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Single gene links rare and unrelated cancers

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Scientists at the BC Cancer Agency, Vancouver Coastal Health Research Institute, and the University of British Columbia are excited over a discovery made while studying rare tumour types.

Dr. David Huntsman, genetic pathologist and director of the Ovarian Cancer Program of BC at the BC Cancer Agency and Vancouver Coastal Health Research Institute and Dr. Gregg Morin, a lead scientist from the Michael Smith Genome Sciences Centre at the BC Cancer Agency, led a team who found mutations in rare, seemingly unrelated cancers were all linked to the same gene, known as DICER.

The research team set about sequencing rare ovarian, uterine, and testicular tumours, expecting to find that their genomes would be distinct with specific, differing abnormalities. They were amazed to discover the same fundamental mutation in the DICER gene showed up as the common process underlying all of the different cancers they examined.

The findings are published today in the New England Journal of Medicine.

"DICER is of great interest to cancer researchers" says Dr. Huntsman, who also holds the Dr. Chew Wei Memorial Professorship in the departments of Obstetrics and Gynaecology and Pathology and Laboratory Medicine at UBC. "There have been nearly 1300 published studies about it in the last 10 years, but until now, it has not been known how the gene functions in relation to cancer."

The gene plays an important role in maintaining health. It has as a "factory style" function, chopping up microRNA molecules to activate them. These microRNA molecules in turn control hundreds of other genes. "This discovery shows researchers that these mutations change the function of DICER so that it participates directly in the initiation of cancer, but not in a typical "on-off" fashion," says Dr. Morin who is also assistant professor in the department of Medical Genetics at UBC. "DICER can be viewed as the conductor for an orchestra of functions critical for the development and behaviour of normal cells. The mutations we discovered do not totally destroy the function of DICER rather they warp it—the orchestra is still there but the conductor is drunk."

This finding is the third of a series of papers published recently in the New England Journal of Medicine in which the Ovarian Cancer Research team has used new genomic technologies to unlock the molecular basis of poorly understood types of ovarian cancer. This breakthrough is particularly pivotal because it could lead to solutions for treatment of more common cancers.

"Studying rare tumours not only is important for the patients and families who suffer from them but also provides unique opportunities to make discoveries critical to more common cancers – both in terms of personalized medicine, but also in applying what we learn from how we manage rare diseases to more common and prevalent cancers," says Dr. Huntsman "The discovery of the DICER mutation in this varied group of rare tumours is the equivalent of finding not the needle in the haystack, but rather the same needle in many haystacks."

"This breakthrough will be of interest to both the clinical and the fundamental science communities," says Professor Phillip A. Sharp, Institute Professor at the Massachusetts Institute of Technology and co-winner of the 1993 Nobel Prize in Physiology and Medicine for the

discovery of the structure of genes. "Huntsman, Morin and colleague's very exciting discovery of specific mutations in DICER, a factor essential for syntheses of small regulatory RNAs in ovarian and other human tumours, could lead to new approaches to treatment."

The research of the team is now working to determine the frequency and role of DICER mutations in other types of cancers and are expanding their collaboration to discover whether mutant DICER and pathways it controls can be modulated to treat both the rare cancers in which the mutations were discovered and more common cancers.

The Michael Smith Genome Sciences Centre, located at the BC Cancer agency, played a key role in this discovery. A decision was made more than 10 years ago, championed by Drs. Michael Smith, Victor Ling, and others to create and locate this facility within the BC Cancer Agency and in close proximity to Vancouver General Hospital. This location has enabled the multidisciplinary cancer research teams in Vancouver access to state of the art technologies and that is now paying off.

"We are one of less than five places in the world doing this type of work successfully. This discovery is one of a series of recent landmark findings from Vancouver that are reshaping our understanding of many cancers," says Dr. Huntsman. "Since my arrival in Vancouver 20 years ago I have never before sensed such a strong feeling of communal pride and excitement within our research community. Our next task is to bring the discoveries into the clinic."

Provided by University of British Columbia