Australian Prostate Cancer Collaboration

THE AUSTRALIAN PROSTATE CANCER BIORESOURCE SUBMISSION TO THE SENATE SELECT COMMITTEE ON MEN'S HEALTH FEBRUARY 2009

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On behalf of the Australian Prostate Cancer BioResource Management Committee, we welcome this opportunity to make a submission to the Senate Select Committee on Men's Health established to inquire into the availability and effectiveness of education, support and services for men's health. In particular, we would like to focus on the first Term of Reference of the enquiry, that is, the level of Commonwealth, State and other funding addressing prostate cancer. Our submission is also focused on the problem of infrastructure funding, particularly for tissue banks or bioresources, to underpin prostate cancer research.

The Problem

Prostate cancer is now the most common cancer diagnosed in Australian men after non malignant skin cancers with ~ 18,700 new cases diagnosed each year. As with breast cancer in women, prostate cancer has now rightfully been recognized as a killer cancer (~ 3000 men die of prostate cancer each year = to the number of women who die of breast cancer) with a major impact on the lifespan of sufferers. A diagnosis of prostate cancer also impacts on quality of life, due to the current inability to determine and advise the sufferer on the likely course of his disease. This leads then to a combination of clinical and psychosocial impacts on the aging male. This lack of clinical insight is because prostate cancer covers a spectrum of disease that ranges from clinically indolent or "slow growing" to aggressive disease and we do not have the "biomarker" tools to guide clinical decision making. Nor do we yet have a suite of therapeutics (drugs) for non-invasive treatment specifically targeted to this disease spectrum.

Personalized medicine, which would provide such an approach, depends on intimate knowledge of each individual's disease. Medical researchers will undoubtedly uncover the secrets of prostate cancer variability that give rise to this complex disease. Discoveries will come from studying the biology, pathology and clinical outcome of tissues from a large number of men with the disease, and will be translated into new diagnostic approaches for earlier and more precise detection, and innovative therapeutic approaches to combat this particularly painful and intractable disease in its more advanced stages. More importantly, the more cases studied the more likely we will unravel the full spectrum of disease and such a personalized medicine approach will eventuate.

Tissue Banks Provide a Valuable Resource

The discovery of new biomarkers and novel therapeutic targets can only be accomplished by analysing the cancer tissues and biological fluids (blood – serum/plasma, urine) of men with prostate cancer. They, alone, hold the key to the complex intricacies of their cancer. This notion has been the cornerstone of the major translational research discoveries of the last 5-10 years and has been accompanied by a resurgence in tissue banking. The caveat is that these collections must be rigorously controlled in terms of the ethical consent of the patients, collection and storage of samples, access to and storage of de-identified patient

and clinical/pathological information on their disease and clinical follow-up of that disease progression. In the latter case, for prostate cancer, this means 10-20 years follow up given the natural history of the disease. These requirements have led to international dialogue and best practice approaches (such as the International Association of Biological and Environmental Repositories/ ISBER) with a recognition by many organizations worldwide (National Cancer Institute, USA; UK Biobank: Singapore Tissue Network etc) that a significant government financial investment is required to underpin such a valuable resource.

The Australian Prostate Cancer BioResource

The Australian Prostate Cancer BioResource is an initiative of the Australian Prostate Cancer Collaboration that was initially funded by the Commonwealth Bank of Australia, Prostate Cancer Foundation of Australia and Andrology Australia. This funding for the initial development of the BioResource helped leverage a successful Enabling Grant application to the NHMRC (funded from 2004-2009 for $2.1M) to establish an ongoing prospective collection. This was a large undertaking but we now have a 4-year old internationally regarded "best practice" national tissue bank collection containing biospecimens with associated clinical data from almost 2000 men with early stage disease. This is the largest multi-institutional collection of prostate cancer tissues within Australia, with patient recruitment from > 10 hospitals in Adelaide, Brisbane, Melbourne & Sydney and storage in four tissue repositories in those cities. The Australian Prostate Cancer BioResource is now distributing biospecimens to researchers across all mainland states of Australia and major collaborations are being formed to utilize these tissues on an international basis.

The National and International Reputation of the APC BioResource

The Australian Prostate Cancer BioResource has a national and international, rather than a state-based focus, as evident by the alliances it has built over the last 5 years:

- The BioResource has aligned itself with the Australasian Biospecimen Network, with major prostate cancer repositories in USA, Canada & Ireland, and with multi-stream tissue banks in Singapore, UK & Netherlands through ISBER (International Association of Biological and Environmental Repositories).
- The BioResource Project Manager is embedded within the ISBER committee structure to facilitate global harmonization of biobanking policies and procedures.
- The BioResource has formed an alliance with ANZUP (Australian & New Zealand Urogenital and Prostate) Clinical Trials Group to facilitate tissue collection following therapeutic manipulation for translational research studies.
- The BioResource has given its support to an international/national Queensland initiative – the Australian Canadian Prostate Cancer Research Alliance (funded for $2M 2008-2010) - cognisant that Australian researchers will need high quality tissues for any research collaborations funded under this program.
- The international "best practice" operations of the APCB have provided the model for the South Australian Cancer Tissue Bank initiative. A/Prof Horsfall is helping to co-ordinate that effort.

