877 6000 x 2194
www.bccancer.bc.ca/PPI/copingwithcancer

My Cancer Journey
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not recurred since then.

I believe that a combination of my tumour's biology and its responsiveness to treatment, but also my personal fight against the cancer, resulted in this success. My personal battle has involved meditation, exercise, prayer, art, top-notch care at the BCCA and most importantly a very close network of family and friends. I felt blessed and happy that in February, 2007, I could return to the GSC almost exactly three years since the day my life changed forever.

Although I had attempted to keep up with the fast moving state of genomics research and DNA sequencing, it didn't really hit me how much the technology had changed in my time away until I came back. What quickly became apparent was that with the decreasing costs of DNA sequencing and our ability to acquire significantly more data, sequencing cancer genomes was becoming a reality. In 2009, I was involved in characterizing a form of cancer, adenocarcinoma, before and after treatment. By 2010, I was contributing to the analysis of a cohort of brain cancer patients diagnosed with oligodendroglioma (ODG) under the direction of Drs. Stephen Yip and Marco Marra.

Through the Brain Tumour Support Group at the BCCA, I have met many courageous and inspiring people who have been diagnosed with this type of cancer. They were often in my thoughts while I worked with the massive amount of data, and they contributed to my sense of motivation to learn and do as much as possible to help characterize this disease. In our case, we discovered a new mutation in a gene called *CIC* that appears to be specific to ODG when we compare it to other forms of brain cancer and also other types of cancer. We are continuing this research and hopefully one day these efforts will lead to a cure. Before that time comes, we're already seeing the benefits of attaining the genetic signature of a patient's cancer as a way of deciding on the best course of treatment. I am honoured to be involved in this research and privileged to have the perspective that I do on brain tumour diseases.

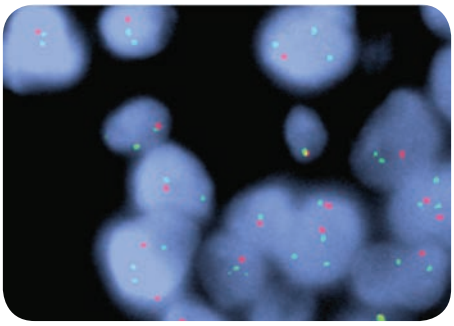
To read a summary of Yaron's recent publication in the Journal of Pathology, see this link: http://onlinelibrary.wiley.com/doi/10.1002/path.2995/abstract

For more information about Yaron Butterfield, see this link: www.braintumour.ca/2367/the-many-faces-of-spring-sprint

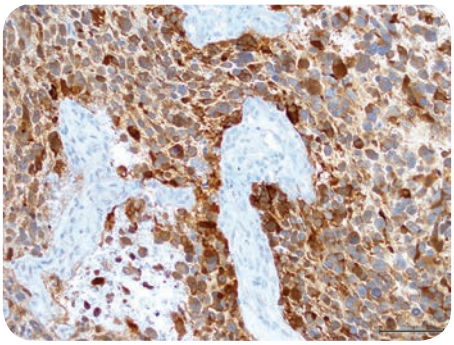
By Yaron Butterfield

Molecular Diagnostics in Neuro-Oncology

ADVANCES IN MOLECULAR DIAGNOSTICS have transformed the practice of clinical neuro-oncology. Approximately one half of brain tumour patients with oligodendroglial–type tumours (that is, both pure oligodendrogliomas and mixed gliomas, also called oligoastrocytomas) respond favourably to chemotherapy. Studies have identified a unique genetic change,



1p FISH of an oligodendroglioma probed with green control probes for chromosome 1q and red test probes for chromosome 1p. A majority of the blue tumour cells display binding by two green probes and only one red probe, demonstrating relative loss of 1p. A separate test is done for chromosome 19q.



Oligodendroglioma cells demonstrating positive staining by this antibody. The tumour cells demonstrate strong cytoplasmic brown staining which means they express the mutant form of the IDH1 protein. Note that the cells lining the blood vessels are not stained in the reaction because they do not express the mutant protein.

Photos courtesy of Dr. Stephen Yip

present in 50-80% of oligodendroglial tumours, that is associated with better outcomes in these patients. This sub-type of oligodendroglial tumours lacks genetic material on the short arm of chromosome 1 (1p) and the long arm of chromosome 19 (19q). Tumours with this change are said to be "co-deleted," or to have loss of heterozygosity *(LOH)* at 1p and 19q. The other major type of glioma, astrocytoma, often harbours isolated loss of 19q but not 1p. The loss of 19q alone is not associated with improved clinical outcomes. This discovery has revolutionized the care of glioma patients in the 21st century.

Treatment planning relies on multiple factors including the patient's age; clinical performance (meaning, how well the patient is); the radiological appearance of the tumour, for example on magnetic resonance imaging (MRI) or computerized tomography (CT); pathological features of the tumour; and proximity of the tumour to critical brain structures. The status of chromosomes 1p and 19q in the tumour, taken in context with other specific features, allows treatment to be tailored to an individual and can mean the difference between "watchful waiting," chemotherapy alone, radiotherapy alone or combined radiation and chemotherapy.

