'THE HEART OF THE MATTER IS UNDERSTANDING WHY TISSUE IS IMPORTANT'

AUSTRALIAN MELANOMA CONSUMER ALLIANCE

tissue is the issue

Conference Proceedings and Outcomes

Contents

Foreword

This Tissue is the Issue' forum was an initiative of the Australian Melanoma Consumer Alliance (AMCA) which also incorporates the Melbourne Melanoma Project Consumer Reference Group (MMP CRG).

This forum brought to the fore one of the most important issues facing medical research into melanoma and for that matter any similar type of disease.

That issue is the collection, availability and sharing of information derived from tissue.

The 'Tissue is the Issue' forum saw presentations from leading researchers in the field of melanoma as well as an internationally respected melanoma consumer representative participating from the United States – Ms Valerie Guild. The forum was also attended by many sufferers and survivors of melanoma who contributed significantly to the forum debate.

Through the presentations, panel debate and audience discussion, the forum delivered several key outcomes and recommendations. They were:

- The willingness of patients to have their tissue easily accessible to researchers
- The need to establish a framework for engagement with front-line health care professionals
- Removing barriers that prevent cost effective and timely collection, storage and research of primary melanoma tissue specimens
- Creating a roadmap for future work

We believe this forum has resolved several of the previously conflicting views on this matter and has established a strong framework through which to pursue the issue of tissue collection. Further, the forum has clearly highlighted the need for tissue to enable better research outcomes and ultimately better treatments for melanoma sufferers.

Professor Grant McArthur
Lead Investigator, MMP

Campbell Rose
Founder AMCA (incorporating the MMP CRG)

Acknowledgement of Sponsors

The convenors of the forum acknowledge the generous contribution of the sponsors who have made this essential debate possible.

Synopsis

WILLINGNESS OF PATIENTS TO HAVE THEIR TISSUE EASILY ACCESSIBLE TO RESEARCHERS

The central aim of the 'Tissue is the Issue' forum was to discuss a pathway to melanoma tissue collection in Australia. That process must begin with consent from patients to have their tissue collected for research purposes.

Melanoma survivors who attended the conference expressed unanimous support for the collection of their tissue for use in research purposes.

This is a key outcome of the forum. However, it is clear that patients cannot operate in a vacuum - awareness needs to be raised giving the consumer the option at the point of excision to donate their tissue for research purposes.

ESTABLISHING A FRAMEWORK FOR ENGAGEMENT WITH FRONT LINE HEALTH CARE PROFESSIONALS

The forum established that there is an obvious lack of awareness among both patients and front line health care professionals around tissue donation, in particular dermatologists operating outside specialist clinics.

In addition, even if aware of the tissue donation process, many front line health care professionals such as GPs and dermatologists don't have a satisfactory generic consent form which would enable consent for tissue to be collected at the initial consultation point. A general consent form needs to be developed so patients can instruct their GP or dermatologist that any remaining tissue sample beyond that which is required for the patient's pathology and treatment will be appropriately stored and used for research.

The variety of health care professionals who are required to participate in the collection, storage or research was also identified as a conflicting component of this agenda. The forum identified that there was an ethical responsibility of health professionals to work together cooperatively to ensure that the process of tissue collection occurs for every patient, particularly at the point of collection of primary melanoma tissue.

REMOVING BARRIERS THAT PREVENT COST EFFECTIVE AND TIMELY COLLECTION, STORAGE AND RESEARCH OF PRIMARY MELANOMA TISSUE SPECIMENS

One of the barriers often mentioned during the panel discussion was the current lack of human resources to deal appropriately with the many requirements of patient tissue collection. The forum also identified a shortage of adequately trained anatomical pathologists as a major barrier to the processing of tissue.

It was noted that the experience in the United States had shown that front line health professionals in this sector (either dermatologists or GPs) were not sufficiently equipped to undertake the ancillary functions of taking blood, urine and securing and freezing a sample of the primary melanoma when they consulted with the patient. It was also noted that in Australia, the AMCA would need to advocate to appropriate bodies for the training of more pathologists.

The solution found in the US to this problem was the placement of specifically dedicated and appropriately qualified personnel to undertake this activity in centres willing and able to collect tissue. This was especially important for fresh unfixed primary melanoma tissue – an area of significant research need.

It was concluded at the forum that there was a need for investment in staffing around this tissue collection process. It was also agreed that the cost of this up-front tissue collection would be offset by the preventative health and research dividends provided by the investment.

There is also an obvious associated cost with bio-banking and it was agreed that increased funding should be sought through both government and private sector investment. Further it was agreed that an informatics and health economics case needed to be built to advocate to government.

CREATING A ROADMAP FOR FUTURE WORK

It was clear from the forum that there were four key areas that needed to be examined.

- **Consent from patients:**

The forum confirmed that patients wanted their tissue donated for research purposes. Therefore streamlining of the informed consent process is a high priority.

- **Collection of tissue samples:**

This will require investment to better coordinate and fund the collection of tissue at the initial interface between patient and front line health care provider. The fundamental importance of obtaining clinical data and follow-up information pertinent to each tissue sample was highlighted. In fact, this is arguably a bigger, more expensive and logistically complex challenge than the collection of tissue itself. However, if done properly, the collection of this 'annotated' data adds immense research value to the tissue. The development of electronic medical records linked to research infrastructure would be highly useful.

- **Collaboration:**

There were differing opinions between clinicians at the forum around the best ways to share tissue for research. It was decided that this issue would require the formation of a working party of health care professionals in order to establish an action plan to resolve an effective way forward. The AMCA will drive the establishment of this working party.

- **Funding:**

It was decided that whilst the issues of collection and collaboration were explored further, an immediate approach should be made to both state and federal governments for a coordinated approach to resourcing tissue collection, in particular by engaging in the Council of Australian Governments (COAG) process. In addition to this, the AMCA believes that philanthropic and private donations should be sought to expedite the continued work on this important issue.

Conference Proceedings and Outcomes

TISSUE IS THE ISSUE - A forum to investigate the challenges of melanoma tissue collection for research

WELCOME MESSAGE

- Mr Campbell Rose

The welcome message was provided by AMCA Founder, Mr Campbell Rose who thanked the variety of representatives that had gathered to discuss the issue of tissue collection which aims to tackle the prevalence of melanoma in Australia. Mr Rose underlined the importance of this being a consumer driven initiative – a forum that successfully convened the full spectrum of health care professionals to hear from survivors and sufferers of melanoma who want to see more done to research and cure the disease.

Mr Rose recognised the contribution of the sponsors of the event who had provided financial support to the AMCA, underlining the fact that forums such as this do not happen without such support. The contribution of the Melbourne Melanoma Project (MMP) was specifically highlighted.

Mr Rose noted the apology of Mr Peter Gordon, who was unable to attend the forum due to an urgent professional matter. Mr Rose thanked Dr Mark Shackleton for agreeing to act as the facilitator of the audience and panel debate.

SETTING THE SCENE

- Mr Campbell Rose

The formation of the AMCA was something that began several years ago and an incredible amount of work has been undertaken in arriving at this conference. The success of that work has been underlined by the significant attendance rate that has been achieved, and also the personally expressed apologies of the country's political leaders.

This forum is aimed at addressing four key drivers:

- Awareness of patient concerns
- The need for stakeholder engagement: with patients, health professionals, lawyers, and law makers
- Removal of barriers to achieve success; and
- How we continue to collaborate and progress

THE LATEST ADVANCES IN MELANOMA

- Presented by Professor Grant McArthur (attached as Appendix 2)

Melanoma in Australia

The rate and severity of melanoma in Australia is both significant and concerning. 1 in 14 males and 1 in 24 females will be affected. This equates to a nation-wide 1 in 18 lifetime risk. There are 11,000 cases of melanoma each year. Whilst Australia accounts for less than 0.5% of the world's population, it accounts for 6.4% of global cases of melanoma, making this problem a very Australian one. Melanoma is the most common cancer among 20-40 year olds and if you suffer from cancer in Australia there is a 1 in 10 chance it will be melanoma.

Melanoma: The Battle Plan

The fight against melanoma has been traditionally fought on three fronts: prevention, early detection and improved treatment.

There is evidence to suggest that prevention is working particularly in younger people, but it is clearly not sufficient to

tackle the issue completely. The rate of melanoma is escalating.

Early Detection has also helped decrease the spread of melanoma phases beyond the primary site, eg, secondary or metastatic disease. But again, early detection (even accompanied by increased awareness) is unlikely to be sufficient alone to tackle the disease given the high propensity of cells from thin melanomas to spread.

What we need is an improved treatment regime and that will only be possible through further research – specifically on melanoma tissue.

Researchers need tissue in order to understand why melanoma acts in the way that it does; why it spreads to phases beyond the primary site and how it is possible to scientifically interrupt that process. We need tissue in order to understand why that staging and spreading of melanoma happens. If we don't have tissue, we cannot establish what mutations drive this process.

The current way that tissue samples are used is as follows: provisional or clinical diagnosis, sample fixed and sent to pathology laboratory, sample examined microscopically for diagnosis, sample tested and stored long term.

From a research perspective this is an ineffective use of the tissue sample and if there was a system in place that enabled tissue samples to be shared with researchers, then advanced research techniques could be applied. This isn't happening.

Whilst patchy, tissue donation does occur and it is one of the only ways that research is able to be conducted. The best example of this is the process of BRAF (see appendix 2) which has made extremely strong progress- none of this is possible without tissues donation. Without tissue, research advances and innovation will remain limited.

Advances in science – specifically molecule amplification- mean that even small amounts of tissue are able to be used for research. But those advances will continue to be limited without tissue collection.

THE US EXPERIENCE - CHALLENGES AND OPPORTUNITIES FOR TISSUE DONATION

- Ms Valerie Giuld (attached as Appendix 3)

After the death of her daughter Charlie, at the age of 26, Valerie Guild spent a year figuring out how she could, with a non-scientific background, help address the disease of melanoma.

It became clear after consultation with many health professionals that the most significant issue facing the health community was the collection of tissue.

There are four major issues facing the establishment of a central tissue collection research facility

- Consenting
- Collection
- Collaboration
- Cash

Consent

Consent in the US has been the least problematic, and when queried, most people who oversee bio banks say that in their experience patients hardly ever object to having their tissues used for research, and that most patients want their disease experience to benefit someone else.

In the US all of the cooperative cancer groups have made bio banking consents a standard part of the protocol for almost all cooperative group trials. It is also common practice at large hospitals that are engaged in research to include a bio banking consent for all newly admitted patients.

These consents tend to be very broad, with patients giving blanket permission for their specimens to be used for unspecified research by unspecified researchers.

Collection

The next area that needs to be addressed is collection and here the issues are threefold: the actual logistics, quality control, and exactly what should be collected. Although many of these are the same for all types of tissue Ms Guild focussed on the primary tissue samples.

The logistical problem is of course that most primaries are not removed in a hospital surgical setting but in a private practice office. In the US that typically means the dermatologist's office.

It was simply impractical to expect a dermatologist in this setting would be willing, or had the ability, to consent, draw blood, get urine samples, take a full medical history and temporarily store the excised tissue. Because of that difficulty, the US model uses only dermatologists at large institutions or their affiliated hospitals.

Each of these institutions has a dedicated trained bio bank person on-call to perform all of these activities once it is determined that there is a patient in the dermatologist's office with a suspicious lesion. After the primary is excised and put into the solution of choice, the bio bank person will ensure that it is immediately brought to the location where it can be flash frozen and stored.

The US also chose this model because the second area of concern in collection is guaranteeing that all of the tissue collected is of the highest quality. Participating institutions have agreed to abide by the guidelines agreed upon for sample documentation, collection, processing, storage and retrieval. As well, all sites are regularly audited by an external organisation.

Lastly, The US understands that both clinical and laboratory data are crucial to this process, as well as prospectively tracking patient outcomes. The goal of the US system is a fully annotated bank with all participating institutions entering the same data in the same way for each patient.

Collaboration

The area of collaboration was the most difficult component of the plan in the US. There was an understanding that in orphan diseases such as melanoma that no one institution was able to collect enough tissue for their own research- much less for the research community at large. In spite of that, it was difficult to find primary investigators who were willing to commit to pooling their tissue, even though that clearly offered them the only way of acquiring the steady stream of tissue needed for their own projects.

When that concept was attacked more broadly through the suggestion that once their own need for tissue was satisfied, that they allow the bank to be opened to outside researchers who would have to meet stringent criteria, the takers became even fewer.

Clearly, there is no easy solution for this lack of collaboration. And this issue was evident at the forum through the panel discussion below. In the US, Ms Guild was able to find four dedicated melanoma department heads who understood the need and were sufficiently eager to assist and go about making these scarce resources available to the research community at large.

That challenge is yet to be tested in Australia, but one of the key outcomes of this forum was that health professionals had an ethical obligation to work together to enable better research and through that, better treatment, for melanoma sufferers in Australia.

Funding

Ms Guild spent significant time educating the government and private funding agencies about the importance and benefits of bio banking. Through this process of education, the money began to flow in.

The US experience taught Ms Guild that public and private funding was rarely made for infrastructure to store the tissue, although it should be noted that this is not necessarily a parallel which should be transferred to Australia. The forum did establish that with an appropriately positioned argument – led by consumers and fleshed out by health professionals – that government would seriously investigate the preventative health economics of funding both a facility and a system of collection.

