

# EUROPE BIOBANK WEEK

SEPTEMBER 13-16, 2016  
VIENNA - AUSTRIA

**Heather Thorne: "CASCADE: A CANcer tiSsue Collection After DEath programme to improve our understanding of the progression from primary stage cancer to metastatic, treatment-resistant disease."**



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# CASCADE

A CAncer tiSsue Collection After DEath program to improve our understanding of the progression from primary stage cancer to metastatic, treatment-resistant disease.

Sub-title:

How we enhanced our bio-bank to facilitate research activity

Peter Mac 

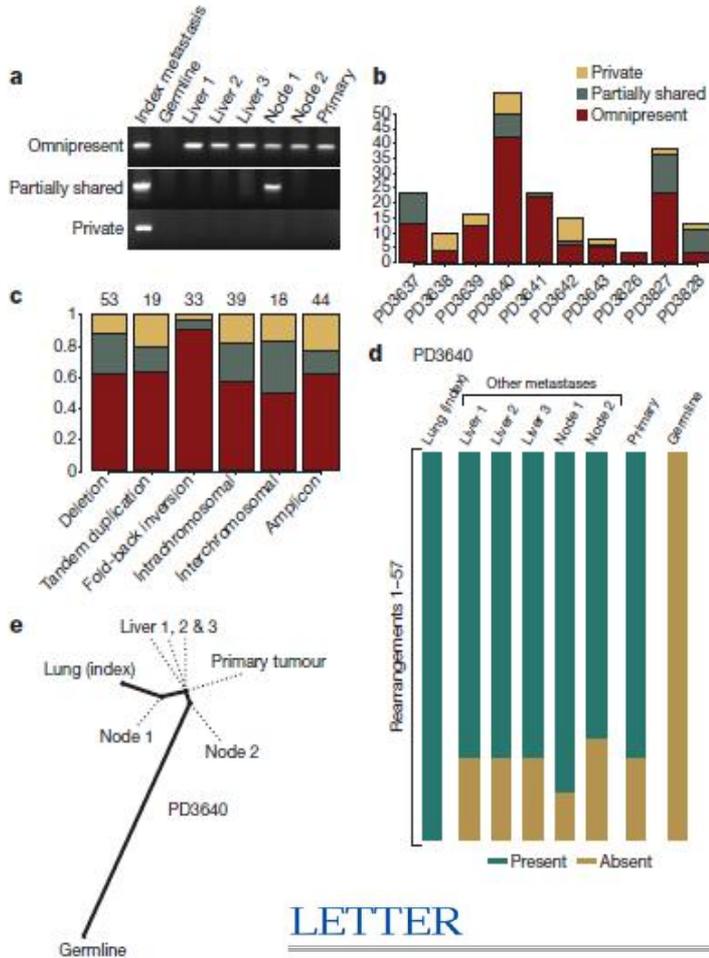
# Why study metastatic tissue?

- Systematic genomic studies, including The Cancer Genome Atlas (TCGA) and the International Cancer Genome Consortium (ICGC), have provided an unprecedented map of driver mutations in human cancer.
- These studies have overwhelmingly utilised primary tumour material, as this is the most common time of surgical intervention in the clinical management of cancer patients.

# Why study metastatic tissue?

- Most people with cancer die because of metastatic disease that is treatment resistant
- There is an urgent need to identify and characterise resistant mechanisms in order to understand how cancers can evade even the best cancer treatments and kill patients.
- By being able to study metastatic tissue we are hoping to be able to unlock some of the properties of tumours, including intra- and inter- tumoural genetic heterogeneity (ITH)
- We established the program CASCADE in September 2012: kConFab, AOCS and the Melbourne Melanoma Group.
- It is a 24/7 operation

# Why study metastatic tissue?



- There has recently been a few very elegant papers using deep sequencing to examine ITH, and the relationships of different metastases within a patient

- Investigators have been able to identify that different metastatic clones are present in different organs, as well as some genomic rearrangements that are common to many metastatic sites within a patient

