Shorelines

NEWSLETTER OF THE PROBUS CLUB OF NORTH SHORE VANCOUVER

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Past Years Newsletters
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probusns2021

Monday, June 14th Zoom Meeting - 9:30AM

with guest speaker

Steve Macdonald, the Pacific Science Enterprise Centre

"The Pacific Science Enterprise Centre: a new way for the delivery of Science-based knowledge to the Department of Fisheries and Oceans. "

The Pacific Science Enterprise Centre: a new way for the delivery of science-based knowledge to the Department of Fisheries and Oceans. What Goes On Behind the Long Green Fence On Marine Drive in West Vancouver.

Dr. Macdonald has over 45 years of experience as a biological scientist with a specialization in fish and invertebrates on the east and west coasts of Canada. During 37 years with Fisheries and Oceans he has managed several multi-disciplinary programs and developed cooperative research relationships with representatives from other government agencies, universities, First Nations and the forest industry.

Dr. Macdonald is a senior scientist at the Department of Fisheries and Oceans research facility in West Vancouver. He is currently preparing for retirement. During the last 25 years he has held the position of the Centre's Director (DSO) and has been responsible for the supervision of most of the federal staff based at this site. Research at the facility ranges from the investigation of freshwater habitat health and carrying capacity in relation to the effects of timber harvesting, mining, pulpmill effluent, agriculture, urban water withdrawal and energy generation issues; to the investigations of the aquaculture industry and its influence on the environment and natural fisheries. Dr. Macdonald's research has assisted in the development of models that for the first time, allow salmon spawning escapement targets to be adjusted to compensate for unfavourable environmental conditions or early migration behaviour. With the prominence of climate change issues, these models provide a means to produce realistic pre-season management targets and *Continued on Page 2...*

Mark Your Calendars with These Important Dates

Pop-Up Zoom Meeting - Monday, June 28, 2021, 10:15AM

Monthly Zoom Meeting - Monday, July 12, 2021

Guest speaker John Atkin, Historian, " *Downtown Eastside History Relative to Hogans Alley and the Viaducts*"

President's Notes

Further to the provincial announcement of May 25th, Dr. Henry stated that the recent, more aggressive vaccination program has successfully lessened the incidence of COVID 19 in the population of B.C.

With a greater percentage of us receiving our second shot very soon, the public restrictions are being relaxed and the prospect of in-person meetings and renewed socialization is on the horizon. While this is positive news for future in-person probus meetings, it also poses challenges in identifying available meeting space.

Your Management Committee has been advised that the Capilano Golf Club does not intend to re-open for public meetings until January 2022 and the North Vancouver School Board will be making a decision re rental of their meeting space following September 2021. Although the committee is in contact with other options, most North Shore organizations do not appear to be interested in renting meeting space in the immediate future.

In the interim, all club members are to be commended as the meetings on Zoom during the last 10 months have been consistently well attended by 80 to 120 members. As it appears necessary that Zoom will continue to be utilized for our meetings in the near term, may I encourage you all to continue to attend in support of the speaker and the club.

Our speaker on June 14th, Dr. Steve Macdonald of the West Vancouver based Pacific Science Enterprise Centre, promises to be most interesting and relevant as he addresses the subject of "a new way for the delivery of science-based knowledge to the federal department of fisheries and oceans".

On behalf of the Management Committee, thankyou for your continued support of the Club and I look forward to "seeing" you all at the June meeting.

Ron Wood

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Speaker Steve Macdonald Cont'd.

provide direction for in-season fisheries. He is also involved in several multidisciplinary research programs designed to promote an understanding of ecosystem processes in watersheds in the interior of B.C.

Most recently Dr. Macdonald has led the development of the Pacific Science Enterprise Centre (PSEC); a pilot program to develop a new method to deliver government science based on collaboration within the government and among industry and other academic institutions. This program engages the community through outreach activities and believes supporting community science initiatives has mutual benefits for citizen scientists and government objectives.

Dr. Macdonald holds adjunct faculty positions at both the UBC Faculty of Forestry and the SFU School of Resource and Environmental Management. He was a founding member of the Cooperative Resource Management Institute based at SFU and has taught university level courses in resource management and experimental design both locally and abroad in Wuxi China. His work has led to recognition from a variety of sources including several Regional Distinction awards and the National Prix du Excellence in 2009 for his work on forestry-related environmental impacts.