PANEL DEBATE AND AUDIENCE DISCUSSION

- Moderated and facilitated by Dr Mark Shackleton

The Panel for the forum consisted of doctors, dermatologists, nurses, carers, oncologists, surgeons, pathologists, ethicists, consumers, lawyers and researchers.

This was a talented panel which provided a full spectrum of insight into the 'tissue issue'- from the consumer who consults with a front-line health professionals through to researchers who could use samples to research and devise new ways of tackling the disease.

Mark Shackleton, acting as the moderator, approached the discussion from two perspectives. Firstly, he asked the panel to consider the issue from a consumer perspective. That is, the patient who first presents to a front line health care professional with a potential melanoma. Secondly he asked the panel to consider the issue of collection; what barriers may be encountered and what solutions could be deployed.

On the first issue it was agreed that there was no concern from a patient perspective about tissue being collected. Significantly, it was also pointed out that the a patient's willingness to donate tissue is not simply for the benefit of future sufferers – there is a utility in having primary samples collected and catalogued for research which could examine secondary and metastasised melanoma for that patient, should the cancer progress. This would provide the capacity for an individually targeted research that could benefit the patient into the future of their treatment. This is particularly the case when oncologists want to test potential treatments such as BRAF on secondary or metastasised melanomas.

It was noted that when patients go to front line health care professions, the most important question a patient wants answered is whether the skin condition is a cancer. Patients generally do not focus on other considerations such as the use of additional tissue for research or preserving adequate tissue to ensure an accurate diagnosis can be made. However, subsequent panel discussion resolved that the size of a melanoma does not determine whether or not it can be used for research. Small tissues can be effectively used for research. In some cases all researchers need is one cell.

One of the important issues raised was that there is a general lack of awareness among patients and front line health care professionals that there is the capacity to donate their tissue. And the challenge is that a patient can't work in a vacuum- they need awareness in order to donate. It was agreed that a general consent form needs to be developed so patients – when approaching their GP or dermatologist – can consent to donating a tissue sample beyond that which is required for the patient's treatment. It was resolved that there is a role for AMCA in raising awareness in the community to address the lack of awareness from a patient's perspective around the possibility of donating their tissue. It was noted that it was essential to secure consent at this initial stage of consultation.

All survivors of melanoma at the forum indicated that they would want their tissue collected for research.

An additional issue that was flagged was that the vast majority of tissue that is taken for testing is actually benign. However, it was noted that whilst this may make some tissue less relevant for research purposes, it did not constitute a sufficiently significant barrier to progress the collection process.

The moderator then asked the panel and audience to consider the prospect of the 'tissue issue' from the point of collection.

It was resolved that whilst some melanomas are small, there is almost always enough excess tissue for the sample to be stored for future research.

It was noted that the current laws in Australia require that the tissue specimens are to be kept for 11 years and that once that time has expired it is up to the operator who stores the specimen as to whether they want to discard or keep the specimen. It was agreed that this legislative position lacked sufficient rigour.

Ms Guild noted that the most commonly used front-line health care professionals for skin checks in the US were dermatologists. And that in the general dermatology community there was a lack of willingness to undertake the ancillary functions of taking blood, urine and securing and freezing a sample of the melanoma when they consulted with the patient. This is why in the US they needed to acquire dedicated personnel to undertake this activity

It was noted that there needed to be further investigation of how sufficient human resources could be established at this initial patient-clinician level for tissue to be taken for both testing and storage whilst also completing the necessary additional functions of urine and blood collection and the establishment of a thorough medical history. This was agreed on the basis that it would be difficult to comply with the logistics from a GP point of view.

Despite the associated costs of bio-banking, there is a significant preventative health component to this and it was noted that by establishing such a tissue collection and research process, the "healthenomics" of this investment far outweighed the cost of establishing the system.

It was agreed that funding from government and the private sector should be sought immediately.

There are current research projects already underway that, with tissue, could address some fundamental tissue research issues. However, there is insufficient funding and resources to collect the tissue in a timely manner and to analyse the data quickly.

From a research perspective, three key issues were raised and discussed:

First, that melanoma is a very complex disease that remains poorly understood. The use of fresh and archived human tissue is now allowing researchers to address important fundamental questions relating to melanoma that have until recently remained elusive, including the ways that melanoma can change and spread throughout the body and how this disease responds to treatment.

Second, these studies are at the forefront of melanoma research and would not be possible without access to banked human tissues. In order to continue research with a strong potential for rapid translation into the clinic, researchers need access to high quality, annotated human samples in a range of states ie. fixed and embedded in wax, fresh frozen and fresh viable.

Third, through research with donated human tissues scientists have a powerful tool to identify new ways to combat this disease, including discovery of disease "drivers", biomarkers for prognosis and potential for therapy-response, novel targets for effective drug design and more relevant and rapid models for preclinical drug testing.

What is the "End Game" of Tissue Collection?

The moderator then turned to the potential optimal yield from achieving the collection of tissue for research purposes. Four key markers were identified in relation to this question:

- International tissue comparisons
- Better understanding of the disease
- Creating better treatments and ultimately cures for melanoma sufferers

Summation and preliminary reflection

- The most important issue the forum established was that patients want their tissue donated.
- There is a lack of coherency in tissue collection and a large amount of tissue languishing in labs and not coordinated into an investigative research capacity.
- Health professionals are ethically obligated to act upon this and are similarly obligated to collaborate to resolve barriers to the implementation of such a system.

- A consent form should be developed for patients to sign at the initial diagnosis point of patient interaction – a GP or dermatologist.
- Those tissues should be annotated so that researchers are able to quickly and reliably gain access to patient tissue data/samples.
- Funding should be sought immediately.
- There is a human resources issue that needs to be resolved- both in terms of front-line collection capacity as well as the pathology level where the assessment and investigation of tissue takes place. This is another issue that should be discussed with government.

CLOSING REMARKS

- Mr Campbell Rose

- Universally agreed that patients want better treatment and would consent to tissue collection.
- The AMCA will be actively lobbying government for funding on this issue.
- There is an ethical obligation for health care professionals to continue to collaborate to resolve any barriers so that this process can begin.

Appendix 1: Attendees

Alan Rose – *General Practitioner*

Amanda Ross – *Biobank Coordinator*

Anne Fennessy – *MMP Project Coordinator*

Anne Spence – *Cabrini Human Research Ethics Committee*

Anne Thompson – *Executive Officer*

Anne Woollett – *MMP Project Coordinator*

Bill McHugh – *AMCA representative*

Brian Loughran – *HREC member, Bendigo Health*

Campbell Rose – *AMCA Founder*

Clare Fedele – *Post-doctoral Research Scientist, Peter Mac*

Clinton Heal – *AMCA representative*

Damien Kee – *Medical Oncologist*

Daniel Bowles – *AMCA representative*

Diane Shepheard – *AMCA representative*

Donna Milne – *Melanoma Care Coordinator*

Esther Yeoman – *Nurse Consultant*

Grant McArthur – *Head Melanoma Unit, Peter Mac*

Hannah Burrell – *Melanoma Care Coordinator*

Jane Palmer – *Research Nurse*

Jay Allen – *AMCA representative*

Jeanette Raleigh – *Biomarkers Researcher*

Jeremy Hoglin – *Biobank Coordinator*

Joanne Mercuri – *Healthscope Limited*

John Dunn – *AMCA*

John Kelly – *Dermatologist*

Julie Johns – *Data Utilisation Manager*

Karen Barfoot – *Public Affairs Manager*

Karen Bruce – *Product Specialist Representative*

Kate Thompson – *Manager*

Kim Ong – *Biobank Coordinator*

Laura Galletta – *Biobank Coordinator*

Leanne Bowes – *AMCA representative*

Libby Paton – *ANZ Melanoma Trials Group*

Lisa Devereux – *Australasian Biospecimen Network*

Lisa McPhail – *Biobank Coordinator*

Lois Whiteoak – *MMP participant*

Louise Marshall – *AMCA representative*

Luke Mannix – *Roche*

Madeleine Whiting – *Director of Devlopment St Vincents*

Margaret Otlowski – *Lawyer and Ethicist*

Mark Shackleton – *Medical Oncologist and Group Leader, Melanoma Research Laboratory, Peter Mac*

Paul White – *AMCA Chairman*

Professor Tom Kay – *Director of St Vincents*

Rachel Conyers – *Research student*

Rhonda Mawal – *Life pool Project Manager*

Richard Scolyer – *Pathologist*

Rob Jarvis

Rosemary Savino – *Pathology Manager*

Roz Kaldor Aroni – *AMCA Administration*

Rynska Aleksandra – *Molecular pathologist*

Smantha Boyle – *Researcher*

Stephen Fox – *Head of Pathology services*

Stephen Wong – *Research Scientist, Peter Mac*

Tass Stylianopoulos – *Australasian Biospecimen Network*

Valerie Guild – *AIM Founder*

Valerie Jakrot – *Melanoma Institute of Australia*

Victoria Mar – *PhD student, Peter Mac and Alfred*

Wayne Phillips – *Peter MacCallum Cancer Centre Ethics Committee*

Will Kerrkitof – *Melanoma Patients Australia*

Yue Li – *Bioinformatics Officer*

Zdenka Prodanovic – *Biobank Coordinator*

Rachel Whiffen – *VCOG*

Laura Vella – *Post doctoral Researcher*

Louise White – *Emily's foundation*

20 – *MMP participants*

Appendix 1: Apologies

Dr Tom John – *Resarcher Ludwig*

Colin Anderson – *Bendigo Hospital Pathology Services*

Matt Hanrahan – *Northern Sydney/Central Coast Health*

Craig Bennett – *Peter Mac Callum Cancer Centre*

Dr Arthur Chiang – *General Practioner*

Associate Professor Alex Dobrovic – *Head of Molecular Pathology, Peter Mac*

Sunshine Coast Day Surgery

Jim Yong – *Pathology Manager*

David Raven – *Pathology Manager*

The Hon. Julia Gillard MP – *Prime Minister*

The Hon. Tanya Plibersek MP – *Federal Minister for Health*

The Hon. Nicola Roxon MP – *Federal Attorney General*

Trent Kear – *Chief of Staff, Federal Minister for Health*

The Hon David Davis MLC – *Minister for Health, Victoria*

The Hon Lawrence Springborg MP – *Minister for Health, Queensland*

Dominic Stefanson – *Chief of staff, Minister for Health and Ageing, South Australia*

Dr David Swan – *Chief of Staff, Department of Health, South Australia*

Mark Compton – *St Luke's Hospital*

Mathew Daly – *Secretary Department of Health, Tasmania*

Mary Lou Chatterton – *Governance Officer, Barwon Health*

Dr Simon Donohue – *Surgeon*

Professor John Thompson – *Surgeon*

Dr Tony O'Connell – *Director-General*

Dr David Speakman – *Surgeon*

Dr John Spillane – *Surgeon*

Dr Andrew Haydon – *Medical Oncologist*

Dr Craig Underhill – *Medical Oncologist*

Jacqueline Mathieson – *Melanoma Care Coordinator*

Dr Craig Underhill – *Hume RICS*

Professor Michael Henderson – *Surgeon*

Bill Murray – *Head of Anatomical Pathology*

Professor Nick Hayward – *Laboratory Head, Onogenomics QMIR*

Professor Paul Waring – *Head of Pathology, Melbourne University*

Jo Hawking – *MMP Coordinator*

Victoria Beshay – *Molecular Pathologist*

Anthony Bell – *Molecular Pathologist*

Catriona McLean – *Pathologist*

VCOG Consumer representative

Esther Yeoman – *Nurse Consultant*

Libby Paton – *ANZMTG Tials Group*

Ian Roos – *Cancer Voices*

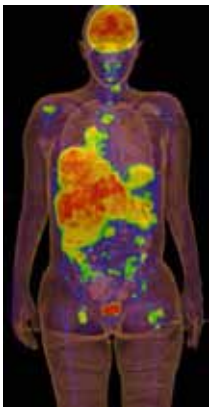
Katie-Lee Alexander – *Biobank Coordinator*

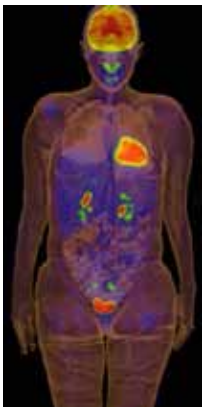
36 – *MMP Participants*

Appendix 2:
Presentation by Professor Grant McArthur

"Tissue the Key to Make The Latest Advances in Melanoma"

Grant McArthur MB BS PhD
Peter MacCallum Cancer Centre
Melbourne, Australia

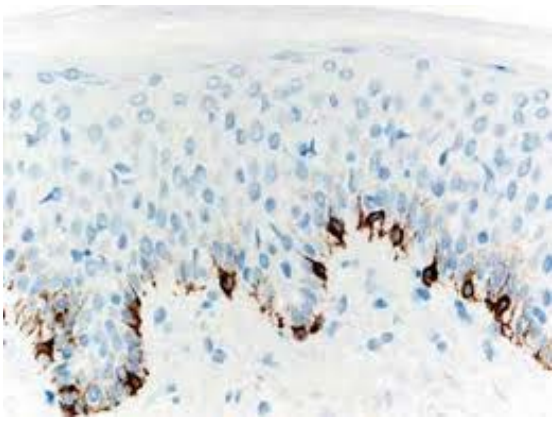


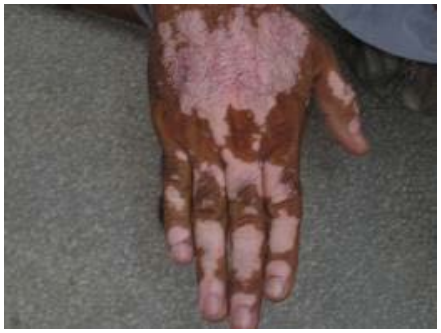


MELBOURNE MELANOMA PROJECT

What is Melanoma?