Strategic Initiatives of the APCB

The Australian Prostate Cancer BioResource operates on a 5 year strategic plan. The current plan for 2005-2009 finishes this year concurrent with our NHMRC funding. Our forward Strategic Plan 2010-2014 is currently in preparation. There are 4 major aspects to the proposed Strategic Plan:

1. Continued recruitment of men diagnosed with prostate cancer and collection of samples of their prostate cancer tissue, blood, and clinical data (see #1 below);
2. Implementation of a web-based central database to enable tissue selection by researchers;
3. An immediate need to embark upon production of tissue derivatives (value-added reagent program);
4. Engagement with national & international cancer gene discovery programs, and Australian clinical trials groups;

1. Continued collection and importance of data annotation:

The accrual of patient biospecimens needs to be continued until at least 2014 to create a resource spanning 10 years. At the current rate of accrual (500 men/yr), this will ensure recruitment of over 4,500 participants. An important outcome in 2014 will be that up to 50% of the patients (those accrued between 2005-09) will have 5-8 years clinical follow up. Ideally, 10-15 years is required for optimal outcome analysis particularly as the relevance of data from research and genomics studies using well annotated samples has gained prominence as new blood and tissue markers are shown to be associated with disease outcome. This is the way in which new biomarkers and therapeutic targets of the future will be discovered.

2. Web-based central database

A central database linked to our website is required for optimal usage of the prospective collection and tissue derivatives. Researchers will be able to view the collection on the database online to determine which patient tissues are relevant to their research study, downloading their needs directly to the Project Manager, while obtaining the Tissue Access Policy and Application Forms from the website (www.apccbioresource.org.au).

3. Production of Tissue derivatives (Value-added Reagent Program)

Value-added reagents are products derived from blood and prostate tissue such as : serum and plasma extracted from blood, DNA from blood cells and prostate cancer tissue, RNA from prostate cancer tissue, and micro-arrays of tissue cores of selected prostate pathologies and disease outcomes. These materials are used for the discovery of markers of diagnosis, prognosis and therapeutic response, and for determination of cancer-related mutations and predictive genetic variations (polymorphisms). Micro arrays allow a high throughput assay of large cohorts of tissues, with comprehensive data annotation, resulting in considerable tissue conservation. Providing these resources instead of the primary tissues is a more cost effective way of distribution and ensures greater longevity of the BioResource collection.

4. Genomic and proteomic discovery programs

The value-added reagent program will permit the Australian Prostate Cancer BioResource to engage with major national and international genomic and proteomic discovery programs (large scale studies of cancer genes and the proteins they produce to discover novel diagnostic and therapeutic modalities), where pre-requisites for entry is a demonstrated availability of DNA, RNA or protein, both of high quality and in large cohort numbers. Tissue samples (blood, prostate) from patients in clinical trials, where the patients are treated with novel drugs alone or in combination with existing drugs are especially important to these gene discovery programs.

Strategic Partnerships and Future Funding

Whereas some State Governments now have a funding focus on multi-cancer banks within their respective states, the successful national focus of the Australian Prostate Cancer BioResource predated those initiatives. Our premise is that a national disease driven resource is more cost effective for prostate cancer than being part of a multi-tumour bank particularly due to the complexity of this disease (prostate cancers frequently arise as numerous independent cancers of varying degrees of aggression) compared to the other solid tumours like breast, colorectal and renal cancers and the associated difficulties in tumour collections. It is important to note too that the national NHMRC funding does not fully fund the BioResource's activity and it relies on a not inconsiderable in–kind support from all of its chief investigator's institutional affiliations. Cost recovery is an oft stated way forward for sustainability, but in our experience it is difficult to find the right level of "cost recovery" that is not prohibitively expensive to the researcher yet demonstrates the value of the research material offered. So true cost recovery could never be effected in Australia. We have estimated that > $2M/year will be required to fully fund the ongoing prospective collections at its current rate and the new initiatives described above. Current funding of $420,000 per annum from the NHMRC concludes December 31st 2009.

A major question now is how best to fund the continuation of this national resource to the benefit of all Australians with prostate cancer?

We envisage that a partnership with several like-minded organizations will be required to underpin the BioResource for the next 5 years. We understand that the NHMRC is currently reviewing its funding arrangement for infrastructure such as ours. While we are confident that the NHMRC will continue to support these endeavours, we are mindful that the NHMRC cannot fully fund them. In this regard we have had discussions with organizations who have supported us in the past such as the Prostate Cancer Foundation of Australia and Andrology Australia who are supportive, in principle, of a co-funding partnership. Similarly, Cancer Australia and the Cancer Councils Australia are also supportive of the need for a national prostate tissue bank of our capacity and quality to underpin prostate cancer research. State Government Health Departments or entities such as the Cancer Institute NSW will also be approached for their involvement. The latter, in particular, will be more conducive to being involved if there is a strong Federal component to this partnership. The imprimatur of the Senate Select Committee on Men's Health would carry considerable weight.

Recommendations

For consideration by the Senate Select Committee on Men's Health:

- That a national prostate cancer tissue bank or BioResource is a key requisite to underpin current and future research which will lead to new diagnostic and prognostic biomarkers and therapeutic targets for prostate cancer and ultimately improved clinical management of this disease;
- That the Australian Prostate Cancer BioResource has the established national and international credentials and track record to continue this endeavour for the forseeable future; and
- That funding for this key initiative should be federally driven but also engage additional national and State based stakeholders in a multi-partnership.