

**TERRY FOX RESEARCH INSTITUTE**  
***REPORT OF***  
**PAN-CANADIAN BIOMARKER WORKSHOP**  
**Saturday October 27 – Sunday October 28, 2007, Toronto**

**Summary**

The objective of the meeting was to identify areas of opportunity for a national Terry Fox Research Institute (TFRI) biomarker initiative, to define process to identify projects with the shortest – term / biggest impact, and to coalesce groups to start preparation of business plans for funding. The meeting agenda is provided as Appendix 1, and a list of participants as Appendix 2.

**Context**

Dr. Victor Ling (Scientific Director, TFRI) explained that the TFRI will be officially launched on Monday October 29, 2007 as a ‘virtual’ institute, initially with four provincial nodes across Canada – in Alberta, BC, Ontario and Quebec. (see [www.tfri.ca](http://www.tfri.ca)) The focus of the Institute will be translational cancer research, and it has become apparent from the large number of expressions of interest that there are many excellent ideas for biomarker discovery and translation projects. In the context of the Canadian healthcare system, a significant opportunity exists to build national teams to complete statistically powered Canada-wide studies to validate biomarkers within a three to five year timeframe. It is desirable to involve other provinces beyond the nodes if possible.

Dr. Clayton Smith (BMT/Leukemia Program Director of BC) provided a current status of the ‘roadmap’ for implementation of biomarkers (see Appendix 3). Workshop participants identified a complex set of drivers (discoveries, economics of personalized medicine), commercialization (pharma business models, IP considerations); and resistors: regulations (‘moving’ regulatory framework of FDA, response of HPB, CLIA opportunities, provincial reimbursement), barriers (tissue collections, ethics, funding models, medical practice, healthcare funders) which slow down progression along the ‘roadmap’.

Dr. Ling reiterated the strategic goal of TFRI to focus initially upon projects which address near-term goals which move projects along the roadmap towards transfer / application / implementation. The endgame of this effort is to ensure that knowledge is applied for the betterment of patient health and survival.

**Tumour Site Presentations & Discussions**

A small working group (SWG) identified five anatomical tumour sites before the meeting and invited champions to present discussion papers for pan-Canadian Biomarker Initiatives.

**(1) BREAST CANCER**

Dr. Peter Watson (Pathology & Tumour Tissue Repository, BC Cancer Agency) surveyed the strengths and expertise of breast clinical research groups in Canada. Three clinical problems were presented for discussion as ready for a pan-Canadian effort: (1) biomarkers of therapeutic resistance in invasive disease; (2) biomarkers of detection / prediction in DCIS/LCIS (~3,500 cases/yr in Canada); and (3) biomarkers of response probability in invasive disease. Dr. Morag Park (McGill) reported that a

strong consensus was achieved within the breast breakout group's discussion to pursue (1) and (2) above as pan-Canadian initiatives.

The first project ((1) above) could provide deliverables within a 3 – 5 year timeline. The project would piggy-back on current clinical trials (CT) for Herceptin, Herceptin + Avastin and anti-estrogen drugs with the aim of identifying / validating biomarkers in tissues resistant to these therapies in the neo-adjuvant setting. There is an urgent need to do this for economic and quality of life reasons. The opportunity exists to validate potential markers (single genes, multi-gene signatures as well as proteins) in these CT cohorts.

The second project ((2) above) would have more long-term deliverables, and would enable biomarker discovery research into early stage breast cancer, to answer such questions such as predictive value for health outcomes for DCIS + an anti-angiogenic switch turned on or off. A pan-Canadian approach, with incentives for tissue collection and live-cell banking, does require a small change in clinical practice, but would accrue sufficient samples over time. This project would build upon some unique strengths of the Canadian healthcare system. This approach could also be applied to other cancers.

**NEXT STEPS:** The CBCRA is organizing a biomarker workshop in February 2008, which would be an opportunity to establish a TFRI/CBCRA partnership, and advance discussion with a broader breast cancer community to prioritize projects of mutual interest.