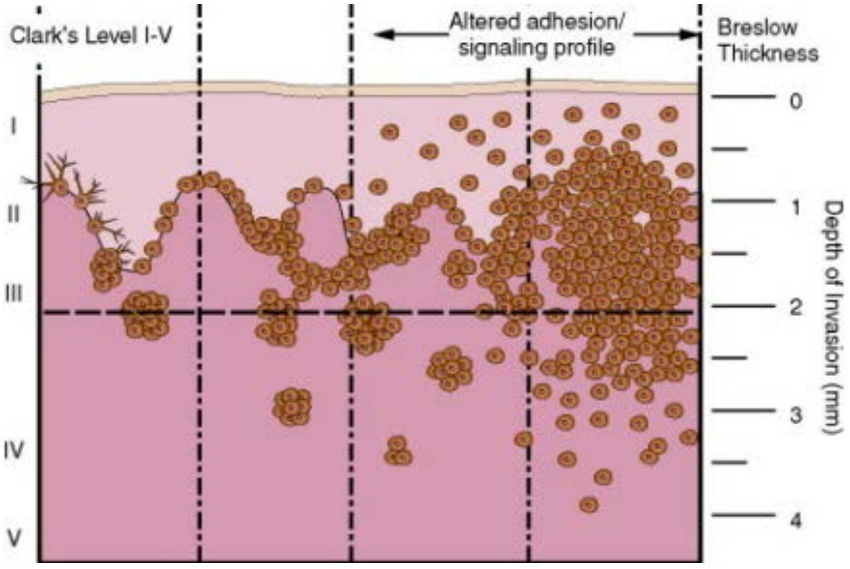
- Cancer of melanocytes





MELBOURNE MELANOMA PROJECT

The Progression of Melanoma- How Does it Spread?



Mendelsohn. *The Molecular Basis of Cancer.* Saunders 2001.

MELBOURNE MELANOMA PROJECT

Melanoma in Australia

- 1 in 18 lifetime risk (breast cancer 1 in 16)
- 1 in 14 (males) ; 1 in 24 (females)
- ~11,000 cases a year (6.4% global cases)
- Most common cancer 20-40 yo
- 10.2% of all cancers (breast cancer 12.2%)
- Death rates increasing by 0.5% pa (males, especially those aged over 60)

MELBOURNE MELANOMA PROJECT

Melanoma- the battle plan

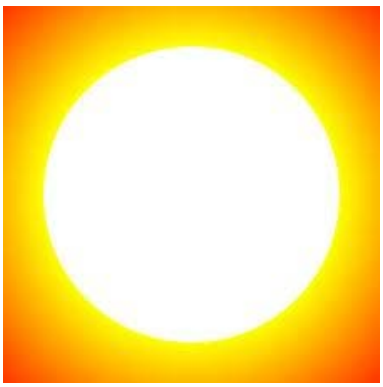
Prevention

Early Detection

Improved Treatment

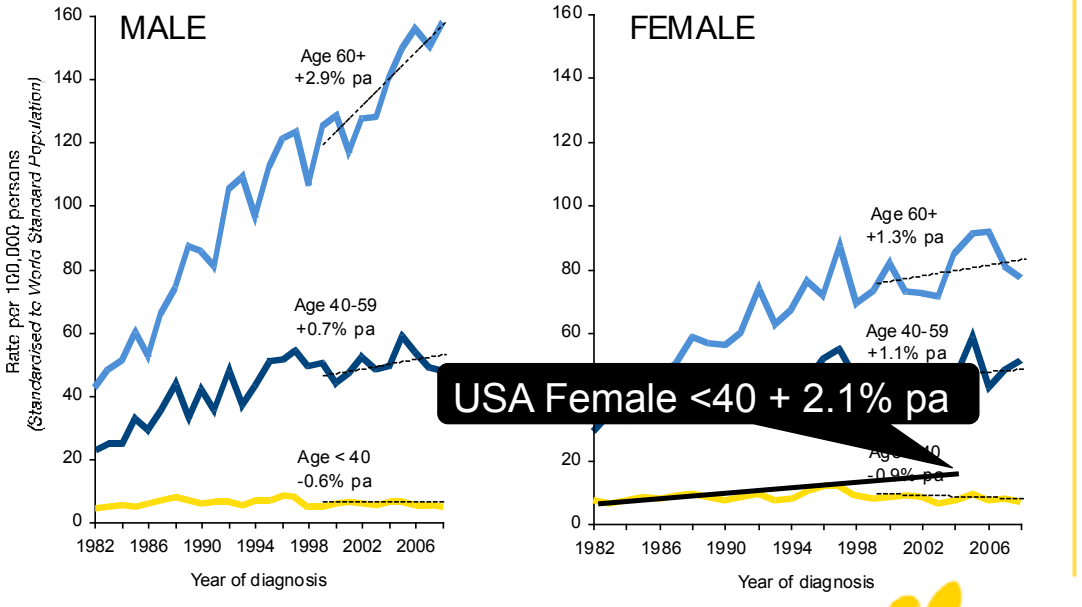
MELBOURNE MELANOMA PROJECT

Preventing Melanoma



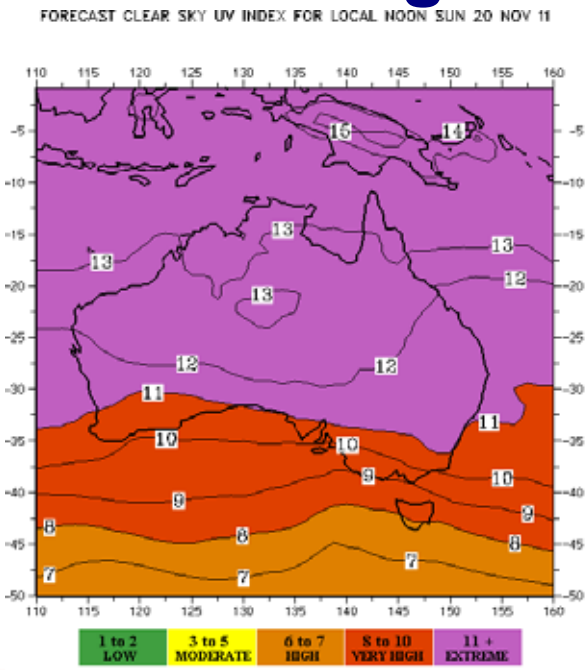
MELBOURNE MELANOMA PROJECT

Melanoma incidence trends by age group



Cancer Council Victoria

Preventing Melanoma

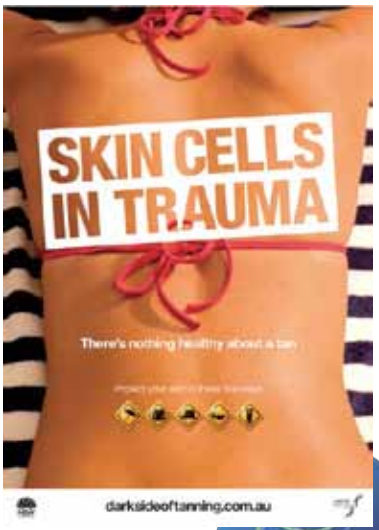


Midday Nov 20 - Spring!

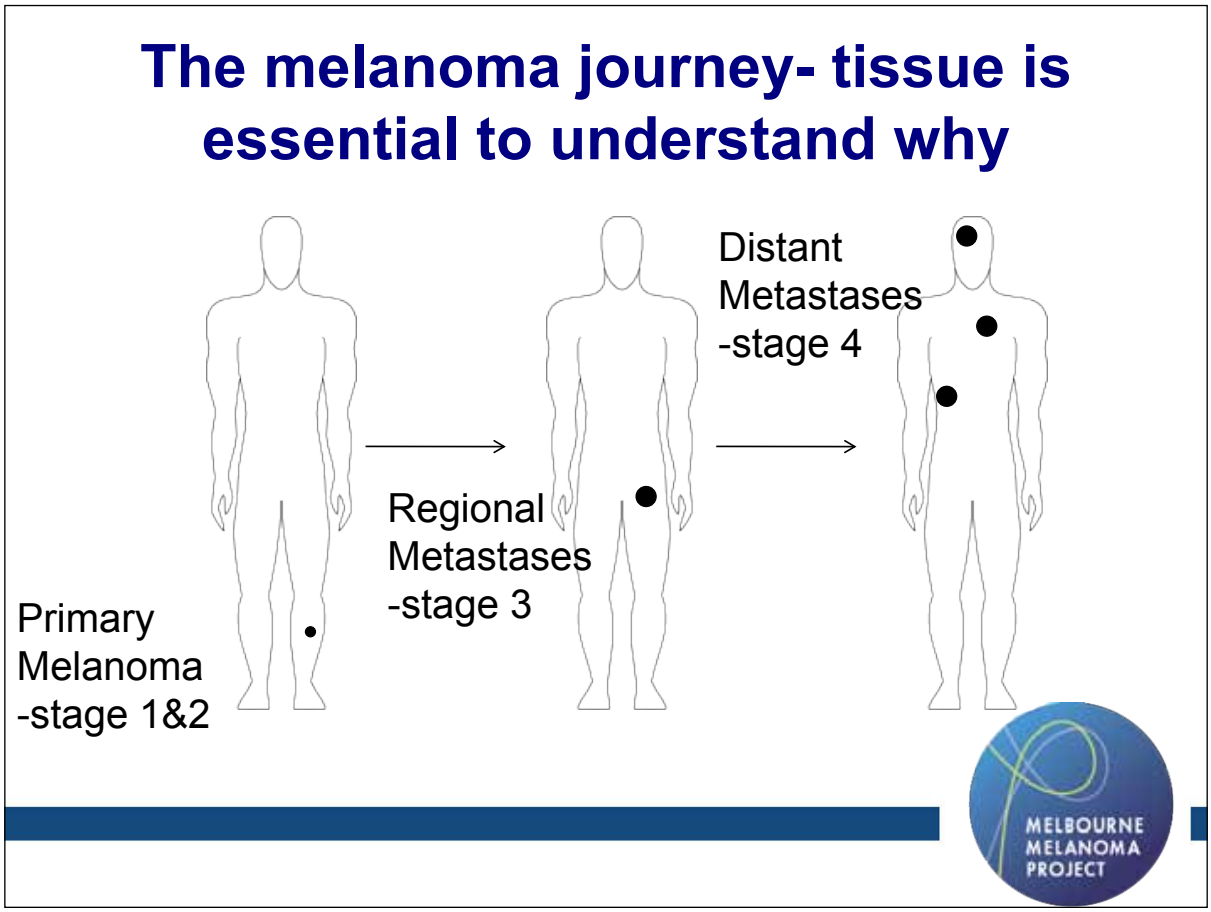
MELBOURNE MELANOMA PROJECT

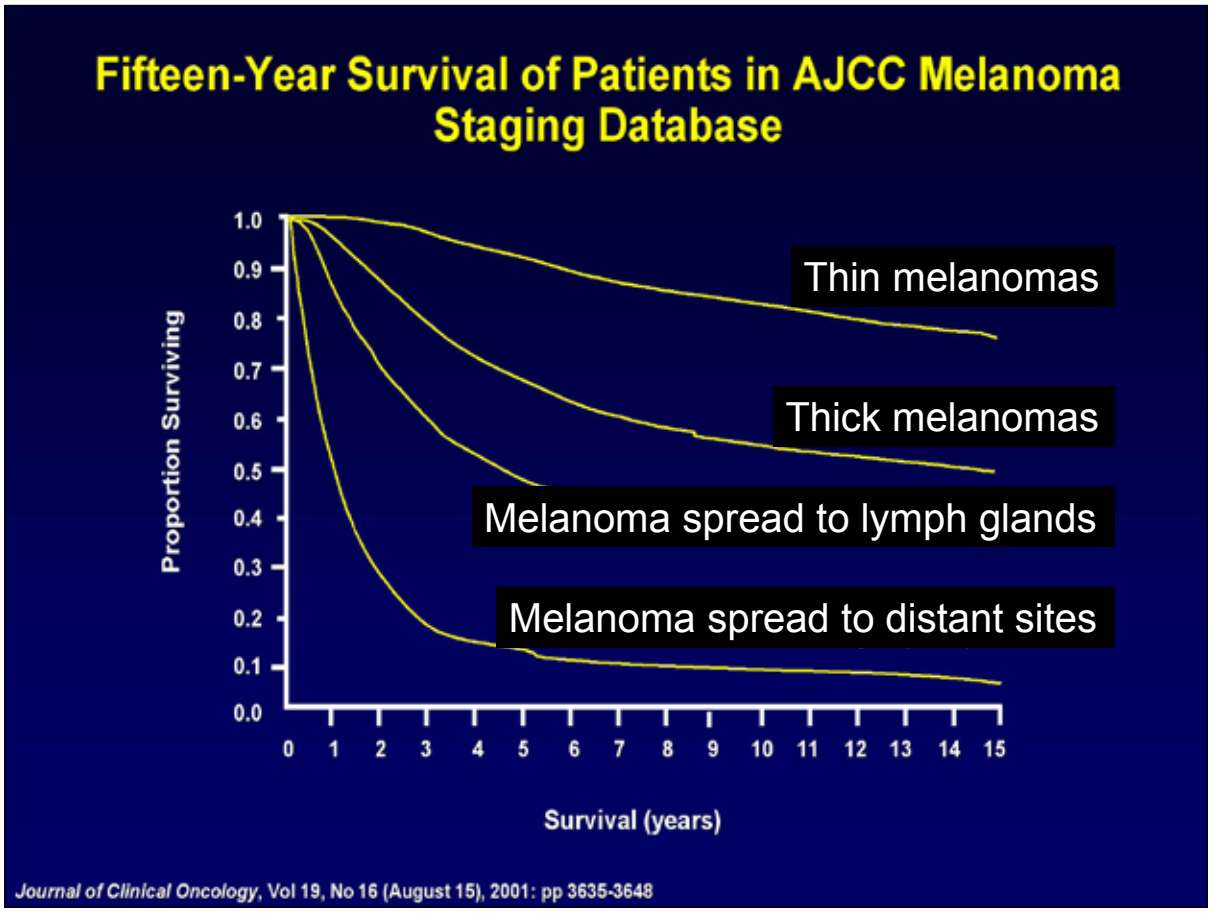
Detecting Melanoma Early

Awareness!

