In Cancer's Genes

Pauline Helle, Co-President of Think Pink McGill

Recent and even controversial findings give an astonishing glimpse into the future of research, prevention and potential cure for breast cancer

Professor Anne-Lise Børresen-Dale, Head of Department of Genetics at the Institute of Cancer Research at the Norwegian Radium Hospital, specializes in molecular oncology of breast and ovarian cancer. She has served as Member of the Board of Directors in the American Association for Cancer Research (AACR), as President of the European Association of Cancer Research (EACR) and as Member of the Board, the European Cancer Organization (ECCO). Her publications include over 350 scientific papers and 30 chapters in books and invited reviews.

Professor Børresen-Dale is a pioneer in gene-based cancer treatment. By decoding the genetic material of a patient' s tumor, researchers can determine the tumor's "Achilles' heel," its weak point, and thus the optimal treatment. This approach is known as " personalized treatment" and may eventually lead to "personalized prevention," whereby researchers are able to foresee genetic dispositions towards particular diseases and prevent them from occuring. Hand in hand with her genetic research work, Professor Børresen-Dale works as an avid advocate for the development of translational sciences. Translational science refers to the concept of converting results from basic research into applied research and product development, also described as translating bench science into bedside clinical practice. With personalized treatment potentially redefining our approach and experience in breast cancer research, we asked Pr. Børresen-Dale ten questions about the future of breast cancer.

Think Pink: *What is the financial cost of codifying a patients genes in 2010 and can it be standardized?*

Pr. Børresen-Dale: Today, if we put this into the clinics it would be too expensive to be a standardized procedure. Partly because we currently are not able to reduce the time in finding the Achilles' heel which could lead us to the best treatment. This process is costly if

we are going to do full mapping and sequencing of each cancer gene. Today, the cost is close to 20,000 dollars, but that is not all that is needed. What must follow is an extensive interpretation of the data and we do not yet know the best way of doing that.

Think Pink: *Do you think this technology will be something my generation could benefit from within our lifetime?*

Pr. Børresen-Dale: I definitely think so because the technology is moving so fast. The informatics, how you handle the data, is escalating. We get more and more sophisticated tools helping us to really see the structures in the data, revealing information which we haven't thought about at all. Then we may be able to identify the Achilles' heel in that particular tumor. The cost of sequencing a genome is moving down to 10,000 dollars and the aim is to get it down to 1,000 dollars within the next five years. As it is today we are still struggling to find the Achilles' heel in each patient. So for the time being what we need to do is molecularly characterize as many tumors as possible with good clinical annotations that we can use for further modeling.

Think Pink:*Do you see this technology ultimately leading to more of a preventive than a curative approach?*

Pr. Børresen-Dale: That is where we need to go to be able to effectively combat cancer. Indeed we need to do more to prevent it. We have for some time been talking about more personalized treatment, but we also have to dare to start talking about **personalized prevention.** It's not good for everyone to eat carrots everyday. You need to know "who is at risk for what?" This is ultimately the goal, but I think it comes together with knowing more about the cancer itself and what triggered that cancer in that particular patient. . We should not limit our research to the tumor but go on to acquire knowledge about the genotype of each patient and the patient's lifestyle and environmental exposure and ask the question: What kind of cancer did the woman with that genotype and that environmental exposure develop? This is part of a **whole system** of biology, and when you can decipher that for each individual, you may be able to predict the type of cancer that a particular woman might develop. At this point, you can start individualized prevention.

Think Pink: *Do you have other personal goals?*

Pr. Børresen-Dale: One of my dreams is to do an image type of analysis, without involving any invasive sampling, where you capture the status of all the molecular components and then get a high digitalized image that shows the structure. When you see a particular image, it will identify a specific type

of tumor and the precise nature of its Achilles' heel. This will immediately tell you how to treat that patient. It may look like science fiction, but I really do think it is possible in the not too distant future.

Think Pink: *Are there any warning signs that one may develop breast cancer or other cancers?*

Pr. Børresen-Dale: I think the first thing to look for is the family history. If you have a close relative that had lung cancer and smoked, don't smoke! Physical activity prevents a lot of diseases including breast cancer so exercise and stay slim. Some infections may stimulate certain cells to grow, possibly occult tumor cells, and thus become a risk factor for developing cancer. The same can be said for surgery, which may also stimulate cell growth so avoid unnecessary operations. There are also reports that the healing process after injuries, for example in knees, may stimulate tumor cell growth. So I think we need to broaden our scope and to start looking at other diseases like diabetes, rheumatism and other autoimmune diseases to determine how they affect one's system and how that system affects the risk of cancer. Such studies are starting to take place. We see that similar genes may be involved in several different diseases, with the same genes affording protection against one type of disease but indicating susceptibility for another. It can go both ways. Again, we need to be much more open-minded when looking at the similarities between different diseases. As previously mentioned, we need to consider diseases at a systems biology level.

Think Pink: *The question of nature vs. nurture (genetics vs. lifestyle) remains an issue with breast cancer and cancer in general. Now we hear about anti-cancer food or that severe depression or anguish can trigger breast cancer is there any truth in all this?*

Pr. Børresen-Dale: It's never only environment; it's never only genetics. **It's a gene environment interaction all the time.** The younger you get the cancer the more likely it is that the genetics play a major role and the older you are it's more likely that the environmental factors are stronger. Take stress for example. Stress causes you to start to hyperventilate, you get anaerobic metabolism, and you get a lot of bi-products which may harm your DNA. If you have a very good repair capacity it doesn't matter. Then again, for some people stress is more dangerous than others; but for the time being we don't know who is and who isn't at greater risk. Similarly, I think nutrition may be protective for some people but not for

all.