Last Month Speaker - Dr. Marra

Dr. Marco Marra is the UBC Canada Research Chair in Genome Science, a member of the Order of British Columbia, Director of Canada's Michael Smith Genome Sciences Centre and Professor of the Department of Medical Genetics in the Faculty of Medicine at the University of British Columbia. A recipient of numerous awards, Dr. Marra is one of the world's most cited scientists in the field of molecular biology & genetics with more than 500 scientific publications. On April 28, 2021 he was inducted into the Canadian Medical Hall of Fame.

Dr. Marra has spoken to Probus members before (April 2017), and he brought us up to date with how the research has matured since then to identify and provide life- altering treatment options for patients with advanced cancer. Dr. Marra and his assistants thank the Probus members for attending his presentation.

He shared a video which provided an overview of POG (Cancer Personalized OncoGenomics Program), which originally began in about 2008 with the first person in the world to have their entire genome and RNA fully sequenced to identify a vulnerability in their cancer cells and a treatment designed for that vulnerability. Now, a world-leading clinical study is underway integrating genomic sequencing into patient care and clinical decision-making

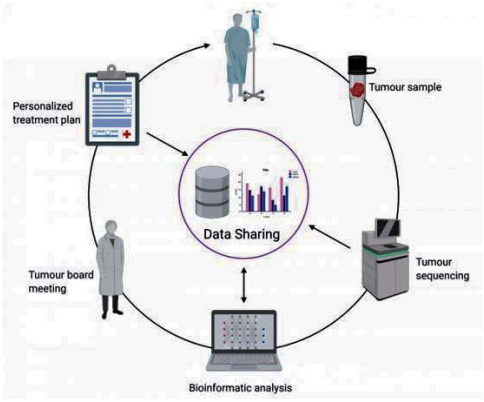
for individuals with advanced and hard-to-treat cancers. It is a learning cycle where POG is constantly learning what works and what doesn't for each case, and that information is also recorded for sharing.

The process starts with the receipt of samples which arrive at the echelon site and sequenced using a suite of very advanced robotics. The sample material fits onto a microscopic slide of glass and is inserted into the reader. A second machine is on its way thanks to BC Cancer and UBC that will allow sequencing of 18,000 genomes a year. This number aligns with the number of new cancer cases in a year – 20,000 with more than 10,000 of these being incurable cancers. With 2 machines, it will allow a significant increase to the POG program. Other kinds of sequencing machines are also used, the thinking is evolving. The technological innovation of looking at single cancer cells and analyzing the DNA of that single cell is brand new and in place now. The computational facility which handles the data is a very powerful super computing system with 30,000 cores of compute power. This is one of the limiting factors in the program, and funding is being obtained in order to scale this up.

The Genome Sciences Center celebrated a milestone of having sequenced 3 Quadrillion (3,073,774,488,981,789) base pairs of sequence information. Printed out – double sided, 8x11, no margins, 6/8 point font- the stack would be 1,800/2,000 kilometres high i.e. an enormous amount of information! This information is analyzed by a core of very sophisticated biometricians who reduce it down to a form that can be used to make valuable insights into cancer. The report is presented to the Molecular Tumour Board – part of the POG team – on a weekly basis. 39% of the POG team are medical oncologists in B.C., and 80% of these oncologists have enrolled at least one patient in the program. B.C. has the most sophisticated clinical interpreters of genomic information compared to any other jurisdiction in the world. This cadre of very sophisticated oncologists is one of the most important things the POG program has built. Other important facts about POG:

- 1,197 enrolled cases, 869 samples from 836 cases sequenced. 28 cases with a serially sequenced biopsy (progressed disease).
- 81 consenting oncologists, all of whom have enrolled at least one patient.
- 78% of cases presented at POG tumour board have a clinically actionable finding.
- 320 POG directed treatments for 255 patients: 66 CT (62 patients); 146 SOC (131 patients); 108 off label/ other (99 patients).
- 2 collaborations with clinical train initiatives (CAPTUR, CAPTIVS)
- Defined the ethical and data sharing framework now being leveraged in the Marathon of Hope Cancer Centres Network.

Despite all this, not all patients can be treated due to medications not being indicated for the condition they have. How we align medications to disease conditions needs to be re-thought. POG is provoking this conversation and is extremely important in the big picture.