- Evidence of selection and adaptation

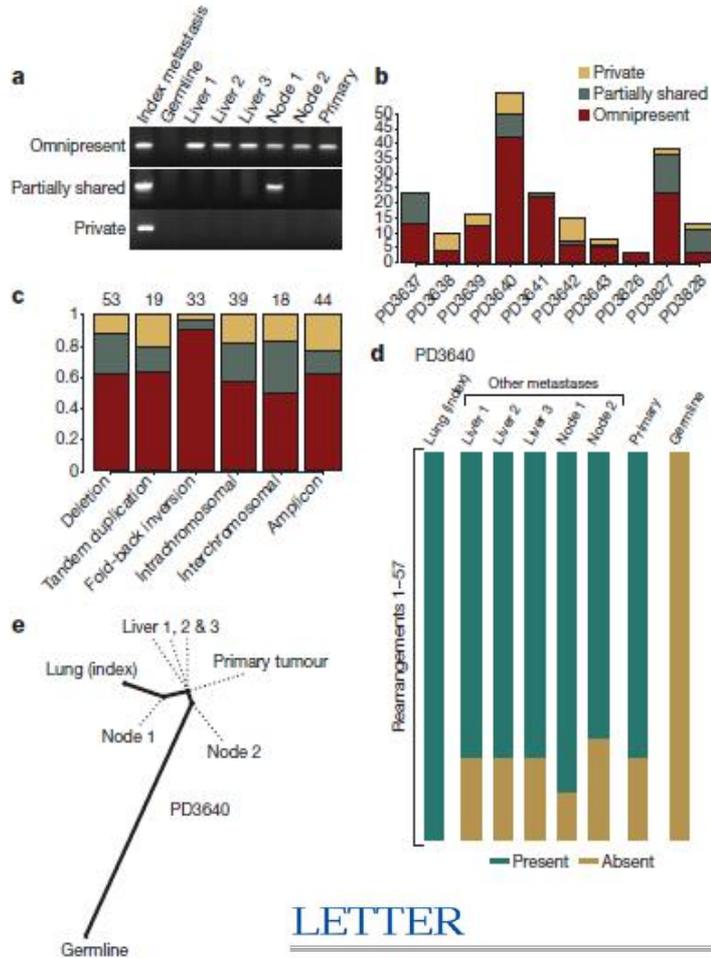
## LETTER

doi:10.1038/nature09460

### The patterns and dynamics of genomic instability in metastatic pancreatic cancer

Peter J. Campbell<sup>1,2\*</sup>, Shinichi Yachida<sup>3\*</sup>, Laura J. Mudie<sup>4</sup>, Philip J. Stephens<sup>5</sup>, Erin D. Pleasance<sup>6</sup>, Lucy A. Stebbings<sup>1</sup>, Laura A. Moraberg<sup>7</sup>, Gaili Lattimer<sup>8</sup>, Stuart McLaren<sup>9</sup>, Meng-Lay Lin<sup>1</sup>, David J. Mellor<sup>10</sup>, Ignacio Varela<sup>11</sup>, Serena A. Nik-Zainal<sup>1</sup>, Catherine Leroy<sup>12</sup>, Mingming Jia<sup>13</sup>, Andreu Munoz<sup>14</sup>, Adam J. Butler<sup>15</sup>, Jon W. Toogood<sup>16</sup>, Constance A. Griffin<sup>17</sup>, John Burnton<sup>18</sup>, Harold Swerdlow<sup>19</sup>, Michael A. Quail<sup>1</sup>, Michael R. Stratton<sup>1,4</sup>, Christine Iacobuzio-Donahue<sup>2</sup> & P. Andrew Futreal<sup>1</sup>

# Why study metastatic tissue?



- On a basic clinical level, treatment decisions in the relapse setting are often made on what we know about primary tumours.
- Understanding the development of resistance and treatment failure is the next critical step in the development of personalised medicine