Until recently, it has been a big problem for epidemiology research aiming at finding risk factors for breast cancer that we have been looking at breast cancer as one single disease. We clearly know today that it isn't. The risks for the different groups are probably very different. If you look at smoking for example, it is quite interesting that some women, who carry mutation in the BRCA1 gene, have a reduced risk for breast cancer if they smoke! So their smoking works the other way around for the risk of breast cancer, probably by lowering the hormone level. But no one talks about that because smoking is bad, and of course smoking presents risks for many other diseases. Quitting smoking will always be beneficial for one's health; however, what is interesting to me is that it's not about smoking per se, but what smoking does to your body to reduce the risk for cancer in these individuals. That is what's important. It may lower your estrogen level and that again protects you if you have a high risk of developing cancer. We must **rethink for the individual.** But it's hard for a government to promote strategies that must vary for individual to individual and to be able to say, "this is good for this group and will work for them, but not for this other group that needs different advice." This problem gets even more difficult when dealing with a heterogeneous population.

Think Pink: *What is the upcoming main challenge for breast cancer research from a genetics point of view?*

Pr. Børresen-Dale: I would say that breast cancer is actually a success story. If you are diagnosed with breast cancer in Norway today, you have almost a 90% chance of being alive after 5 years, which is extremely good. On the other hand, we know that we do "**over-treat**" and that some individuals suffer severe long-term side effects as a result of treatment. The challenge is to identify those that need the heaviest treatment and those who can receive less and still survive. We have not really started to treat in a personalized manner yet. We do not dare NOT to treat. The treatment itself contains carcinogenic substances, and may cause development of a second cancer, so avoiding that is the biggest challenge. It has been estimated that by 2015, every 4th or 5th patient diagnosed with cancer will actually be a previous cancer patient having developed a second cancer as a result of the exposure from the treatment of the first cancer. If blood tests existed that could alert us to the presence of cancer formations at an early stage, and if there were tests that could monitor the efficacy of the therapy, I think we could prevent much of the over-treatment. We are not there

yet, but we are working hard on this concept.

Think Pink: *What are the goals for translational science in breast cancer research and for patients?*

Pr. Børresen-Dale: Women are not mice so we need to do research involving women. We, the scientists, need to be able to follow the patients in order to produce new drugs and, by using them in early experimental trials, determine if the treatment is beneficial. So, a very close and good collaboration with the clinicians and with the patients is needed. We must explain what we are doing to the patients and give them the necessary knowledge so that they can make informed decisions on further treatment. We must work hard to educate the public. Lay groups could help in reaching out and that is why your (Think Pink) request was so interesting to me, because indeed you have to start with educating the young ones. They have to get the knowledge before it is too late. Many of the patients participating in research projects say "I don't do this for myself; I do it for my daughters." So the daughters should be aware; they should know what we are doing. In return they can be supportive. We need young advocates for our cause. We need to demystify cancer. People are living longer and at the rate of one in four contracting cancer in his or her lifetime we know that virtually every family will have to face this disease in some way.

The hope is not to have to not wait 10 years for the FDA to approve new promising treatments. We want to shorten the time between acquisition of new knowledge and possible new treatment. We need to dare to fail and go back again. Part of translational science and research is to be able to go back and forth between bench [science] and patient.

Think Pink: *What are some of the barriers of translational sciences cultural, linguistic?*

Pr. Børresen-Dale: One of the challenges is the internalization of the idea of translational sciences and being open about what you know. Some competition is always good, but sharing data and knowledge will enhance the field faster. You may experience having your ideas stolen by a competitor, but that might occur two or three times in a lifetime. The risk and personal harm is nothing compared to what you get back from being open! That is one of the things I really hope to see happen a more open **sphere of dialogue**, especially between the different professionals, the basic researchers, the clinical staff, the clinical scientists and, of course, the patients. If we could get this

rotation of feedback and of **knowledge spinning, we would be much better informed much faster.**

Once, while working with a team at the Yale University, I experienced a challenging situation. There was a whole group of experts, including epidemiologists, oncologists, pathologists, radiation oncologists, molecular biologists and geneticists. Each had different information at hand with respect to the patient's genotype, exposure, family history, the size of the tumor, etc. They discussed how to best treat the patient based on all this information. After going through all the data and the possible options for the patient for a personalized treatment, a final question was asked: "what kind of insurance does she have?" Many of the treatment options that had been proposed had to be abandoned because of insufficient medical coverage!!! This is unfair!! Medical improvements for the patients are slowed down by non-medical factors.

Think Pink: *Do you have any advice for women between 18 and 25?*

Pr. Børresen-Dale: If you should be presented with a cancer diagnosis, be positive. I am certain that having a positive attitude during treatment affects how you experience it and fight it. Don't feel guilt, thinking "I should have" and "I shouldn't have." We still don't always know why cancer happens. I hope that one day we will be able to give that diagnosis, so the patient can get that relief, that answer. But today, we don't know.

Despite all the advances made in recent years and her promising research, Prof. Børresen-Dale does not hesitate in stating that, " we should not be nave and think we will eradicate breast cancer or cancer from the human population. Cancer comes from our genes. If we stop our genes from changing and developing, we are stopping evolution." On a brighter note, she adds that the next step is rather to change the outlook. "We hope to change how we will live with cancer. By 2015, 25% of the population will be affected by cancer at one point in their lives. We must learn not to die of cancer but how to live with it. The hope is to minimize the pain and suffering around cancer."

Think Pink is a student-run McGill club dedicated to raising breast cancer awareness and fundraising for the Quebec Breast Cancer Foundation (QBCF). For more information visit http://thinkpinkmcgill.ca/.