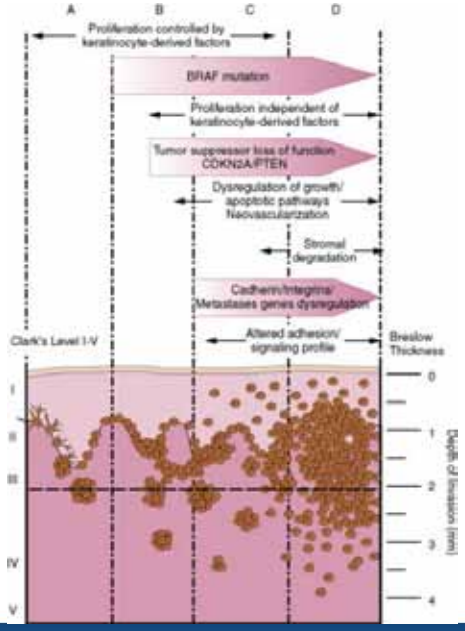


MELBOURNE MELANOMA PROJECT


The melanoma journey- tissue is essential to understand why
Distant Metastases -stage 4
Regional Metastases -stage 3
Primary Melanoma -stage 1&2
MELBOURNE MELANOMA PROJECT


Fifteen-Year Survival of Patients in AJCC Melanoma Staging Database
Proportion Surviving
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Survival (years)
Thin melanomas
Thick melanomas
Melanoma spread to lymph glands
Melanoma spread to distant sites
Journal of Clinical Oncology, Vol 19, No 16 (August 15), 2001: pp 3635-3648

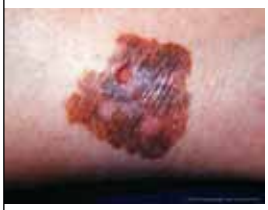
Gene mutations in melanocytes are central to the development of melanoma

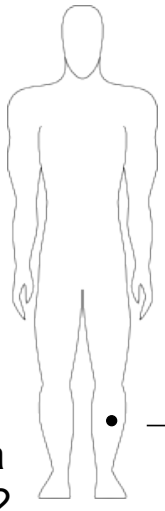


Mendelsohn. *The Molecular Basis of Cancer.* Saunders 2001.

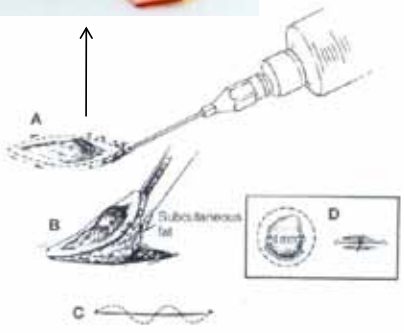
MELBOURNE MELANOMA PROJECT

The melanoma journey- tissue is essential to understand why



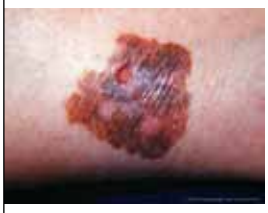


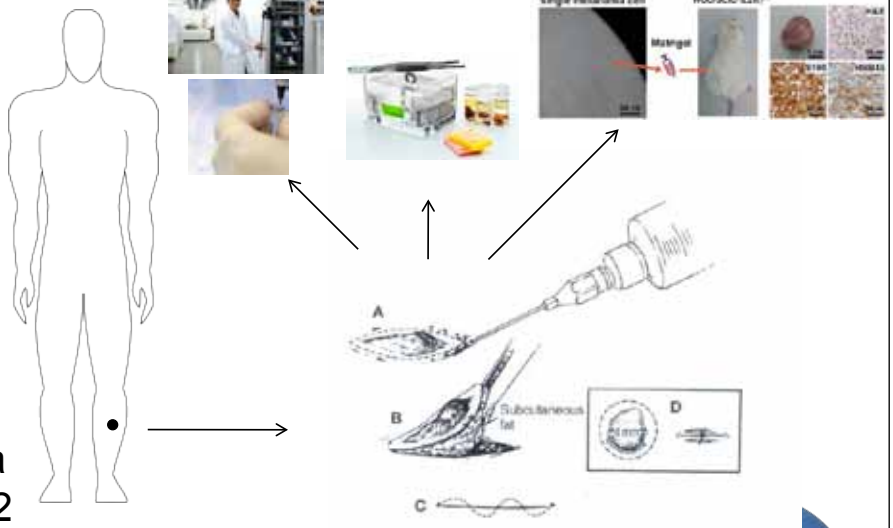
Primary Melanoma -stage 1&2



MELBOURNE MELANOMA PROJECT

The melanoma journey- tissue is essential to understand why

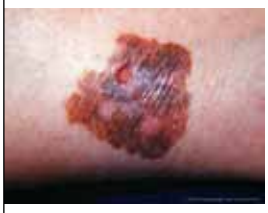


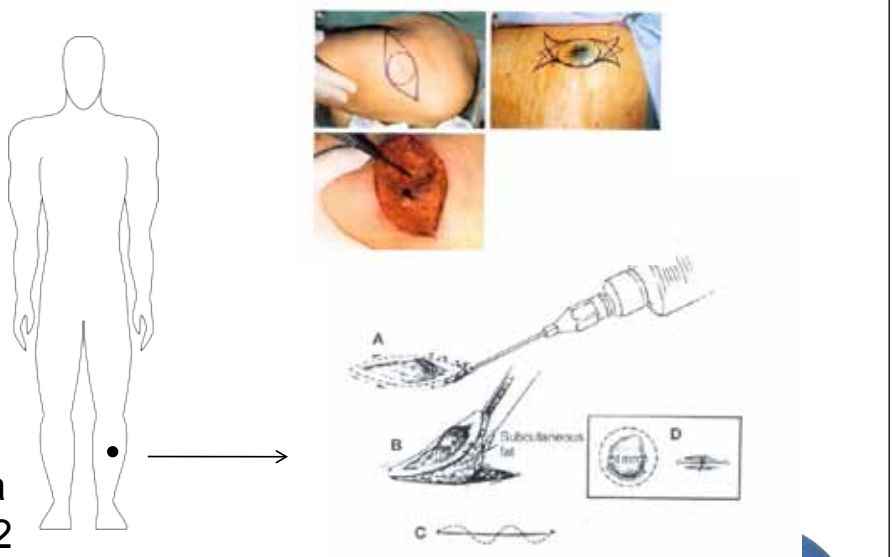


Primary Melanoma -stage 1&2

MELBOURNE MELANOMA PROJECT

The melanoma journey- tissue is essential to understand why

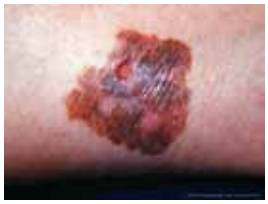


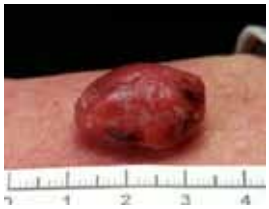


Primary Melanoma -stage 1&2

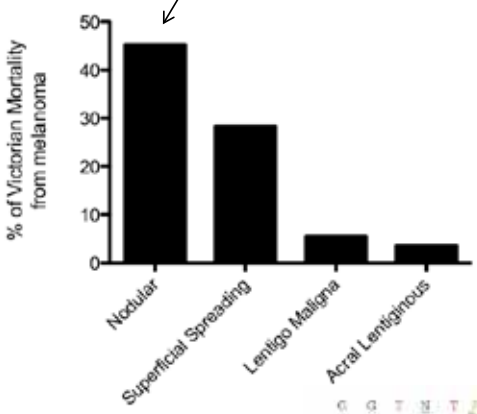
MELBOURNE MELANOMA PROJECT

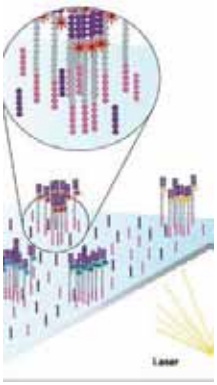
Research on primary melanoma

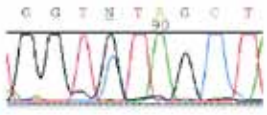




Only 8.5% of melanomas

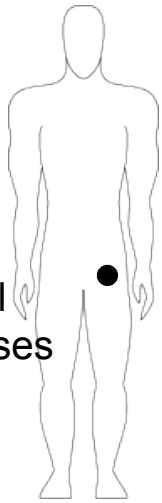




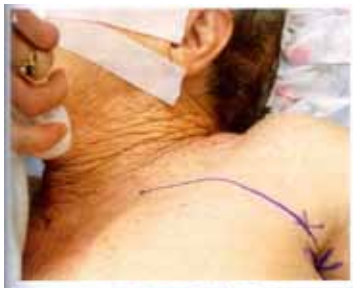


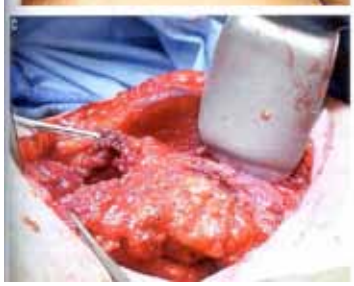
MELBOURNE MELANOMA PROJECT

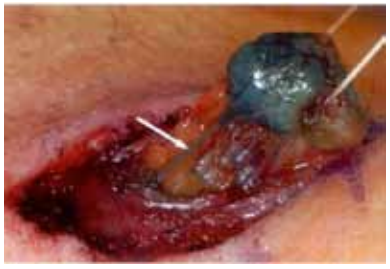
The melanoma journey- tissue is essential to understand why



Regional Metastases -stage 3



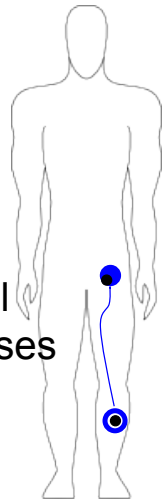




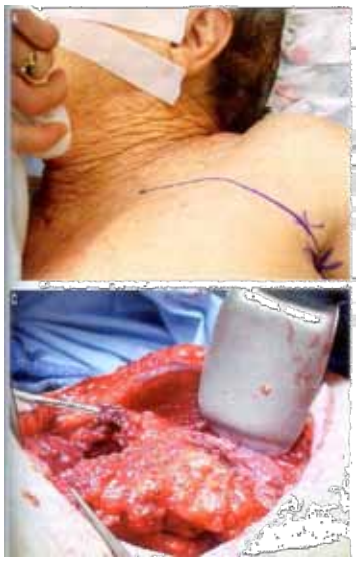
MELBOURNE MELANOMA PROJECT

Balch et al – Cutaneous Melanoma, QMP, 2009

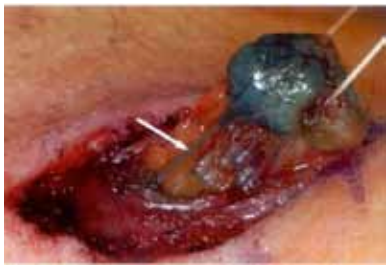
The melanoma journey- tissue is essential to understand why