## LETTER

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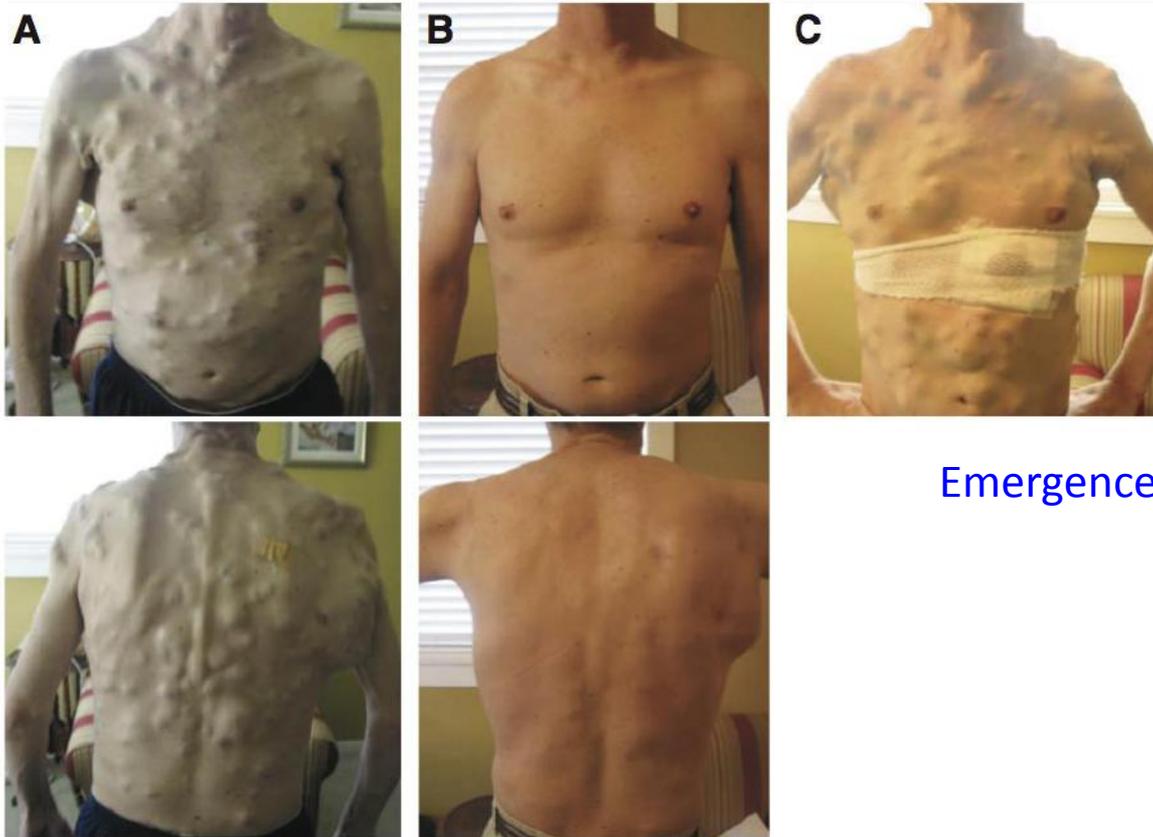
# Resistance to targeted therapies becoming a new clinical challenge



Prior to treatment

15 weeks after treatment: targeting of the BRAF kinase with Vemurafenib

# Resistance to targeted therapies becoming a new clinical challenge



Prior to treatment

15 weeks after treatment

# Benefits of a rapid autopsy program

- Patients with advanced disseminated disease are unlikely to undergo surgery as it is not routine clinical practice – CT/imaging
- Autopsies provide an opportunity to obtain a comprehensive survey of tumour deposits
  - Large amounts of material
  - Multiple locations – patterns of spread and determinants of growth in different organs
- Tumours from the same patient have a shared clonal origin, which reduces the background ‘noise’ that confounds comparisons of tumour genotypes from different patients.

