

The Canadian Prostate Cancer Biomarker Network (CPCBN)

We would like to thank you for your interest in participating in the project by proposing one or more biomarkers of interest in prostate cancer. The CPCBN is a program that regroups several researchers from four different Canadian provinces. The main objective of the CPCBN is to address important issues dealing with prostate cancer diagnosis and management. The CPCBN has assembled a cohort of 1500 radical prostatectomy specimens arrayed on tissue microarray (TMA) (1-2 normal cores and 2-4 tumor cores per patient). In addition, two different cohorts of 250 biopsy specimens were also assembled from an intermediate-risk group of patients treated by radiotherapy and from low-risk patients followed by active surveillance. All these patients' specimens are associated with diagnosis, treatment and clinical outcome data.

The project has 2 specific goals:

1. To develop a multi-parametric test on prostate biopsy to help stratify patients with apparently low-stage/low risk disease that will not progress and could be safely put on a surveillance protocol and avoid the risks of therapy from those whose disease will evolve and require active treatment.
2. To define a set of prognostic markers on radical prostatectomy specimens or biopsies from radiotherapy treated patients that will add to the currently used clinical and pathological parameters, to identify patients at high-risk of cancer recurrence and or progression that may benefit from adjuvant or neo-adjuvant therapies.

Data from both approaches will be combined within nomograms, along with age, comorbidity profile as well as clinical and pathological characteristics, to more accurately risk stratify the host-adjusted, individual risk-characteristics of each prostate cancer.

Please be advised that the CPCBN is a validation rather than a discovery platform. Thus it is primordial that the biomarker you are about to propose has preliminary data to its potential usefulness in prostate cancer management. Indeed, your proposal will be reviewed by the CPCBN-Study Committee who will, according to specific criteria, decide if your proposal is to be accepted or not. Thus, it will be important for you to provide the study committee with enough details to assure proper evaluation of your proposal. In addition, due to the heterogeneous nature of prostate cancer and TMA design, we would request that a pathologist or a fellow in pathology participate in the scoring. Indeed, as specific normal and tumor cores are present on the TMA it will be important to evaluate the specific zone and if a modification of the definition of the core is performed (normal/PIN/tumor), the CPCBN should be notified.

Flow chart of your proposal

- 1) Submission of the proposal along with required documents and images by email to Veronique Ouellet, the project manager of the CPCBN
- 2) Evaluation by the study committee.
- 3) For approved project, accession to the optimisation-TMA
- 4) Evaluation of the staining by a professional having received the approval of the study committee.
- 5) Accession to the test-TMA of 250 patients.
- 6) Evaluation of the results (statistical analyses) by the study committee. You will be asked to submit the scoring datasheet and associated TMA images (whole TMA scan) to the CPCBN. If your biomarker does not meet criteria, the data may be used, in the future, in multivariate analyses. If your biomarker demonstrates usefulness, accession to the remaining samples will be possible
- 7) Accession (or not) to the remaining 1250 patients of the RP cohort.
- 8) **You will be asked to submit the scoring datasheet and associated TMA images (whole TMA scan) to the CPCBN**
- 9) Evaluation of the results (statistical analyses) by the study committee

Should you have any questions/comments please contact

/DDQH0HXQHUpURQTXH0UUqV
8807RXU 9HU
UXH 6WHQM6XWH5
0RQWUpDO4F
‡ \$
3KRQHWH

Email : EREDQTXHUUFDQFHUFKXP#VVVRXYTFFD



Biomarker(s) ID (short name) If you are performing a multiplex assay, please state the name of all biomarkers evaluated on the same section):	
--	--

Study Title	
--------------------	--

1- CONTACT INFORMATION

a) Principal Investigator's contact information including complete name, address and email

--

b) Resource person's (contact person) contact information including complete name, address and email Same as PI

--

c) Shipping address as it should appear on the Fedex package

--

d) Co-Investigators(s) Please indicate complete name and affiliation

--



2- DESCRIPTION OF PRELIMINARY DATA

a) Brief description of the biomarker: function in normal and cancer context / Pathways involved / Partners. Were these partners/pathway members known in PC? Will you validate them on the CPCBN cohort?

b) Size and specification of the cohort used for preliminary data (ex. number of patients, radical prostatectomy, TURP, high/low risk cohort, pre/post treatments, etc.)

c) Experimental approach (summarize the technique used and specificity of the methods used)

d) Scoring technique used for IHC/IF (see appendix A for description)

e) Describe the scoring technique used for FISH (control to normal, cut-off, etc.)



f) Criteria used for scoring (cytoplasmic, nuclear, cut-off, scoring algorithm/software used or not – Please specify and provide an image representative of the scoring)

g) What does the biomarker predict: latent vs aggressive, disease progression, recurrence, death, and/or metastases?