Regional Metastases -stage 3



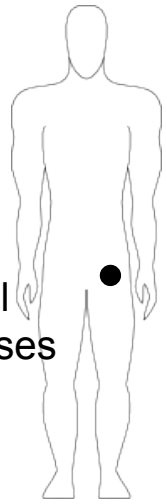
Sentinel Lymph Node Biopsy



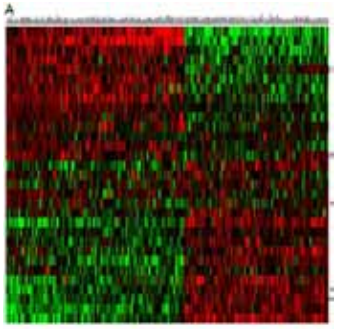
Balch et al – Cutaneous Melanoma, QMP, 2009

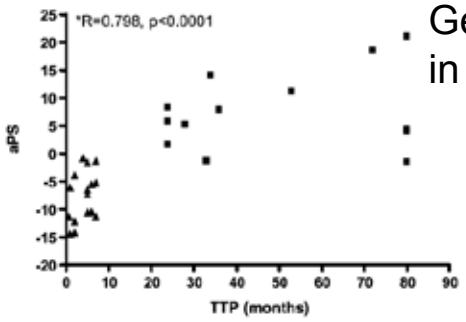
MELBOURNE MELANOMA PROJECT

Research on Regional Melanoma



Regional Metastases -stage 3



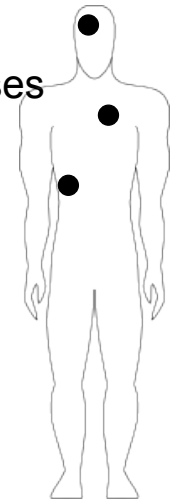


Genes involved in immunity

MELBOURNE MELANOMA PROJECT

The melanoma journey- tissue is essential to understand why

Distant Metastases -stage 4



Balch et al – Cutaneous Melanoma, QMP, 2009

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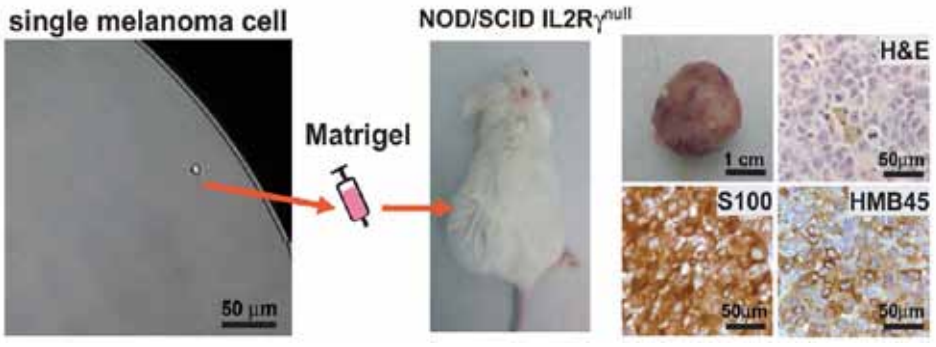
Research on Distant Metastases



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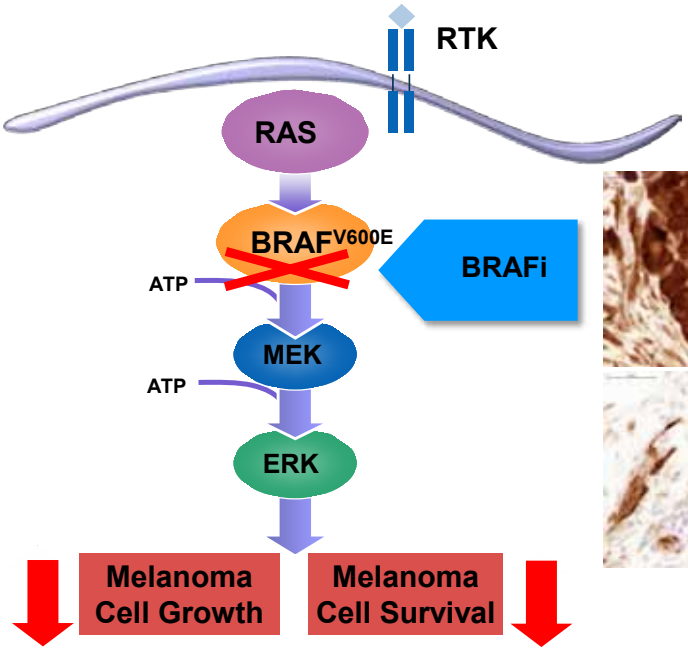
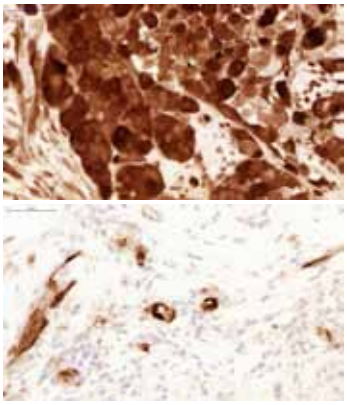
Understanding how BRAF inhibitors work



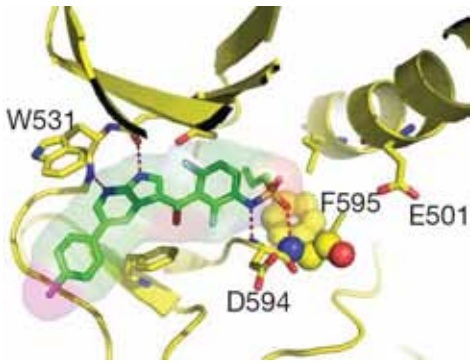


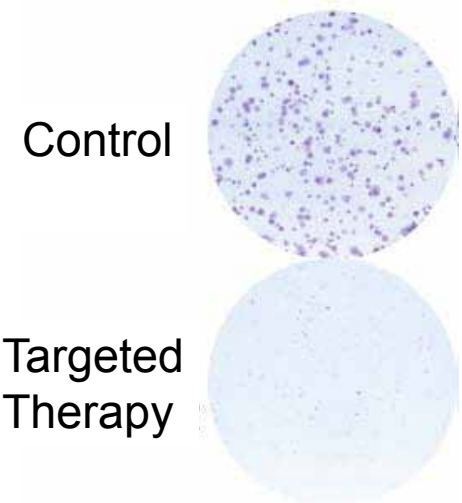
BRAF On

BRAF Off

MELBOURNE MELANOMA PROJECT

Targeting Melanoma- BRAF



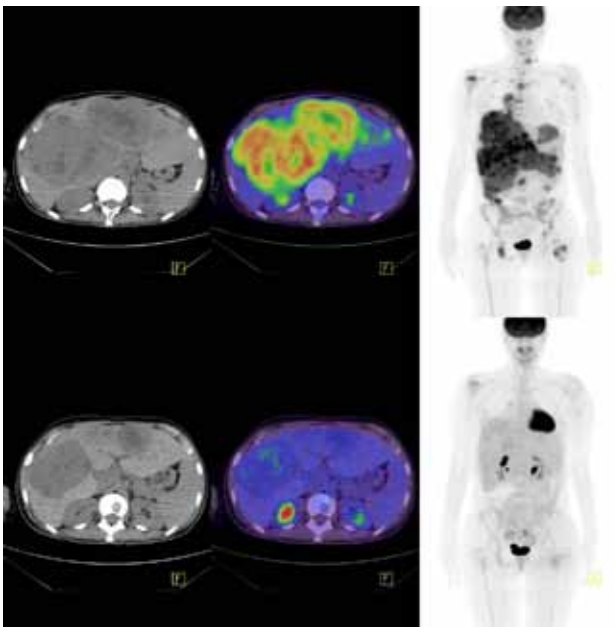


MELBOURNE MELANOMA PROJECT

Turning off the genes driving melanoma- BRAF

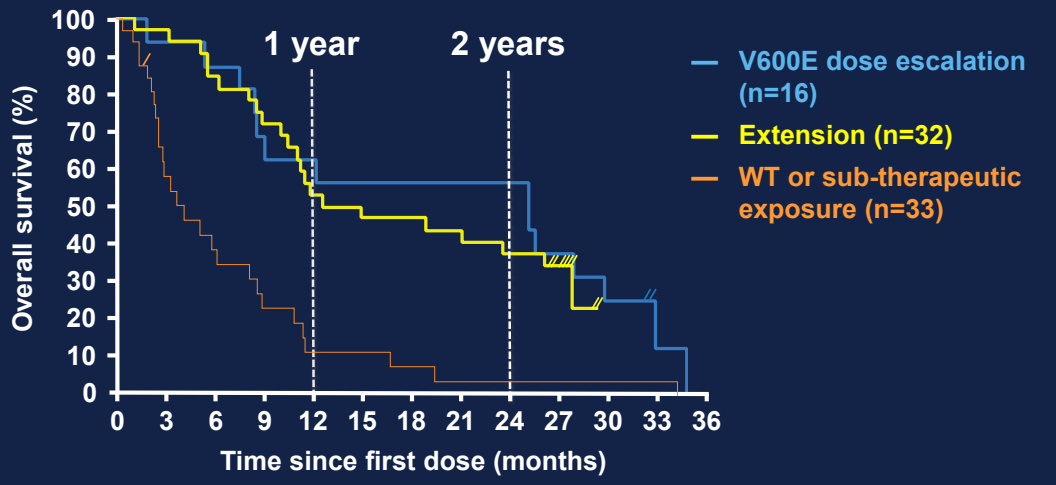
Baseline

2 weeks of Targeted Therapy with BRAF Inhibitor



McArthur et al, Journal of Clinical Oncology 2012

Vemurafenib phase I overall survival: Updated KM estimates (Aug. 2011)

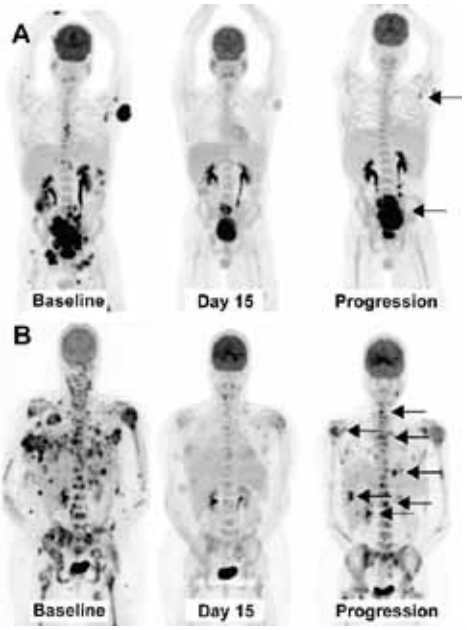


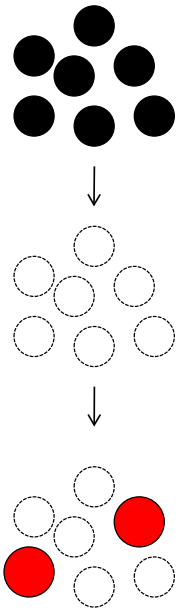
Median OS (month)	
Dose escalation	25.2
Extension	13.8
WT or sub-therapeutic.	4.18

Extension cohort landmark
Estimated survival: 1 year = 50%, 2 years = 38%

McArthur et al, ESMO, 2011

Research and more clinical trials are vital





Baseline

Response

NRAS Mutation

Progression

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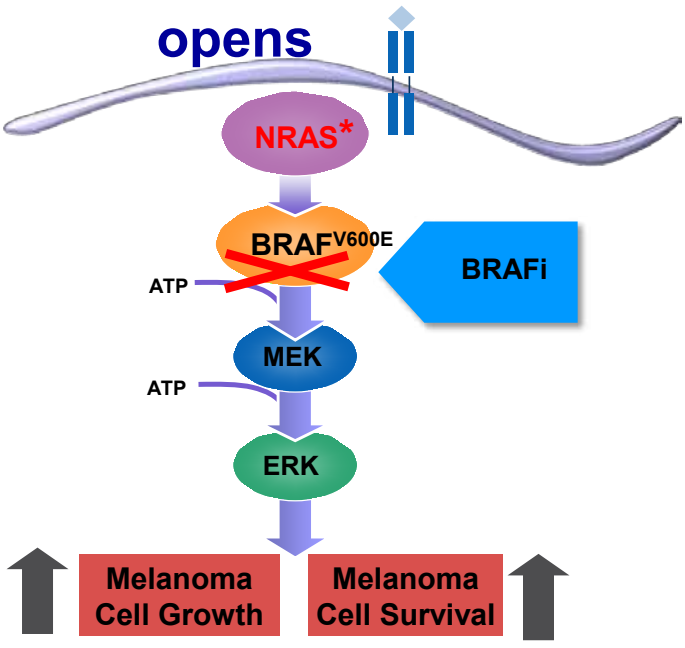
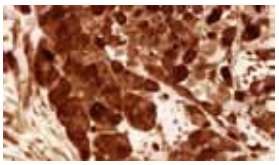
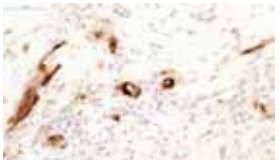
Mechanisms of Resistance to BRAF Inhibition – Biochemistry opens new doors





