Predicting Tumour Growth with Genomics

By Stephanie Roberts

A senior scientist at Sunnybrook Health Sciences Centre is one of four principal investigators in a multidisciplinary program that has received $3.36 million to study the metastasis of breast cancer. Dr. Arun Seth, a leader in genomics research, is the sole Toronto recipient of an award funded by a special competition of the Canadian Breast Cancer Research Alliance (CBCRA).

Seth's project, one of four in the program that aims to speed the development of metastasis-specific diagnostics and therapeutics, will receive $860,000 over five years to study how to predict which tumours in the breast will spread to bone.

"There is no model so far that allows you to predict that this tumour will go to bone, that this one will go somewhere else," says Seth. That's why he and bone biologist Jane Aubin, a co-investigator who is at the University of Toronto, created a unique mouse model that allows them to put human bone into it and then inject tumour cells into the bone to see if the cells grow. The model is the first that will enable scientists to use the same microenvironment – human cells and human bone – to study how breast cancer spreads. In the past, scientists have injected human cells into a mouse-only microenvironment, which doesn't allow for confidence in interpreting results.

"My idea is to predict early on whether a tumour will metastasize, first of all, and second if it will go to bone or the liver or the lungs," says Seth. He and his colleagues will do this by dividing a tumour sample into at least two parts and injecting one part into the bone in the mouse. If it spreads, they will remove it and do a genetic analysis to compare its molecular make-up to that of the sample that remained outside the mouse.

"What we hope to find is that the genetic makeup is already altered. That way we'll know if there are common changes. Then we can tell what will happen without waiting for metastases to occur, and those women can be treated aggressively," explains Seth.

When cancer spreads to bone, it often spells dire consequences for women. Being able to predict which tumours might spread based on a genetic profile taken at the biopsy stage means clinicians could treat women early, thereby radically improving outcomes.

All of the molecular analyses will be done at Sunnybrook Research Institute's Centre for Genomics, which Seth directs, using equipment funded by the Canada Foundation for Innovation. Dr. Harriet Khan, a pathologist at Sunnybrook, will provide the tumour samples. Dr. Albert Yee, an associate scientist and orthopaedic surgeon will provide the bone samples.

The three other PIs in the program, each of whom is leading a funded project, are Dr. Shoukat Dedhar (program lead) at the British Columbia Cancer Agency, and Drs. Chris Overall and Calvin Roskelley at the University of British Columbia. All of the molecular analyses for the projects will be at Sunnybrook's Centre for Genomics. Seth notes that multi-investigator funding like this from the CBCRA is crucial for this kind of translational work. "If you tried to do the research separately, it wouldn't work."

CBCRA's special grant competition was created to encourage and support the generation of multidisciplinary teams who will use new technologies and/or innovative approaches to develop preclinical models to understand metastases.

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