## **(2) OVARIAN CANCER**

Dr. Diane Provencher (CHUM) surveyed the status over ovarian research in Canada. The Society of Gynecological Oncologists in Canada (GOC) provides a small, but cohesive focus for ovarian cancer services and research across Canada, with the opportunity to implement change in practice evidence rapidly. Ovarian cancer is a silent killer, plagued by late diagnosis, histopathologic subtyping, and ultimately resistance to treatment. Ovarian tumour banks with good clinical data exist at the major centres (FFPE tissues with >10 year clinical data), and will need to be linked due to the small number of new cases regionally if biomarkers are to be validated. Dr. Anne-Marie Mes-Masson (CHUM) presented four ideas of potential projects raised during the ovarian breakout group discussion:

- a) A program focused on early detection and here the idea was two-fold. One was to pool early stage disease material for an early detection study since detecting cancers earlier in ovarian cancer would have an immediate health impact. The other was based on the observation that some very early disease is missed by pathology because it occurs in the fallopian tubes, and that standardized protocols would need to be developed to help existing banks capture this material which then could be included in an early detection study.
- b) The program would capture all high grade ovarian serous cancers and test for BRCA mutations by high-throughput sequencing. Identification of hereditary forms of ovarian cancer would impact not only on prognosis (and eventually treatment modalities as they evolve) but would have an impact in ovarian and breast cancer prevention in the families of these patients.

- c) To propose a companion study to piggy-back on a recently approved NCIC CTG of intraperitoneal chemotherapy. This study would validate known biomarkers (and provide the study material for new investigation if these fail) that could be incorporated into a decision nomogram for identifying women most likely to benefit from this intervention, which has both cost and important quality of life issues associated with it.
- d) Lastly, to design a pan-Canadian study to advance histology / molecular sub-typing to achieve a more molecular subtyping of endometrial, serous and clear cell carcinomas. Identifying key molecular pathways associated with specific histopathologies will impact the choice of more selective therapies being offered.

NEXT STEP: The ovarian cancer group proposed to arrange a workshop to involve a more complete interdisciplinary group than was present at this workshop.

### **(3) LUNG CANCER**

Dr. Stephen Lam (BC Cancer Agency) reviewed the dismal prognosis for lung cancer patients, and the importance of early detection to improve five year survival rates. Dr. Lam presented a screening study for discussion, involving six centres across Canada. In contrast to other epithelial cancers, the human lung comprises different components: the central airways and a complex branching system. Various imaging technologies have been employed to improve detection rates, and physicians now can detect lung tumours < 1mm. However this has led to over-diagnosis and utilization of healthcare resources. Since the prevalence of lung cancer is low (~2%) even in high risk groups, better screening strategies are required. Discovery recently of a plasma marker by Dr. Lam and publication of results of 2 large international gene association studies within the coming year provide an excellent opportunity to validate improved screening methods with greater sensitivity and specificity within a 4 year time frame. The addition of epidemiological and health economic studies add significant dimensions for the rapid implementation of results of the proposed study.

Dr. Sandy McEwan (Cross Cancer Institute) described discussion of the project by the lung breakout group. If successful, this project will have a significant impact upon lung cancer screening, and can be implemented rapidly. Lung cancer is an under-funded research area, that other organizations (e.g., CPAC) would likely wish to support. Concern was expressed about deficiencies in handling and analysis of images, and it was recommended that a centralized system with at least two independent reviewers be used to score images. This would add to the cost of the study, but will more rigorously support the conclusions.

The general consensus was the lung project is ready to go, and should be supported. TFRI should ask Dr. Lam to arrange a principal investigators project planning meeting as soon as possible. .

### **(4) LYMPHOID CANCERS**

Dr. Clayton Smith (BMT/Leukemia program of BC) presented the discussion paper submitted by Dr. Randy Gascoyne (BC Cancer Agency), who was unable to attend the meeting. Through its 20 year longitudinal clinical database, BC is recognized for its international leadership in lymphoid cancer sub-typing. Other Canadian centres have also developed strong research interactions. Questions remain, such as which

patients with diffuse large B cell lymphoma will fail the current (expensive) targeted treatments? Can we identify the ~20% of Hodgkin lymphoma patients who will fail current therapy?