**A O C S**

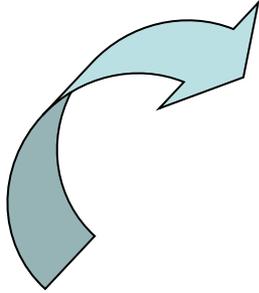
Australian Ovarian Cancer Study



**Patient Identification  
Clinician Driven**

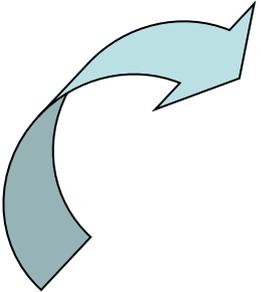
- Consent conversation can take place over a number of weeks
- Seek the consent of the patient to participate
- Consent Form asks for NOK witness who will be directly involved once the patient passes away
- Outlines the implications of the collection, but also the storage of biospecimens and data indefinitely for research purposes
- Full treat history is obtained

**Patient Identification  
Clinician Driven**

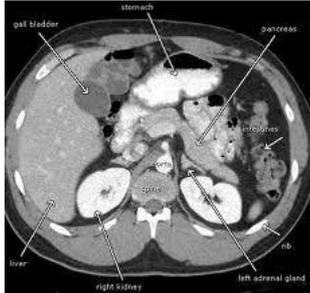
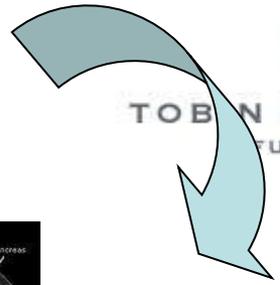


