GCIG Translational Research Committee

Thursday 30th May 2013

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Agenda

- Patient derived xenografts – Clare Scott (ANZGOG)
- Tumour heterogeneity – Jessica McAlpine (NCIC)
- Digital droplet PCR – Paul Speiser (AGO-Austria)
- Co-ordination of complex samples - McNeish
- Peace and Harmony – Natalie LeFur

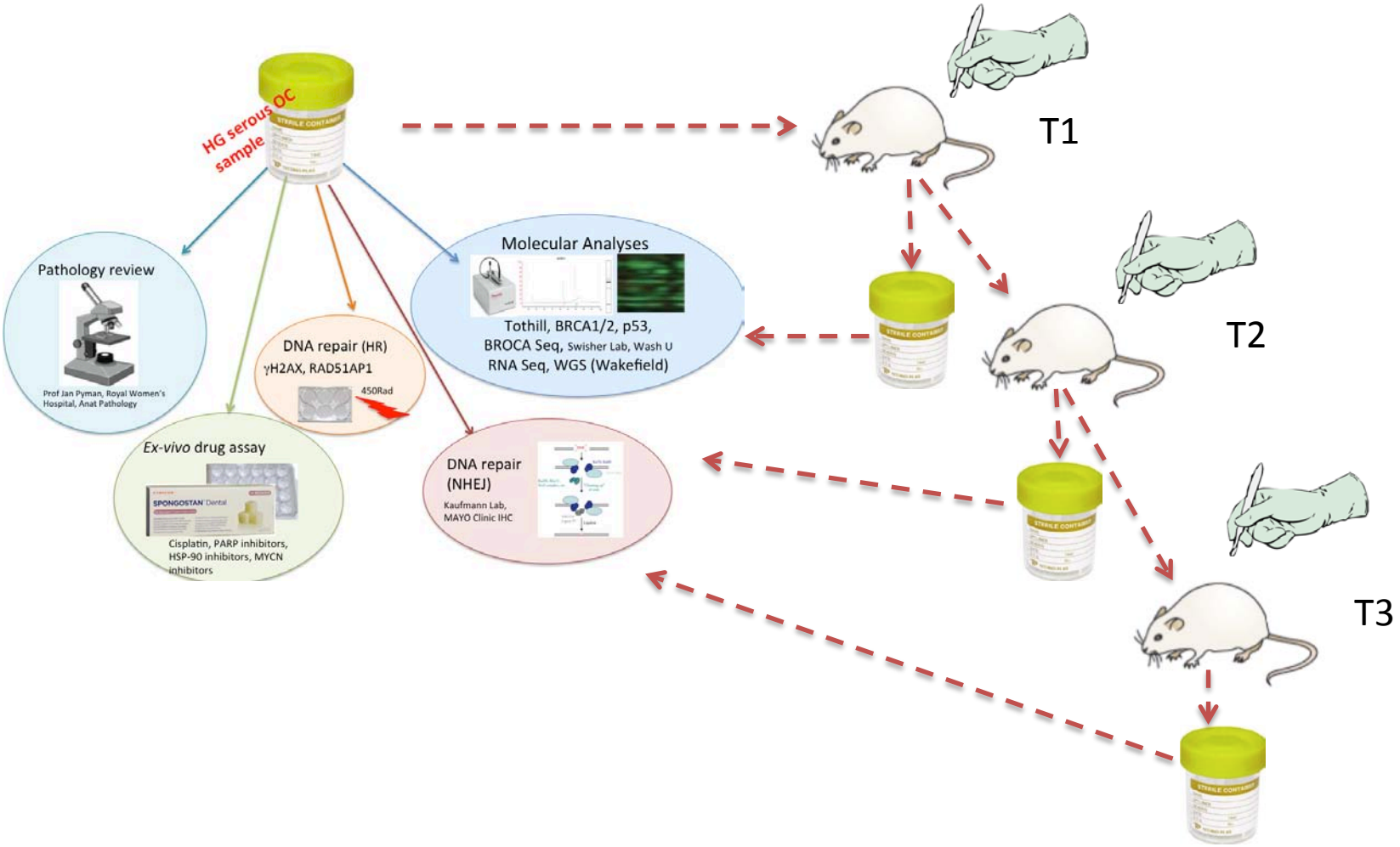
Platinum response and molecular correlates of human high-grade serous ovarian cancer patient-derived xenografts (PDXs)