BRAF On



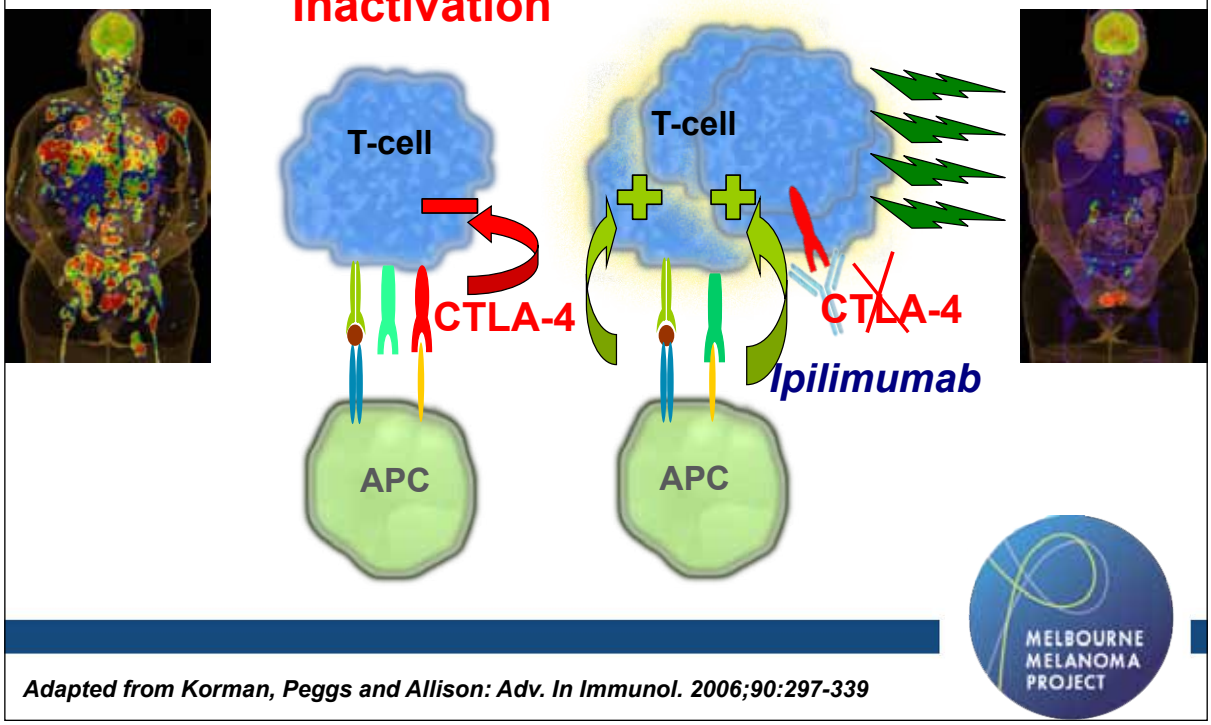
BRAF Off

BRAF On

Poulikakos….Rosen, Nature 2010; Nazarian…..Lo, Nature 2010

MELBOURNE MELANOMA PROJECT

Unlocking the Immune system –targeting CTLA4



Adapted from Korman, Peggs and Allison: Adv. In Immunol. 2006;90:297-339

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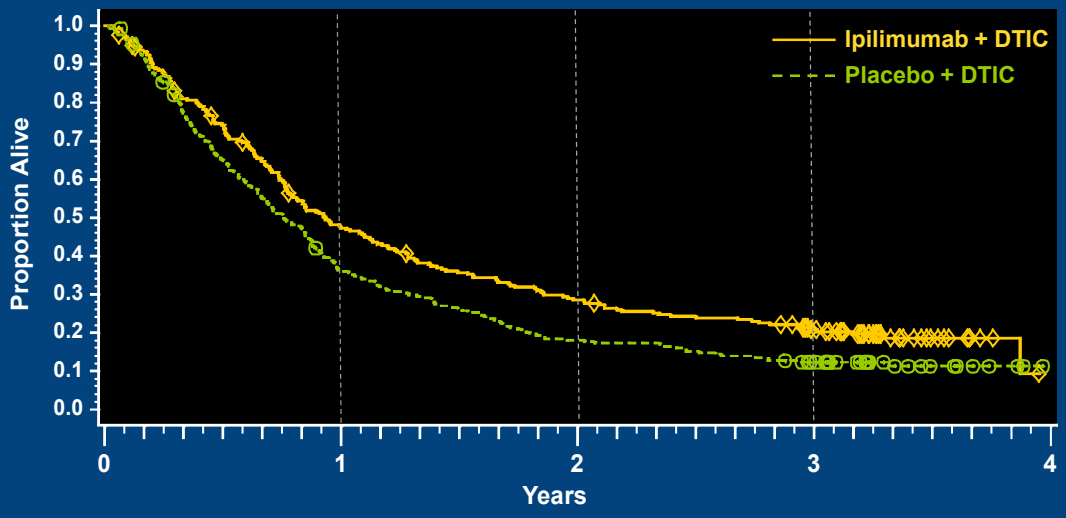
Study 024: Overall Survival



Estimated Survival Rate	1 Year	2 Year	3 Year*
Ipilimumab + DTIC n=250	47.3	28.5	20.8
Placebo + DTIC n=252	36.3	17.9	12.2

*3-year survival was a post-hoc analysis

PRESENTED AT: ASCO Annual '11 Meeting

Wolchok et al, ASCO 2011

29

Melanoma- making advances

Prevention

Early Detection

Improved Treatment

Melanoma- making advances

Team Approach

A Global Coordinated Approach

-Community
-Scientists/Health Care professionals
-Industry
-Government

Appendix 3:
Speech from Ms Valerie Guild

Valerie Guild serves as the President of the AIM at Melanoma Foundation, the largest international melanoma organisation focused on melanoma research, education, awareness, and legislation. She holds an MBA and an MS in Education. After spending 25 years in the private sector, Valerie started working in the area of melanoma advocacy in 2003 after the death of her daughter from melanoma.

My daughter Charlie died of melanoma at the age of 26. In an attempt to try to understand what I could possibly contribute, I spent the year after her death traveling around the US, interviewing melanoma researchers, clinicians, industry people, and advocates from other cancer areas.

I came away from that experience realizing that one of the great unmet needs in the world of melanoma was the lack of fresh frozen primary and metastatic tissue. That was almost 8 years ago. I can say that in the year 2012 the need for fresh frozen tissue is as great as ever.

The goal of AIM has been to launch a primary melanoma tissue bank, and I would like to speak today to the challenges we have faced and how we have chosen to deal with them,

Although we are certainly not there yet, as a by product of that work, under the auspices of the International Melanoma Working Group, a think tank launched by AIM, of which Grant McArthur is a founding member, we will soon launch a brain mets bank, with Australia as one of the partners. The size and scope of that bank will greatly depend on further funding.

But back to lessons learned. I would say that there are four major issues anyone attempting to create a repository for a rare cancer needs to be cognizant of, and they are consenting, collection, collaboration, and cash.

Consenting seems to be the one area that the US has handled relatively successfully. When queried most people who oversee biobanks say that in their experience patients hardly ever object to having their tissues used for research, and that most patients want their disease experience to benefit someone else.

In the US all of the cooperative cancer groups have made biobanking consents a standard part of the protocol for almost all cooperative group trials.

As well, it is also common practice at large hospitals that are engaged in research to include a biobanking consent for all newly admitted patients.

These consents tend to be very broad, with patients giving blanket permission for their specimens to be used for unspecified research by unspecified researchers.

The next area that needs to be addressed is collection, and here the issues are threefold; the actual logistics, quality control, and exactly what should be collected. Although many of these are the same for all types of tissue I'm going to focus on the primary.

The logistical problem is of course that most primaries are not removed in a hospital surgical setting but in a private practice office, in the US that typically means the dermatologist's office.

It is simply impractical to expect a dermatologist in this setting will be willing, or has the ability. to consent, draw blood, get urine samples, take a full medical history and temporarily store the excised tissue, so in our model we are using only dermatologists at large institutions or their affiliated hospitals.

Each of these institutions will have a dedicated trained biobank person on call to perform all of these activities once it is determined that there is a patient In the dermatologist's office with a suspicious lesion. After the primary is excised and put into the solution of choice, the biobank person will assure that it is immediately brought to the location where it can be flash frozen and stored.

We have also chosen to use this model because the second area of concern in collection is guaranteeing that all of

the tissue collected is of the highest quality. Participating institutions have agreed to abide by the guidelines agreed upon for sample documentation, collection, processing, storage and retrieval. As well, all sites will bei audited on a regular basis by an external organization.

Lastly, we believe that both clinical and laboratory data are crucial to this process, as well as prospectively tracking patient outcomes. Our goal is a fully annotated bank with all participating institutions entering the same data in the same way for each patient.

The area of collaboration is a difficult one. We all understand that in orphan diseases such as melanoma no one institution is able to collect enough tissue for their own research, much less for the research community at large. Yet I can tell you that it was a challenge finding primary investigators who were willing to commit to pooling their tissue, even though that clearly offered them the only way of acquiring the steady stream of tissue needed for their own projects.

When I broadened that request and also asked that once their own need for tissue was satisfied, that they allow the bank to be opened to outside researchers who would have to meet stringent criteria, the takers became even fewer.

Clearly, there is no easy solution for this lack of collaboration, and luckily I was able to find 4 dedicated melanoma department heads who understood the need and were as passionate, or more passionate than I, about making these scarce resources available to the research community at large.

And finally we talk about the cash, more discreetly known as the funding.

I would like to tell you that by educating gov't and private funding agencies about the importance and benefits of biobanking the money will flow in. I can only speak of my own experience. In the US, gov't research grants and the vast majority of private foundation grants specifically exclude the funding of infrastructure.

Industry is only willing, when it is willing at all, to fund the collection of tissue for it's specific trial or therapy.

Yet there are tissue banks in the US for rare cancers such as multiple myeloma and inflammatory breast cancer, and they have been funded and overseen by patient advocacy groups. As opposed to those bank housed in large-scale, clinical research centers, the ones under the auspices of advocacy groups are founded on the principle of sharing the tissue among the research community at large.

And taking it a step further, in the multiple myeloma model patients are encouraged to go to a participating center in order to have their scheduled bone marrow aspirate and blood draw. They now have 2700 samples in their bank and 17 participating centers.

And, as an aside, they have become the premier industry source for fresh tissue samples, which benefits the patients and also offsets the cost of maintaining the bank.

If I am heartened by anything, it is the fact that I was invited last week to speak on tissue banking at a European patient meeting in Brussels, and I am here today in Melbourne speaking on that self-same topic.

Patients and their families are beginning to connect the now popular topics of biomarkers and personalized medicine, to the need for tissue.

I am flying back tomorrow to be in Chicago for a large fundraiser we are holding for our "National Melanoma Tissue Bank". We have cultivated and educated over 200 families during this past year about the need for a repository and we will see on Thur. how successful we have been.

Our hope is that once this bank is launched in the US the next step will be collaborations, through the IMWG, with Australia and Europe. Since these are virtual banks at the very least we should be able to share our bioinformatics, and at best, our tissue, in pursuit of a better tomorrow for melanoma patients worldwide.

All I can say is stay tuned.

Appendix 4:
Panel facilitator's notes: Dr Mark Shackleton

GENERAL ISSUES

1. **Expectations of what happens to tissue:**
   - Consumer perspective - future use for my own care?
     - – Is it needed – what contexts?
     - – How much is needed?
     - – What happens to the rest?
   - Other expectations?
2. **Is there a 'duty' of contributing tissue to research?**
   - Whose duty is this?
     - – consumer, clinician, pathologist, researcher
   - Should contribution default be 'opt-in' rather than 'opt-out'?
3. **If a consumer wants to donate tissue, how does he/she do it?**
   - Is this a relevant question?
   - Do consumers want to be involved?
   - What are the barriers?
4. **What should be stored with the tissue?**
   - matched normal tissue, other clinical data, family history
5. **Who owns tissue that is stored for clinical care or research?**
6. **Who should look after tissue and clinical data that is stored for research?**
   - consumers, pathology services, research resources (e.g. Biobanks)
7. **Who should pay for tissue and data collection and storage?**
   - Researchers, consumers
   - What does it cost – per sample?
8. **Who should have a say in how tissues are used?**
   - consumers, researchers, ethics committees

RESEARCHER WANTS SOME STAGE 1/2 MELANOMA TISSUE FOR A PROJECT

1. **What sort of research requires such tissue?**
2. **How does human tissue actually help the research? What about other models?**
3. **Where is such tissue usually available? sources**
4. **What are the current limitations for a researcher in obtaining such tissue?**
   - supply – no. of samples made available
     – GPs, dermatologists, surgeons, pathologists
   - processing procedures – fresh, formalin
   - amounts per sample that are made available
     – pathologists
     – what criteria determine how much is offered
   - logistical – timeliness
   - administrative – ethics
   - cost
   - quality of annotation
   - availability of matched normal tissue

RESEARCHER WANTS SOME STAGE 3 MELANOMA TISSUE FOR A PROJECT

5. **What sort of research requires such tissue?**
6. **Limitations?**

RESEARCHER WANTS SOME STAGE 4 MELANOMA TISSUE FOR A PROJECT

7. **What sort of research requires such tissue?**
8. **Limitations?**

SUMMARY/COMMENTARY FROM DR MARK SHACKLETON:

- Widespread agreement on the primacy of consideration of patient welfare in protocols to collect tumor tissue for research

– Recognition that in the foreseeable future, it will continue to be important to keep stored samples of melanoma tissue in order to perform future tests and review pathology information that could affect clinical management

- However, the reality is that in many cases the tissue that is removed from a patient is in excess of clinical requirements, even after consideration of future clinical requirements

– Obviously, the smaller the tumor – such as primary stage 1/2 melanomas – the less tissue that is left over in excess

- In the vast majority of cases, excess tissues are stored for at least several years, according to law, before being considered for discard - a wasted opportunity to provide resources for research

- Discussed the possibility of default 'opt-in' consent to donate tissue (i.e. to donate tissue, patients have to opt-out volitionally of consent), incorporated into routine clinical care, as exists in some academic centres in the US

– This could potentially be done at the point of initial dermatology/GP consultation for a pigmented lesion. May not be feasible as a widespread practice, however, could be targeted to 'high-yield' centres and individual practitioners who see a high proportion of cases. Although most pigmented lesions won't be melanomas, the resource would be very valuable of stored non-pigmented lesions and of the melanomas that were subsequently diagnosed.