Benefits of POG

- Supports clinical trials and causes them to be created.
- Partnered with Roche to bring new medicines for 200 patients to B.C. and is $20 Million of drug we would not otherwise have access to.
- Most significantly for a future point of view, POG has defined very fundamental properties of doing this sort of work that has informed the creation of Terry Fox Research Institutes Marathon of Hope Cancer Centre Network concept.
- The path forward is the Terry Fox Research Institutes Marathon of Hope Cancer Centre Network. The goal of the Network is to:
- Link Cancer Centers across the country to undertake Precision Medicine cancer research;
- Build collaborations to share and analyze data from cancer patients and their precision medicine treatments; Centers of activity initially will be Montreal and Toronto which will allow all to query data and potentially find other patients that look like the one they are dealing with. Everyone's genome, just like everyone's cancer can be subtly distinct, and so this is extremely important. The more one knows, the better one can act.
- Create the first pan-Canadian cohort of 15,000 fully annotated cancer cases (eventually 100,000) (over the next 15 years) and follow their precision medicine treatments.
- High quality data for precision medicine research and innovation to better help patients. Will drive innovation and relationships between the centers. Patients, regardless of where they are, will have access to a standard

of care that is beyond what they would have had before the program started.

Gratitude and thanks to B.C. donors who since 2008 have provided the vision and support that has brought this program forward.

Questions

Q1 I want to know what drives you Dr. Marra, what gives you hope every day.

A A path forward and to see roll out on a national level. One of the biggest problems we've had is the inability to scale the effort and it has been slower than I would have liked, but the pieces of the pipeline have now been assembled so we can. I believe that there will be a launch this year, and am excited that funding from Federal Government and B.C. donors is being worked out.

Q2 I understand you have lost many of your best research staff who have moved to the US for better support services and salary. How to you propose to compete with US cancer institutes?

A I would not agree that we've lost the majority of our researchers. We have been able to maintain our cohort of research folks with relatively little turnover. In fact, new talent has been hired from the UK and the US to come to BC Cancer and start up new initiatives, and we are growing right now.

Q3 What was one of the more unusual treatments found to be of use after determining what type of cancer cell from the POG?

A There are many examples that exist that I could give you. For a very long time the prevailing science has been that all cells within a cancer are cancer cells and therefore identical to each other. That tends not to be true. Within a given mass or malignancy there can be a very large number of cancer cells that differ substantially from each other, and the single cell technology that has now become available has revealed the extent to which cancers are heterogeneous masses. It is this heterogeneity, these different biological properties that genome science has revealed. So the idea that you could offer one drug, and that one drug might have a global effect on all those biologically distinct cells is not quite right, and we understand that now with a clarity that we never had before because of genome science.

There is a very interesting class of drug that was recently made available and are called immune checkpoint inhibitors and they tend to expose the cancer cells to the action of the immune system. It doesn't work for all people, but where it does, it works very well. With the POG program we are trying to understand what the bio-markers are of the response. An example was given from the pediatric cancer space – a young girl of 8 years with a treatment-resistant cancer was profiled using the technology and approach I described and we couldn't find any of the standard kinds of mutations. But in the RNA we were able to find a signal from a gene that was very on (very high). This gene is not normally expressed except in the embryo and then it is shut off later in the development, so it is normally expressed prior to the development of the immune system. So how is it that this gene is turned on in an 8 yr. old, after the immune system has developed? We hypothesized that if the immune system had seen this gene coming on, it would have seen the cell as expressing itself as foreign. There were other signals in the detail that told that the immune system could not see the cancer cells – they were being hidden by a normal process that keeps your normal cells from being attacked by your immune system. The cancer cells needed to be exposed to the action of the immune system because it needed to see it as foreign. The drug prescribed allowed this to happen with a remarkable effect. There are many examples like this where POG results in a determination that makes available a drug that would not otherwise have been indicated or used, and people can experience benefit for a number of years.

Q4 Are there commercial possibilities, and if so, do we here in B.C. know how to do this, and / or do we want to do this?

A There are many ways to approach this question both philosophically and practically. There likely could be entities that might be engaged, but they would have to make money. How would that happen? It is not an easy problem as it takes very sophisticated (and expensive) facilities to process information here, and in Toronto and Montreal. Clinicians would have to order information from the business entity, which would have to be reimbursed by the province. For this to happen, a health benefit would have to be quantified to ensure Government of its value. This is understood and therefore part of the POG program is health economics. An economist works with POG to develop a valuation for the program. As we move along, and costs go down, at what point is the argument made to create a commercial entity? We are not there yet and the Terry Fox Program will help us with the assessments needed. One of the biggest challenges at the moment is not so much the data gathering but the training of oncologists to use the information as well as having access to drugs. They have been well trained for years and could conceivably access and interpret information from a commercial entity, but they wouldn't have access to the drugs (which government controls), and so would be of little value to patients. The way that we assign drugs to indications now is not up to the task in my opinion, to make this kind of approach broadly available yet.