h) Results (including the statistical analyses performed and results)

i) Assay performance (reproducibility, sensitivity and specificity)

3- PROOF OF CONCEPTS AND FEASIBILITY OF THE STUDY

a) Assay description



Name of the biomarker	Assay performed on		
	FFPE	TMA	Automated system
	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No
	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No
	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No
	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No
	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No

*Please note that in a translational point of view, the CPCBN required the assay to be performed on an automated stainer

b) Biomarker tested in multiplex (ex. multiple protein/genes tested at the same time)

- Yes, Please specify which biomarkers were performed together
 No

c) Specification of the antibody(ies) used

Name of the biomarker	Antibody				
	Commercially available	Monoclonal	Host Species	Specificity tested*	Digital image analysis
	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No		<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No
	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No		<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No
	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No		<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No
	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No		<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No
	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No		<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No

*Control images are requested for evaluation by the CPCBN Study Committee

d) A pathologist or a fellow in pathology is available to perform scoring of the TMAs?

- Yes No

e) A statistician is available to perform the statistical analyses?

- Yes No



4-ADDITIONAL INFORMATION

a) Funding from another institution to support the study

<input type="checkbox"/> Funds not available for this study at the present time <input type="checkbox"/> Study has been submitted for funding. Organization: <input type="checkbox"/> Study is funded or funds are available for this study from another source. Organization:

b) Budget

This is no longer available for researchers

NA

c) Timeline

--

d) Ethical committee approval

<input type="checkbox"/> Approval received <input type="checkbox"/> Project is under review <input type="checkbox"/> Project is not yet submitted

e) Intellectual Property protection process

<input type="checkbox"/> Not patentable <input type="checkbox"/> Not yet done <input type="checkbox"/> In preparation <input type="checkbox"/> Pending / provisional <input type="checkbox"/> Accepted	Patent number :
--	-----------------

f) Industry partnership

This proposal is performed in association with an industrial partner <input type="checkbox"/> Yes <input type="checkbox"/> No
--

5.0 Security and confidentiality

<i>Proposed electronic measures for clinical data safety: (ex: Are computers protected by passwords? Who accesses them)</i>	
<i>Will tissue and/or data treatment and analysis be carried out by outsourced personnel? If yes, please explain</i>	



The Terry Fox Research Institute
L'Institut de recherche Terry Fox

CPCBN Canadian Prostate Cancer Biomarker Network
Réseau canadien de biomarqueurs en cancer de la prostate

A Material Transfer Agreement (MTA) is presently being developed for the TFRI-CPCBN project. I understand that my application may be financed, and I will receive samples, only after this MTA has been approved and signed by all concerned parties. I also understand that the MTA defines the requirement for me to deposit the results and data generated from my experiments with the CPCBN resources into the CPCBN repository, and I agree to these conditions.

Signature: _____ Date: _____

Application checklist

- Completed application form.
- IHC/IF images.
 - Whole TMA scan or high quality images of low and high magnification.
 - Note that you will need to provide a slide scan for the other steps of the process.
 - Please email biobanquercancer.chum@ssss.gouv.qc.ca to receive a Dropbox invitation.
- Images of the staining/hybridization along with their associated scoring.
- Positive and negative controls supporting the specificity of detection of your biomarkers (western blot and/or staining).
- Budget description if needed.
- Antibody datasheet or information regarding the non-commercial antibody.
- Manuscript or paper demonstrating the results.
- REB approval if available, the CPCBN will request your approval prior to send the test-TMA
- Principal investigator cv (short version is sufficient).
- Award letter (if applicable).

Appendix A

SCORING TECHNIQUE DESCRIPTION

1. **BINARY.** A two-point scale. This is defined as either absent staining or staining in a sufficient number of cells so that you are convinced that at least some of the tumor cells express the antigen.
2. **4 POINT SCALE.** Assigning a value on a four-point scale to each immunostain. Descriptively, 0 represents no staining by any tumor cells, 1 represents a faint or focal, questionably present stain, 2 represents a stain of convincing intensity in a minority of cells and 3 a stain of convincing intensity in a majority of cells.
3. **COMPOSITIONAL** Estimation of the percentage of cells (expressed as increments of 5 to 25%) of cells expressing the antigen at each of three levels of reaction product - no expression, faint/equivocal expression, and intense. Methods for obtaining a single number for analysis
4. **CATEGORICAL COMPOSITIONAL (CC)** Expression on a four-point scale of 0 to 3, where 0 equals no expression, 1 equals $\leq 5\%$ of the cells express the antigen, 2 equals 5 to 20% of the cells, 3 represents 20 to 100% of cells.

Kindly provided by the Vancouver Prostate Centre