Current testing of tumour 1p19q status relies predominantly on two techniques that are used in the molecular testing laboratory. Fluorescent in situ hybridization *(FISH)* and LOH polymerase chain reaction *(PCR)* are both well-established and robust tests used to identify genetic status. Currently, any oligodendroglial–type tumour, whether pure or mixed, will undergo molecular testing for 1p19q status. The pathologist selects a piece of the tumour that best represents the tumour overall for DNA extraction. DNA is also taken from blood donated by the patient for comparison. The *LOH PCR* test examines selected molecular markers or microsatellites along chromosome 1p and 19q in samples of a patient's tumour and blood and then compares them in order to determine the status of 1p and 19q in the tumour. *FISH* is a technique which uses fluorescent probes to detect the presence of specific DNA sequences on chromosomes of interest. No blood is required for this test.

Another recent discovery is the identification of recurrent mutations in *IDH1*, which is the gene for isocitrate dehydrogenase, an enzyme used in energy metabolism in the cell. This leads to altered metabolism of the tumour cells. This mutation appears to be an early and critical event in glioma formation. It was initially identified in "secondary glioblastomas," which are typically found in younger brain tumour patients. Secondary glioblastomas are thought to arise from lower grade gliomas. The *IDH1* mutation is found in the tumours of a vast majority of younger patients, but is not found in older patients with primary ("de novo") glioblastomas, Primary glioblastomas start out as aggressive grade IV tumours, not as low grade tumours. More importantly, the *IDH1* mutation is also found in a large percentage of lower grade gliomas, including astrocytomas and oligodendrogliomas.

An antibody recognizes the mutated *IDH1* gene and is used in the clinical pathology laboratory to identify glioma cells carrying this mutation. This antibody

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For more information on how you can support enhanced patient care, patient information and brain tumour research, please contact Sharon Kennedy at the BC Cancer Foundation, 604 877 6160 or 1 888 906 2873 or skennedy@bccancer.bc.ca

Look Good Feel Better

I HAD A GREAT TIME at the Look Good Feel Better® seminar. It was held in a dining room in the Jean C. Barber Lodge across the street from the BC Cancer Agency in Vancouver. There were about four or five cosmeticians on hand to help the 16 participants in attendance. We received step-by-step advice about makeup, and also each received a sturdy box filled with cleanser, highlighter, moisturizer, foundation cream, face powder, eye liner, eyebrow pencil, lip liner, lipstick and other skin care products. There were many different brands of cosmetics, as they are all donated by a number of companies. All of this was ours to take home, and all was free of charge! There was a lot of emphasis on cleanliness during the session, especially important for those whose immune systems are challenged by cancer or cancer treatments.

After that the "wig lady," Vivian, showed us a number of different wigs which we could pass around and even try on. Again for hygienic reasons, we were each given what looked like a kind of mesh head covering to use while trying on wigs. There was even a purple one, just for fun. We all had a few laughs, and were surprised at how natural the right wig looked and felt. She also had scarves, hats, and even a turban which she dressed right up with a man's tie. She was a very down-to-earth person, and had a practical approach to the purchase of a hair prosthesis. She encouraged us to determine a price limit and to communicate that right from the start to the facility where we purchase the wig so that we stay within our limit.

There was lots of information about the difference between synthetic hair, real hair and a brand new prosthetic product that is flame/torch resistant. Most synthetics are flammable so one needs to be careful when bending over a hot oven, etc. Vivian also advised women not to shave their heads as the scalp is quite tender, especially when you are going through treatment. Instead she recommended just cutting the hair short.

At the end of the workshop participants were very appreciative of the time and energy the professionals put into this very informative, fun and worthwhile evening. It made us all feel good!

By Carol Palmer, Kamloops resident and BCCA Vancouver Centre patient

The Look Good Feel Better (LGFB) program is funded by a charitable foundation of the Canadian Cosmetic, Toiletry and Fragrance Association (CCTFA). Since its launch in 1992, LGFB has helped over 110,000 women with cancer to manage the effects of their disease and its treatments on their appearance, and in some cases on their morale. Says one participant, "Looking good through my treatment has helped me stay positive. It's a way of saying to my children, and to myself, that I'm going to be OK." For more information about the LGFB program see the website: **www.lgfb.ca** or contact your Patient and Family Counselling Department.

Molecular Diagnostics

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is of great importance to diagnostic neuropathology since the pathological characterization of low grade glioma is extremely subtle. Low grade gliomas can be indistinguishable from brain inflammation or infection. This antibody specifically recognizes the mutant *IDH1* protein that is only present in tumour cells, and this permits the highly specific and sensitive identification of these cells. In addition, results from early studies have shown that the mutational status of *IDH1* might trump the classical pathological grading of glioma. It has been found that patients with grade IV glioblastomas with *IDH1* mutations have better outcomes than grade III anaplastic astrocytomas without *IDH1* mutation. This finding requires confirmation from larger studies but confirms the importance of novel molecular biomarkers and their role in predicting the behaviour of brain tumours.

For more information about the pathology and molecular genetics of brain tumours, see *Headlines*, Fall 2006, Summer 2009 and Summer 2010.
www.bccancer.bc.ca/PPI/copingwithcancer/specificresources/Neurooncology.htm

By Dr. Stephen Yip, Neuropathologist

Editions of *Headlines* are also available as a pdf download at:
www.bccancer.bc.ca/PPI/copingwithcancer/specificresources/Neurooncology.htm
If you would like to submit an article, ask a question, or serve on our patient and family editorial board, please contact Rosemary Cashman at rcashman@bccancer.bc.ca or 604 877 6072 (phone) 604 877 6180 (fax).

All content by Rosemary Cashman unless otherwise specified.