Final point is that this needs to be a learning system.

We have to learn as we go what the various properties of cancer cells are, how to effectively attack the cancer cells, and how to make cancer treatment better for our province. There are a lot of challenges, but also a ton of opportunity in this space.

Q5 It appears that this work is not applicable to metastasized cancers if a cancer cell is not obtained. Is this a future help for metastasized cancers?

A A focus for POG from the beginning is to work on metastatic disease and more generally, treatment-resistant disease. Most of the observations we have made have been for metastatic patients. The problems have been that not all metastatic sites are safe to biopsy. In order to get the cells, you need to insert a needle into the cancer mass. Doing this carries a risk of morbidity and mortality. It is dangerous and recovery needs to happen in a facility with medical supervision. There are quite a few cases where biopsies could not be safely obtained.

Q6 Without naming names, could you describe a successful use of this technology?

A An example of the 8 year old girl was given in an earlier question. We have processed about 1,200 cases and sequenced ¾ of these. We were able to prescribe more than 300 treatments to more than 200 patients. The major reasons a patient could not receive therapy was that a biopsy could not be obtained or the patient was too ill by the time the data were available, or too ill right from the outset, or the drug was not available because it is approved for a different indication.

Q7 Will patents be involved?

A They, of necessity are involved, as everything we are using is patented. The treatment with the immune checkpoint inhibitor for the 8 year old girl is a patented medication. Another example is a patient that received a DNA damaging agent that preferentially kill cancer cells, but this drug is generic and cheap. We use machines and reagents that are all under patent but we release the data. So the date is shared which is the focus of the Terry Fox Program. There will be intellectual property issues that need to be sorted out. We have investigators within the program that have patented observations which is done to promote the treatment as a licensable entity. Patenting an observation is a pre-competitive discovery. In 2003 the sequencing of the SARS genome – all data was made available 6 days after receiving the sample in the spirit of promoting health.

Q8 Can this technology assist in early cancer detection?

A A really important thing to think about. What is the definition of early cancer? If one has 100 trillion cells in the body and one cell can be a cancer cell, is there any way that we could find it using the technology today? No … the very best use of this technology as a way to identify in an "early" screening sense would be to identify patients at risk. About 15% of individuals seen in POG are carrying a mutation in their normal DNA that represents a known and important cancer gene. That information can then be used to inform the hereditary cancer program which can work with the patient, and their family, to offer them testing. If a high risk form of the gene is detected in a family member they may not have the cancer but are at increased risk for it. This can be managed better by more frequent testing i.e. Colonoscopy or mammogram, which may lead to the early detection of related cancers. As we learn more and more about the genetic material of cancer patients as part of the Terry Fox program, we'll be able to realize that benefit, which will be substantial – imagine 15% early detection for cancers that might arise in those patients.

Q9 Do you see a time when there will be routine screening of the general population to identify a pre-disposition to cancer?

A I do.

Q10 In gest … what is the significance of the car you are standing in front of on your background screen?

A I walk my dog every day and like to take pictures of interesting things … usually of flowers. This interesting vehicle was parked on the side of the road – a VW right hand drive bus -and I took the picture and forgot that I had put it on my backdrop. So no special significance.

Q11 Early in your presentation you mentioned RNA. Is there any cross reference between the MRNA developed for Covid 19 and cancer treatment?

A A very perceptive question, as it is exactly the way we are thinking about things. The observations that have led to the creation of a vaccine are not new, but are from 20-25 years of science, back to the very beginning of the genome project.

What the MRNA vaccines are demonstrating is that with with knowledge of the virus's nucleic acid you can choose in that genome where to design a smaller region as a target, so that the messenger RNA will enter the cell to cause a region of something that looks like the genome to be expressed, and to create an antigen not normally seen by human cells, which creates an opportunity for the immune system to recognize it and generate other immune cells that could respond to the real virus. Referring back to my example of the 8 year old girl, there was a gene that she was expressing on her cancer cells, which was developed before her immune system that we recognized as an antigen her immune system can recognize with assistance from a drug. That concept means that the immune system is an important thing to harness in cancer therapy.

Darlene Dean