NEXT STEPS: From the discussion of the lymphoma breakout group, Dr. Smith reported support for the organization of three separate biomarker workshops should for: (1) leukemia; (2) lymphoma and (3) transplantation. If prospective CTs are arranged, TFRI should support collection of frozen biomaterials for correlative studies.

#### **(5) PROSTATE CANCER**

Dr. Fred Saad (CHUM) presented an overview of Canadian strengths in prostate cancer research. The most significant looming problem in prostate cancer is the need to identify biomarkers which will enable urologists to discuss with patients whether to treat or not. The first task is to conduct a survey to identify what we have in prostate cancer in Canada. Significant collections exist in Montreal and Vancouver. A proposal discussed with the prostate breakout group would involve about 10 centres / leaders in prostate cancer developing a tissue microarray with good clinical follow up data upon which to validate a range of biomarkers already identified.

A mechanism would also be to piggy-back on the START CT to collect tissues prospectively, the results of which analysis would augment the treatment / watchful waiting nonograms currently used in prostate cancer management.

NEXT STEPS: A proposal to hold a prostate biomarker workshop in January 2008, involving key researchers / physicians from across the country.

#### **(6) OTHER CANCERS**

It was recognized at the start of the workshop that the structure adopted does not lend itself to cross-fertilization of ideas across tumour sites. A much larger workshop would have to be arranged to include other groups. Nevertheless, a number of other ideas were raised where a focused workshop would generate ideas and potentially proposals. These included:

- Brain
- Colon
- Kidney
- Melanoma
- Pancreas
- Pediatric where oncologists are tightly linked across Canada in the C17 and COG networks. Significant issues are present in late toxicity effects, and a large number of patients are on CTs. Recommend organize a specific workshop.
- Sarcoma, and
- Radiation responsiveness where 40% of patients have intrinsic resistance and a further 10% acquire resistance. Radiation response is an intriguing area which has the ability to biopsy and treat, and acquire results within a short timeframe, ie., 3 months. Candidate markers have already been identified. Rob Bristow in Toronto might be a good champion for this workshop.

*Friday November 16, 2007*

## Appendix 1

**PAN-CANADIAN BIOMARKER WORKSHOP**  
**Saturday October 27 – Sunday October 28, 2007**  
**MaRS Centre, 101 College Street, Toronto, Ontario, M5G 1L7**  
**Room CR3**

### *AGENDA*

**Meeting Objective:** To identify areas of opportunity for a national TFRI biomarker initiative, to define process to identify projects with the shortest – term / biggest impact, and to coalesce groups to start preparation of business plans for funding

#### Saturday October 27

1. **Introductions, TFRI & Pan-Canadian Biomarker Initiative ( V. Ling)** **3.30 pm**
2. **Opening Strategies** **4 pm**
  - **Towards Roadmaps for Biomarkers (C Smith)**
3. **Presentations by champions (discussion papers)** **4.30 pm**
  - Breast, Ovary, Lung, Lymphoma, Prostate, Others
4. **Dinner and informal discussion** **6.00 pm**

#### Sunday October 28

- Breakfast** **8.30 am**
1. **Synthesis & Technology Considerations** **9 am**
    - **Technologies: Imaging (S McEwan), Genomics (S Jones), Proteomics (T Kislinger)**
    - **Intellectual Property Considerations (S Abraham)**
- Coffee Break** **10.15 am**
2. **Breakout groups to refine proposals (participants to self-identify)** **10.30 am**
    - **Identification of Issues / Challenges / Synergies**
  3. **Plenary Discussion** **Noon**
- Lunch 12.30 pm**
4. **Breakout Meetings of Tumour Site Groups (towards a plan)** **1.30 am**
  5. **Presentation of Initial Plans by each group** **3.30 pm**
  6. **Next Steps / Wrap Up (Victor Ling)** **4.30 pm**

## Appendix 2

### PAN-CANADIAN BIOMARKER INITIATIVE

27 – 28 October 2007, Toronto

### WORKSHOP PARTICIPANTS

Abraham, Sam -Director, Technology Development Office, BC Cancer Agency, Vancouver BC