**Participant Follow Up**

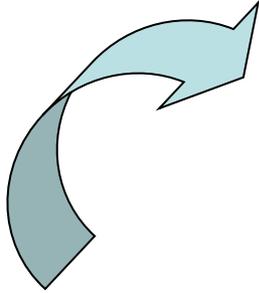
**Participant Follow Up**



**Patient Identification  
Clinician Driven**



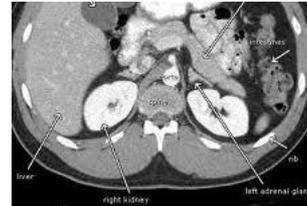
**Tissue Collection  
VIFM – 24/7**



## Participant Follow Up

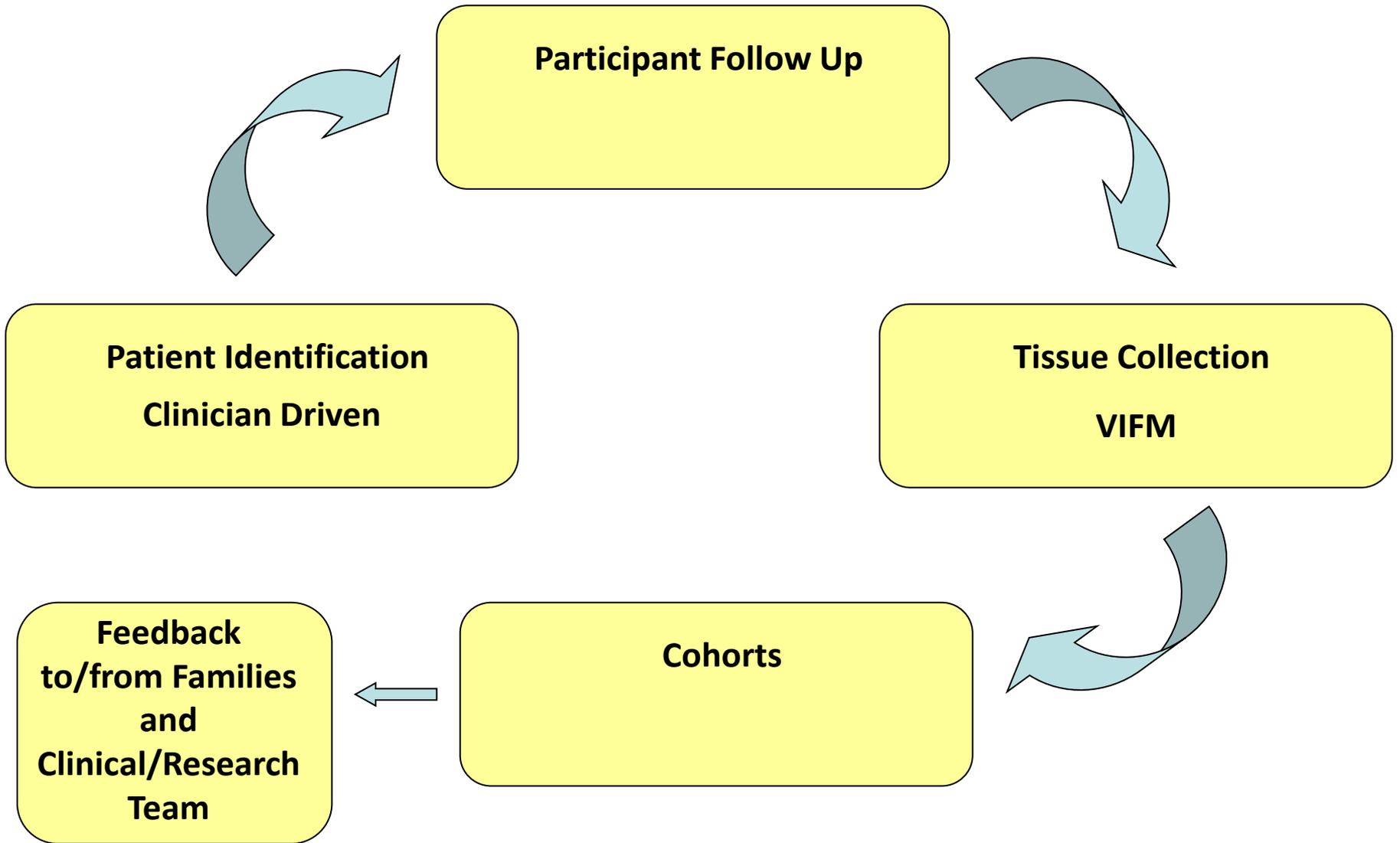
If at the time of death the family become distressed, and decide they do not want to participate, the NOK can make the decision at this stage to withdraw from the program

**Patient Identification  
Clinician Driven**



**Tissue Collection  
VIFM**

- **Priority Driven Collection - Fresh, Frozen, Formalin**
  - **Tissue Collection within 4 - 6 hours**
    - **PDXs established**
- **Every tissue collected is logged: time, tissue type with exact location , pictures.**
  - **A variety of QA performed on all aliquots: DAN/RNA, IHC**
    - **Full histology report available to researchers**



# Overall Overview

Cohort	Primary Tumour	Approached	Accepted	Complete
	Ovarian	17	12	12
	Breast Prostate Sarcoma	8 2 1	8 2 1	8
	Melanoma	19	12	12
Sporadic Prostate	-	7	7	7
Lung	-	1	1	1
		<b>55</b>	<b>42</b>	<b>40</b>

# Tissue Collection Details

		%
<b>Number of Collections</b>	<b>40</b>	
<b>Days Enrolled</b>		
Median	30.5	
Range	0.5 – 380	
<b>Place of Death</b>		
Home	12	30.0%
Hospice	16	40.0%
Hospital	12	30.0%
<b>Hours between Death and Collection</b>		
Median	6.25	
Range	3 - 12	
<b>Number of Sites sampled</b>		
Median	16	
Range	4 – 26	

# Conclusion:

A small number of patients have provided unparalleled insight into the timing and pattern of disease progression, metastatic spread and polyclonal seeding e.g. genomic studies have shown how minor clones found in primary tumours can dominate disease progression and ultimately lead to death

Many of the CASCADE participants and their families have expressed a gratefulness to have the opportunity to participate in such a program. Can help to provide meaning at the end of life for the patient and their families

**A community based model of rapid autopsy in end stage cancer patients. *Kathryn Alsop, Heather Thorne, et al***  
***Publication, Nature Biotechnology, Today.***

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Lisa Devereux

Chris Angel

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All Pathologists and Staff

**Tobin Brothers Funerals**

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