- Need to raise awareness in the melanoma patient community of the importance of tissue banking. Indeed, possible role for consumers in facilitating melanoma tissue collection/storage efforts, including generating funding

- Importance of augmentation of tissue collection with links to other clinical data (diagnosis, pathology review, recurrences, treatment, etc.). Major potential role in this for electronic medical recording. Role for consumers to lobby government/bureaucracy regarding this.

- Funding of tissue banking is a challenge, currently mostly supported by limited-term government grants and community fundraising. As above, there is a major opportunity for consumers to help meet the challenges of funding core infrastructure projects, such as tissue banking, that are essential for supporting research.

- Major limitation to melanoma research is the supply of adequate amounts of tissue. One reason for this is that many primary melanomas are small and not much tissue can be spared without compromising clinical care of the patient in question.

– However, another reason is that, even when tissue samples are big enough so as to provide spare material for research, enthusiasm and expertise is usually lacking from pathologists to ensure that the tissue provided is of adequate amount and quality. At the core of this problem is the inadequate pathology workforce that currently exists. On multiple levels, chronic understaffing by specialist pathologists in public hospitals is a major impediment to medical research. The central role needs to be recognized that is played by pathologists not only in diagnosing diseases such as cancer, but in developing research infrastructure and in contributing directly to research efforts and the discovery of new treatments. Lobbying by consumer advocates to health bureaucracy of the need to reimbursement and supply of pathology services is recommended.

Appendix 5: Tissue is the Issue

A forum to investigate the challenges of melanoma tissue collection for research

This document is authored by xxx Mark Shakleton

SESSION – PANEL AND AUDIENCE DISCUSSION

Session Lead: Dr Mark Shackleton

Expert Panel
- Grant McArthur
- Valerie Guild
- Victoria Mar
- Margaret Otlowski
- Leanne Bowes
- Clinton Heal
- Bill McHugh
- Richard Scolyer
- Anne Thompson

Researchers
- Tom Kaye
- Stephen Wong
- Clare Fedele
- Grant McArthur

Dermatologists
- John Kelly
- Victoria Mar

Pathologists
- Catriona McLean
- Richard Scolyer
- Stephen Fox
- Anthony Bell
- Rosemary Savino (manager)

Private Path
- Joanne Mercuri
- John Dunn

Legal/Ethics
- Margaret Otlowski

HREC
- Wayne Phillips
- Anne Spence
- Brian Loughran

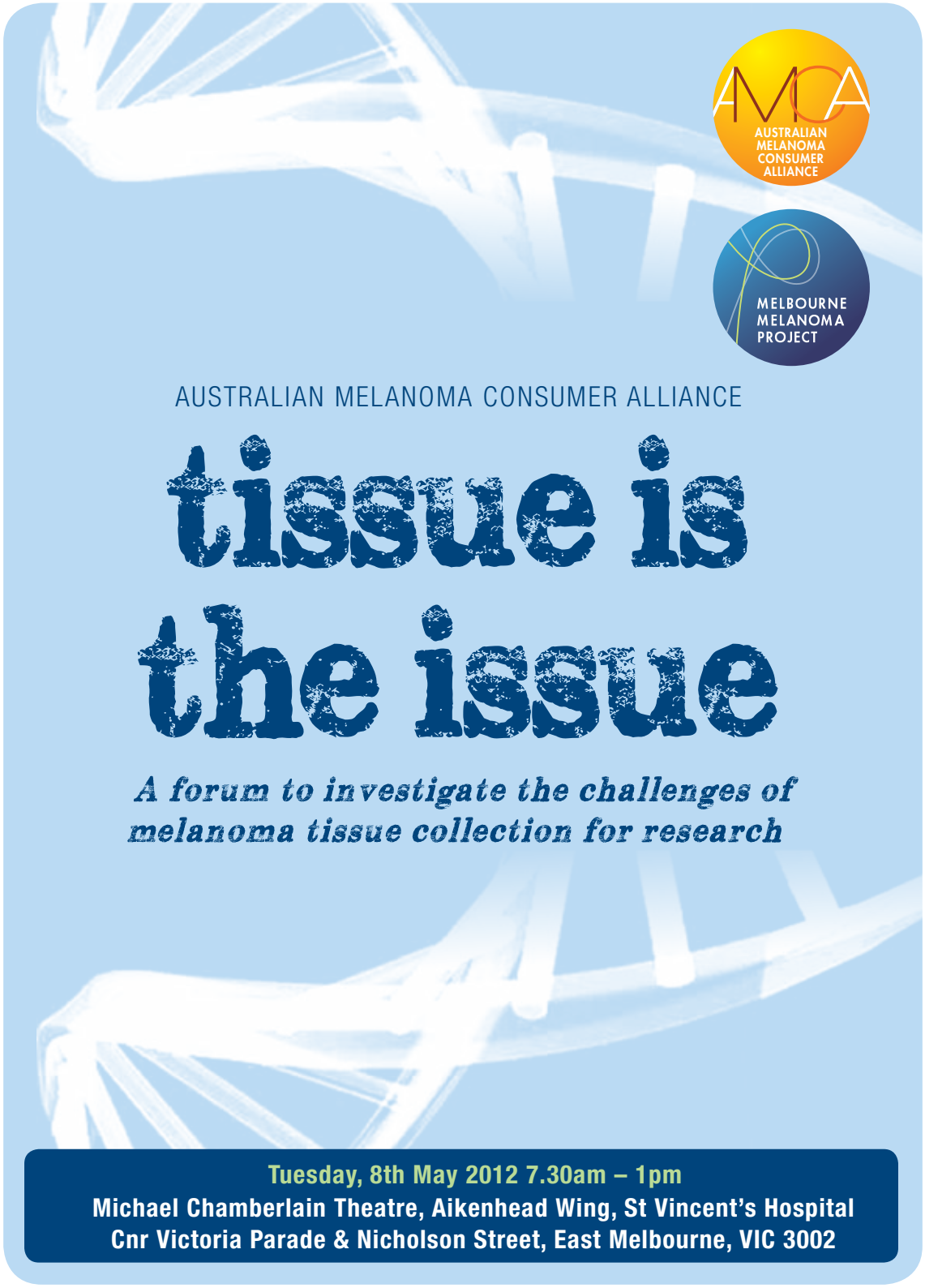
Biobank
- Anne Thompson
- Lisa Devereaux
- Laura Galletta
- Leanne Bowes

MMP
- Maxine Cooper
- Lois Whiteoak

Consumer Advocacy/Lobby
- Ian Roos (Cancer Voices)
- Jay Allen (MIA)
- Clinton Heal
- Bill McHugh
- Valerie Guild

Appendix 6:

'THE HEART OF THE MATTER IS UNDERSTANDING WHY TISSUE IS IMPORTANT'



Foreword

This Tissue is the Issue conference is an initiative of the Australian Melanoma Consumer Alliance (AMCA) which also incorporates the Melbourne Melanoma Project Consumer Reference Group (MMP CRG). Both these groups and their histories are explained in detail further below.

On behalf of the Melbourne Melanoma Project (MMP) it is with pride that from small beginnings, the AMCA with the support of the wider research community have been able to bring to the fore, one of the most important issues facing medical research into melanoma and for that matter any similar type of disease.

This issue is the collection, availability and sharing of information derived from tissue.

We are honoured to be holding this inaugural "Tissue is the Issue" conference and have an internationally respected melanoma consumer representative participating from the United States, being Ms Valerie Guild.

We are also most grateful to have one of Australia's leading Plaintiff Lawyers, Mr Peter Gordon, to host and facilitate our panel discussion.

Further, such strong participation and representation across researchers, pathologist, consumers, doctors, dermatologist, surgeons, oncologists, ethicists, lawyers, nurses and carers is further validation of the need to discuss these issues and find solutions, to provide timely, cost effective melanoma tissue collection and sharing of tissue information.

On behalf of the MMP and the AMCA (incorporating the MMP CRG), it is with pleasure that we bring you "the Tissue is the Issue inaugural conference".

Professor Grant McArthur

Lead Investigator, MMP

Campbell Rose

Founder AMCA (incorporating the MMP CRG)

Purpose

When melanoma is diagnosed at an early stage, surgical resection of the tumour with a wide and deep margin has a favourable cure rate. However, when melanoma progresses to deep invasion into the skin or presents after it has spread, the prognosis is much worse and risk of death from the disease high.

In pursuit of a cure for melanoma, research and translational studies require access to large numbers of melanoma tissue samples from patients, with their associated clinical information to permit discovery and validation of the findings discovered in the laboratory.

This forum is being driven by current and former patients of melanoma (which we refer to ourselves as "consumers") to identify the barriers that are currently preventing the collection of Melanoma tissue for research. The forum will explore ways of overcoming these barriers and examine the benefits of using tissue samples for research purposes.

With Australia experiencing one of the highest incidences of Melanoma in the world, we have a responsibility to use the best possible practice in researching into this insidious disease.

Supporters of this Forum include surgeons, physicians and their assistants, nurses, pathologist, dermatologists, oncologists, health care educators, public health professionals, research scientists, medical students, melanoma patients, their friends and families.

We believe that by bringing this collection of specialists together to share the input from renowned guest speakers, we will be in a better position to progress research outcomes for Melanoma sufferers into the future.

The results of the Forum will identify both Melanoma specific barriers to tissue collection and further actions for the AMCA to pursue in partnership with the health profession and all levels of Government.

Anticipated Conference Outcomes

RAISE AWARENESS OF PATIENTS CONCERNS

Raise awareness to all healthcare professionals (pathologists, surgeons, researchers, ethics, dermatologists, clinicians, allied health and legislators) of patient preference and desire for 'their tissue' to be more readily available for research purposes.

STAKEHOLDER ENGAGEMENT

Seek the engagement of healthcare professionals in acknowledging consumer rights and preferences for tissue donation.

REMOVAL OF BARRIERS

Establish an initiative to remove any structural, legal and or legislative barriers to efficient and cost effect tissue collection, storage and release, for research purposes.

CONTINUATION OF COLLABORATION

This Forum is only the first step in the journey and not the arrival at a destination. Therefore AMCA invites national participation to an ongoing process to address the issue of tissue availability for research.

The Australian Melanoma Consumer Alliance (AMCA)

The Australian Melanoma Consumer Alliance (AMCA) was spawned from the initial work of the Melbourne Melanoma Project (MMP) research requirements whereby MMP researchers had established a Consumer Reference Group in order to be well informed by consumer input. This is explained in more detail below.

As a result of the success of the MMP Consumer Reference Group (CRG) a national approach became a natural evolution. Given the nature of melanoma and the various other organisations that are involved and engaged with the disease at various levels of patient and consumers, the MMP CRG evolved into an organisation with representation and input from a number of other consumer based forums and organisations around Australia. This resulted in the progression of the MMP CRG having representation from various organisations that weren't geographically or regionally based around Melbourne.

This led to the formation of the Australian Melanoma Consumer Alliance incorporating the MMP CRG

In this way, the AMCA was able to fulfil the initial requirements of the MMP to ensure that MMP Researchers were well informed with and by consumer input as well as enabling the AMCA to become a national voice on behalf of melanoma consumers providing an overall umbrella forum (alliance) for the individual support group organisations – those that currently exist, and those that could be still in the making.

Although the AMCA has no current legal structure or independent organisation, it operates as an association amongst individuals all of whom have been touched by melanoma and wish to, through co-operation, pooling of resources, knowledge and information, bring about an informed consumer approach into research and advocacy around the disease of melanoma in the hope of changing its course.

The AMCA is represented with individuals who have an interest in melanoma, those that have been touched by melanoma, carers and nurses who are involved with the disease. These interests are supplemented with representation from organisations around the country including; Melanoma Patients Australia (MPA), Melanoma Institute of Australia (MIA), Australia and New Zealand Trials Group (ANZMTG), Melbourne Melanoma Project (MMP) and Melanoma WA.

The AMCA (has only been in existence in this form for the past 12 months after previously operating as the MMP CRG for some two years.