Baruchel, Sylvain - Professor, Pediatrics & Director New Agent and Innovative Therapy Program, Hospital for Sick Children, Toronto ON

Basik, Mark - Professor, Montreal Centre for Experimental Therapeutics in Cancer, Lady Davis Institute for Medical Research, Montreal QC

Branton, Philip, Scientific Director, CIHR Institute of Cancer Research, McGill University, Montreal QC

Chevrette, Mario, McGill Urologic Oncology Research Group, Dept of Surgery, Montreal QC

Forsyth, Peter - Director, Southern Alberta Cancer Research Institute, Calgary AB

Geary, Peter - Director, CTRNet, Winnipeg, MB

Guha, Ab, Co-Director Arthur and Sonia Labatt Brain Tumour Research Centre, Hospital for Sick Children, Toronto ON

Herst, Stephen - Director, Research Development, BC Cancer Agency, Vancouver BC

Jones, Steven - Head, Bioinformatics and Associate Director, Genome Sciences Centre, BC Cancer Agency, Vancouver BC

Thomas Kislinger - Scientist, Division of Cancer Genomics and Proteomics, Ontario Cancer Institute, Toronto ON

Lam, Stephen - Head, Lung Tumour Group, BC Cancer Agency, Vancouver, BC

Lees-Miller, Susan, Professor, Biochemistry and Molecular Biology, Southern Alberta Cancer Research Institute, Calgary AB

Ling, Victor - Scientific Director, Terry Fox Research Institute, Vancouver BC

Magliocco, Anthony - Associate Professor, Depts of Pathology and Laboratory Medicine, and Oncology. Southern Alberta Cancer Research Institute, Calgary AB

McEwan, Sandy - Director, Oncologic Imaging, Cross Cancer Institute, Edmonton AB

Mes-Masson, Anne-Marie - Scientific Director, Institut du cancer de Montréal and Head of Oncology Research at the CHUM Research Centre, Notre-Dame Hospital, Montreal QC

Minden, Mark - Senior Scientist, Division of Stem Cell and Developmental Biology, Ontario Cancer Institute, Toronto ON

Murray, David -Director, Experimental Oncology, Dept of Oncology, Cross Cancer Institute, Edmonton AB

O'Connor-McCourt, Maureen - Cancer Genomics Project Leader, National Research Council of Canada. Biotechnology Research Institute, Montreal QC

Paige, Chris - Senior Scientist, Division of Stem Cell and Developmental Biology, Ontario Cancer Institute, Toronto ON

Park, Morag - Director, Molecular Oncology Group, Royal Victoria Hospital, Montreal QC

Parkinson, David - President and CEO, Nodality Inc, South San Francisco CA

Provencher, Diane – Director of Gynaecology-Oncology, University of Montreal CHUM Notre-Dame Hospital, Montreal QC

Rottapel, Robert - Associate Professor, Medical Biophysics, University of Toronto, Toronto ON

Saad, Fred - Director of Urology-Oncology, University of Montreal CHUM Notre-Dame Hospital, Montreal QC

Shaw, Patricia - Associate Professor, Pathology and Gynecology-Oncology, Ontario Cancer Institute, Toronto ON

Shepherd, Lois - Blood Bank Director, Pathology, Queen’s University, Kingston, ON

Siu, Michael - Professor of Chemistry, Biology and Director of Research in Mass Spectroscopy, York University, Toronto ON

Smith, Clayton - Director, BMT /Leukemia Program of BC, BC Cancer Agency / Vancouver General Hospital, Vancouver, BC

Tammermagi, Martin - Associate Professor, Dept of Community Health Sciences, Brook University ON

Tonin, Patricia –Associate Professor, Depts of Medicine & Human Genetics, McGill University and the Research Institute of the Montreal University Health Centre, Montreal QC

Tremblay, Michel - Director, McGill Cancer Research Centre, Montreal QC

Tsao, Ming-Sound - Professor, Division of Applied Molecular Oncology, Ontario Cancer Institute, Toronto ON

Watson, Peter - Professor of Pathology and Director, Tumour Tissue Repository, BC Cancer Agency, Victoria BC

## Appendix 3

