NEWS RELEASE

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Significant childhood cancer discovery made by scientists at the BC Cancer Agency

Vancouver – Research published today by scientists at the BC Cancer Agency in *Cancer Cell* brings new hope for the treatment of high-risk childhood sarcomas – a type of cancer that has seen almost no treatment improvement in the last 20 years in spite of intense research efforts.

Sarcomas are malignant – meaning they are cancerous – tumors of the connective tissues, including bones and muscles. They are more common in children and can be extremely difficult to treat because they have a high tendency to metastasize, or spread. Up until now, there has been very little known about the mechanism of how sarcoma cells spread to other organs.

To better understand this mechanism Dr. Poul Sorensen and his team, including Dr. Amal El-Naggar, a post-doctoral fellow, studied a previously unrecognized pathway involving two proteins, YB-1 and HIF1α.

"This research shows for the first time that HIF1α production in sarcomas can be regulated by YB-1, a known drug resistance marker," said Dr. Poul Sorensen, Distinguished Scientist at the BC Cancer Agency and Professor, Department of Pathology & Laboratory Medicine and Johal Chair in Childhood Cancer Research at the University of British Columbia. "This process appears to be specific for tumour cells, which could have profound implications for targeting the YB-1-HIF1α pathway therapeutically."

The researchers found that YB-1, which is highly expressed across virtually all human sarcoma subtypes, can directly stimulate the production of HIF1α when large tumours outgrow their blood supply and become oxygen deficient. It allows oxygen deficient tumour cells to adapt to the stress of low oxygen (called hypoxia), making these adapted tumour cells more hardy and stress resistant, and therefore likely more treatment resistant.

"Dr. Sorensen's landmark study provides real hope that dramatic improvements in the treatment of childhood sarcomas are around the corner. This is a testament to the power of BC Cancer Foundation donors fuelling promising research that will impact families facing a childhood cancer diagnosis in the future," said Erik Dierks, VP, Development, BC Cancer Foundation.

They also showed that when YB-1 drives HIF1α production, this also makes sarcoma cells much more invasive and metastatic. When the process is blocked it makes local tumors more

susceptible to low oxygen conditions, and also dramatically inhibits the spread of childhood sarcoma cells to the lungs.

“In 2008, when my son Finn’s Rhabdomyosarcoma cancer returned and had metastasized, his chance of survival was effectively zero,” said Patrick Sullivan who formed Team Finn to honour his late-son and raise funds in support of life-saving childhood cancer research. “If Finn was diagnosed today, those numbers would be the exact same. As a parent of a child who died of Rhabdomyosarcoma, it is really important to know that the work of Dr. Poul Sorensen and Team Finn is helping to change that story for other Finn's and families around the world.”

This research shows how sarcoma cells adapt to harsh tumour environments, namely by activating a HIF1α pathway that allows them to survive and acquire metastatic capacity. With this knowledge researchers at the BC Cancer Agency are already looking at how to target this pathway in tumour cells as a tumour-specific therapeutic strategy.

There may also be therapeutic applications for other cancers. The data suggests that this pathway is also active in adult epithelial cancers such as breast cancer.

Quick facts:

- Sarcomas are malignant tumors of the connective tissues, including bones and muscles.
- Sarcomas are relatively more common in children, and can be extremely difficult to treat because of a high tendency to metastasize (spread).
- This study is extremely impactful as very little is known about the biology of how aggressive sarcoma cells spread to other organs.
- Dr. Sorensen’s research has identified a significant protein function as a driver in childhood sarcomas.
- This provides proof of a druggable target (YB-1 protein pathway) that may be able to halt the spread of childhood sarcomas.
- There are 12 cases of sarcoma per year in B.C., and approximately 30-40 per cent of patients die of their disease, particularly in high-risk disease.
- The BC Cancer Foundation has donated $500,000 to fund this research, including funds from Team Finn and the Ride to Conquer Cancer.

The BC Cancer Agency, an agency of the Provincial Health Services Authority, is committed to reducing the incidence of cancer, reducing the mortality from cancer, and improving the quality of life of those living with cancer. It provides a comprehensive cancer control program for the people of British Columbia by working with community partners to deliver a range of oncology services, including prevention, early detection, diagnosis and treatment, research, education, supportive care, rehabilitation and palliative care. For more information, visit www.bccancer.bc.ca.

The BC Cancer Foundation is the bridge that connects philanthropic support and research breakthroughs in cancer knowledge. As the fundraising partner of the BC Cancer Agency and the largest funder of cancer research in this province, we enable donors to make contributions to leading-edge research that has a direct impact on improvements to cancer care for patients in British Columbia. We fund with the goal of finding solutions.

Visit www.bccancerfoundation.com to make a donation or to learn how you can make a difference in the lives of those affected by cancer.

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