The principal functions of the AMCA include:

- Representing the interests of consumers
- Advocating on behalf of consumers to ensure that their voice is heard by researchers, policy makers and governments
- Providing input on how consumers may think and feel about certain issues relating to melanoma research
- Contributing consumer experiences
- Ensuring the MMP recognises consumer concerns
- Establishing a protocol for consumer review of melanoma based research
- Contributing to and reviewing patient-oriented resources and tools for clinical trials occurring at MMP and other melanoma research sites.
- Contributing to and reviewing content for the MMP consumer website and e- bulletin
- Connecting with other consumer groups to ensure that information is appropriately disseminated.

Melbourne Melanoma Project

The Melbourne Melanoma Project (MMP) is committed to improving the diagnosis and early detection of melanoma and to offer focused treatments based on the latest research.

The Melbourne Melanoma Project is linking leading programs in melanoma research across Victoria to improve diagnosis and early detection, gain more accurate tools to predict outcome and target new melanoma therapies for the patients at most risk. Peter MacCallum Cancer Centre, Victorian Melanoma Service - Alfred Hospital and the Austin Hospital and Border are all MMP sites.

MMP collects clinical data from consenting patients attending the clinics and linking this information with the molecular analyses of melanoma tissue. This vital information is assisting MMP to develop and progress basic research and clinical trial programmes of new and upcoming therapies, in order to improve the outcomes for patients with melanoma.

A key initiative of MMP is the establishment of a Consumer Reference Group to ensure research programmes are developed with consumer consultation and research findings are shared with the wider community using a multi-faceted strategy. The Group regularly provides expert advice from a consumer's perspective on early research programmes for melanoma. The Tissue is the Issue forum is the first community event arranged by the MMP CRG, aimed at raising awareness on the value of consumer integration into research. Annual forums are planned for the future.

Programme

Tuesday, 8th May 2012 7.30am – 1pm

MC: **Campbell Rose, AMCA founder**
Facilitator: **Peter Gordon, Lawyer, Health Legal**

7.30am	*Registration and Breakfast*
8.15am	**Campbell Rose**: Welcome Message
8.30am	**Grant McArthur**: The Latest Advances in Melanoma
9.05am	**Valerie Guild**: The US Experience: Challenges and Opportunities for Tissue Donation
9.25am	*Morning Tea break*
9.40am	**Peter Gordon**: Panel Debate
11.10am	**Peter Gordon**: Open Discussion and Audience participation
12.10pm	**Peter Gordon**: Summation and Preliminary reflection
12.20pm	**Campbell Rose**: Closing Remarks
12.30-1pm	*Lunch and Networking*

Panel

LEANNE BOWES

Leanne has over ten years experience collecting tissue specimens from patient cohorts across a range of national research studies including Australian Ovarian Cancer Study and Australian Cancer Study and locally VCB. Based at Peter MacCallum Cancer Centre she is also a consumer representative for MMP/AMCA.

PETER GORDON

Internationally renowned Lawyer, Peter Gordon is best known for his work on numerous landmark cases including the first successful asbestos related cancer claim in Australia. Peter has worked at the cutting edge of mass tort and consumer class action litigation as well as residing on the Board of a number of not-for -profit organisations.

CLINTON HEAL

Clinton Heal is a melanoma survivor, and founder of MelanomaWA. As a result of his advocacy work in raising awareness of melanoma prevention and early intervention, he was appointed CEO of the Melanoma Cancer support Association WA,as well as the 2011 WA young Australian of the year.

VALERIE GUILD

Valerie Guild serves as the President of the AIM at Melanoma Foundation, the largest international melanoma organization focused on melanoma research, education, awareness, and legislation. She holds an MBA and an MS in Education. After spending 25 years in the private sector, Valerie started working in the area of melanoma advocacy in 2003 after the death of her daughter from melanoma.

VICTORIA MAR

Dr Victoria Mar is a Consultant Dermatologist at the Victorian Melanoma Service, Alfred Hospital and in private practice. She is undertaking a PhD in the clinical and molecular characteristics of nodular melanoma at Peter MacCallum, the Alfred and Department of Epidemiology and Preventive Medicine, Monash University. She is Honorary Secretary of the Victorian Faculty of the Australasian College of Dermatologists.

GRANT MCARTHUR

Professor McArthur holds a number of posts at Peter MacCallum Cancer Centre, Melbourne, Australia. He is head of the Medical oncology skin and Melanoma Clinical service, as well as head of Molecular oncology and translational research laboratories and head of the Cancer therapeutics programme. He is national and international study co-chair of a number of clinical trials and chapter leader on multidisciplinary care in the 2008 national guidelines for the Management of Melanoma. He has extensive experience in communicating issues on the management and prevention of melanoma to lay audiences.

BILL MCHUGH

Bill McHugh is a member of the Australian Melanoma Consumer Alliance and Melanoma Patients Australia. Bill has extensive experience representing consumer perspectives. He has held numerous positions with the Prostate Cancer Foundation of Australia leading on to consumer representation on Cancer Australia grants and Medical Services Advisory Committee (MSAC).

Panel

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Background Briefing Paper for Discussion

A SUMMARY OF THE ISSUES ASSOCIATED WITH MELANOMA RESEARCH

- Inadequate tissue - The diagnosis of melanoma is complex. Pathologists require almost the entire biopsy tissue from the original cancer for diagnosis and in the main, they do not have the resources to send any remaining tissue to tissue banks
- Limited facilities for tissue banking - Tissue banking is only supported through major hospitals. Many valuable samples are collected outside this structure, in particular private and regional settings.
- Infrastructure and sustainability - A number of activities and infrastructure critical to support a nationally coordinated approach to biobanking in cancer clinical trials are not currently funded or available.
- Lack of awareness within the broader community on the value of tissue donation - Much of this can be attributed to the lack of involvement of the consumer in decision making by the primary care giver and the specialist
- An inadequate supply of biospecimens that have been harvested and stored according to standard protocols – There is no co-ordination for collection of biospecimens using standard protocols and therefore it is difficult to compare many of these samples in research
- Consent Forms - Project specific consent forms which require trained personnel to administer them.
- Lack of Funds for Tissue Collection - Biobanks operate on a cost recovery structure. Significant proportion of translational research grants are used up for tissue collection and acquisition making less funds available for other needed research.

BENEFITS OF HAVING MORE TISSUE SAMPLES

An ample supply of high-quality biospecimens will make the following types of advances possible:

- The identification of specific proteins or other biomarkers associated with various stages or subtypes of individual cancers, which could lead to the development of new screening or diagnostic tests.
- The grouping of patients, based on biomarkers of their disease and their personal genetic characteristics, to receive the most appropriate, most effective, and least toxic treatments.
- The identification (and validation) of new ways to deliver drugs or other agents to cancer cells and to measure responses to treatment

REFERENCES

1. Guiding Principles associated with Tissue Donation and Tissue Banking

There are prudent constraints embodied in the overall approval processes for donating human biological materials (and the pertinent companion clinical data) destined for basic research and clinical research along with the storage and withdrawal of the tissue for approved research.

Observation: These constraints may constitute a limiting factor for the amount of biospecimen collected, banked and subsequently released for approved research.

a) Ethical Conduct in Human Research

The National Statement on Ethical Conduct in Human Research published in 2007 was produced to promote ethically sound human research. Fulfilment of its purpose requires that participants of the research be accorded the respect and protection that is due to them. The statement also involves the fostering of research that is of benefit to the community.

Specifically the National Statement is designed to clarify the responsibilities of:

– Institutions and researchers for the ethical design, conduct and dissemination of results of human research; and

– Review bodies in the ethical review of research.

The National Statement guides researchers with the aim that they meet their responsibilities to identify issues of ethics that arise in the design, review and conduct of human research, to deliberate about those ethical issues, and to justify decisions about them.

b) Ethics Committees in individual Health Care Institutions

These committees are charged with the responsibility to formally approve every individual research project conducted from within their individual organisations. Their role includes the responsibility to critically assess and approve the protocols that have already been approved by collaborating institutions that may receive tissue that has been removed from humans.

2. The Establishment, Management and Governance of BioBanks

Australian Guidelines have been derived for biobanks. These cover research merit and integrity, data usage and consent to the use of the stored data for research. They cover a wide range of data types and methodologies and common types of research using databanks, including epidemiology, pathology, genetics, social sciences and biospecimens.

In terms of the involvement of biobank personnel in the overall process for biobanking those individuals assist with obtaining informed participant consent, the collection of biospecimen from within operating theatres, preparation of the biospecimen for long term storage (along with pertinent patient history/data), its specific storage and, finally, management of requests for access to banked biospecimens.

Both incoming and outgoing protocols for biospecimen processing in themselves can constitute a limiting factor for the amount of biospecimen collected, banked and subsequently released for approved research.

BioBanks aim to recover costs through charging for material and data that they provide for research. The extent of cost recovery is understood to be totally inadequate for the continuing operation of the Biobank, and accordingly BioBanks need to be supported by institutional funding and or Government Grants via NHMRC. On the other hand, the cost to researchers for accessing this resource does present as a barrier that needs to be overcome.

3. Scientific Research and Clinical Trials

Scientific Research constitutes a critically important step in health care and the improvement of medical outcomes. The requirement for human biospecimens is often the next step following the integrated stages of desk research and laboratory research involving animals. Often researchers that have a requirement for human biospecimens do not have direct contact with potential donors of human biospecimen.

On the other hand Clinical Trials are carried out by clinicians who are in direct contact with patients. This relationship affords the clinicians with the opportunity for collecting biospecimens not only for the conduct of a specific trial but also for biobanking allowing use in other research.

4. Disease Clinical Stages with respect to Tissue Collection for Research

Primary melanoma – Stages 0, I and II

These tumours are most commonly removed by GPs or by health care professionals working in the field of melanoma and skin cancer monitoring. The excision protocol is well understood in relation to providing appropriate margins and the excised tissue is sent for pathologic diagnosis. Pathologists retain this tissue as per the legal requirement for professional service to the patient, as and when required.

It is unlikely, but not impossible, that tissue suitable for scientific research could be collected at this stage either at the time of the excision or from the pathologists for biobanking. Given the small amount of tissue obtained there are strict protocols for the attainment and methods of biobanking.

Later stage melanoma – Stages III and IV

Patients progressing to this stage of their melanoma journey are invariably in an established patient/specialist relationship where access to tissue for research has the best prospect for responsible tissue harvesting. For patients with stage III disease (regional lymph node involvement) removal of the involved tissue is the treatment of choice. Stage IV implies the disease has spread to distant organs. There are occasions when tissue is removed as treatment for the Stage IV disease. Tissue collection on those occasions is critically important for broader research requirements, particularly understanding changes that could occur in the cancer itself as it metastasises.

The best potential for harvesting biospecimen will occur where the treatment is provided in a hospital which has in-house pathology services, ethical approval for human tissue collection and proven successful working arrangements with established and networked Biobanks.

In practice, optimising the opportunities for biobanking that occurs in these situations still requires considerable coordination within the hospital for realisation of that goal.

5. Patient Initiation of BioResource Banking

At present there is no established awareness/protocol/opportunity for the individual with melanoma to initiate action for voluntary donation of human biological melanoma materials. Nor is there opportunity for individuals with melanoma to register interest in participating in clinical trials which are deemed to afford the best configuration for biospecimen donation and banking.

Perhaps this is where consumer initiatives could generate patient interest in increasing supply of biospecimen for research. Knowledge of relevant trials would potentially maximise the number of patients that might contribute tissue for research relevant to them or patients in the future.

To further assist with this type of research a register could be established for individuals to put themselves forward for consideration as candidates for clinical trials. That option would involve specific management protocols and processes for individuals to update their personal and treatment records on an annual basis. Perhaps this service could be provided by ANZMTG, a research group within the University of Sydney, funded by Cancer Australia, and a member of the Co-operative Trials Group of COSA.

6. A Protocol Worthy of Consideration

The protocol for Rapid Autopsy for specific procurement of metastatic cancer material already exists in the US. It is a valuable resource for molecular and clinical research.

In overview, patient consent to undergo a directed autopsy after death needs to be obtained while the patient is alive. Autopsies are undertaken specifically to document the distribution of metastases, characterize tumours, harvest fresh tumour and normal control tissues suitable for molecular examination and the establishment of cell lines.

The program requires a multidisciplinary team approach for both the autopsy and the tissue procurement on a round-the-clock basis.

7. Stages of melanoma

Stage 0	The Melanoma is in situ. The abnormal cells are confined to the epidermis and have not invaded.
Stage I	In Stage 1A, the tumour is thinner than 1.0 mm, the cells are slowly dividing and no ulceration is present. In Stage 1B tumours either have the same thickness with a faster dermal mitotic rate or ulceration, or are a bit thicker without ulceration. In Stage 1 there is no cancer in the lymphatic tissue or distant organs.
Stage II	This stage is divided into 3 groups – A, B, and C – based on thicker and/or ulcerated tumours. In Stage II there is no cancer in the lymphatic tissue or distant organs.
Stage III	In Stage III melanoma has spread to nearby lymphatic tissue. The clinical stage includes tumours of any size with lymphatic metastases. Pathologic staging divides tumours into 3 groups based on ulceration and the extent of growth into the lymphatic tissues.
Stage IV	The melanoma has spread to one or more distant sites. Stage IV includes all the a – c subcategories. Although not a criterion for Stage IV the main tumour is often thick.

Notes

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