Clare Scott, MD PhD

Royal Melbourne and Royal Women's Hospitals and Walter Eliza Hall Institute of Medical Research

Sir Edward Dunlop fellowship

Characterisation of Ovarian Cancer patient-derived xenografts (PDX)



HG-SOC PDX: pre-clinical utility

- Transplantatation success rate 83%
- Mutations detected in PDX:

  2x *BRCA1*; 3x *BRCA2*; *TP53* present in all
- *In vivo* cisplatin response defined for HG-SOC PDX as platinum sensitive, resistant or refractory
  - largely consistent with patient outcome.
- Two of three PDX containing DNA repair gene mutations were platinum sensitive whereas over-expression of oncogenes was observed in platinum resistant/refractory PDX.

Intratumoral heterogeneity: the evolutionary dynamics of high-grade serous ovarian cancer and new directions in other gynaecologic cancers

Vancouver CoastalHealth
Promoting wellness. Ensuring care.

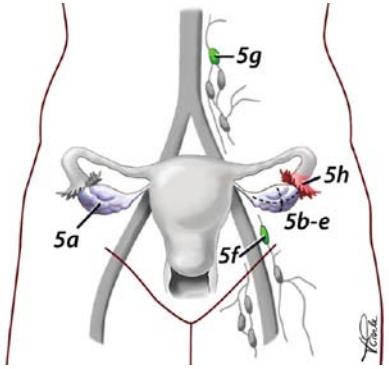
BC'S OVARIAN CANCER RESEARCH TEAM
OvCaRe
CARING WITH RESEARCH

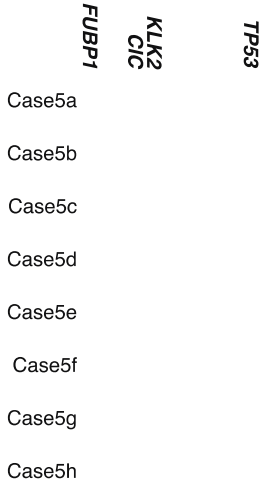
UBC

BC Cancer Agency
CARE + RESEARCH
An agency of the Provincial Health Services Authority

OVCARE
BC'S OVARIAN CANCER RESEARCH TEAM

Regional diversity of mutational profiles





- 52% +/- 31% of mutations present in all samples
- 91% in primary-recurrence comparison
- 10% in most diverse case
- TP53 always in all samples
- Driver mutations PIK3CA, CTNNB1 not present in all samples

Conclusions: spatial sampling of HGS ovarian cancers

- A single sample will only partially represent the mutational landscape of a tumour
- Histologically distinct tumours in the same individual can evolve from a common ancestral lineage
- Mutational and genome architecture profiles are not always compatible – different tumours evolve in different ways

Distinct evolutionary trajectories of primary high-grade serous ovarian cancers revealed through spatial mutational profiling

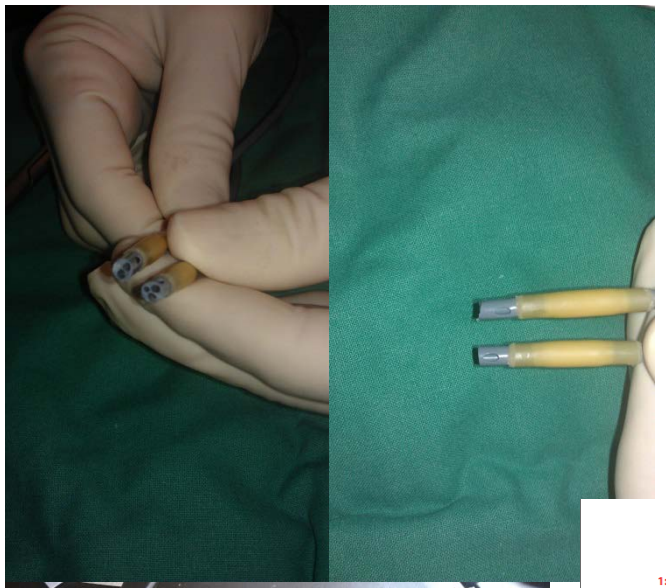
Bashashati et al, J Pathology, In Press

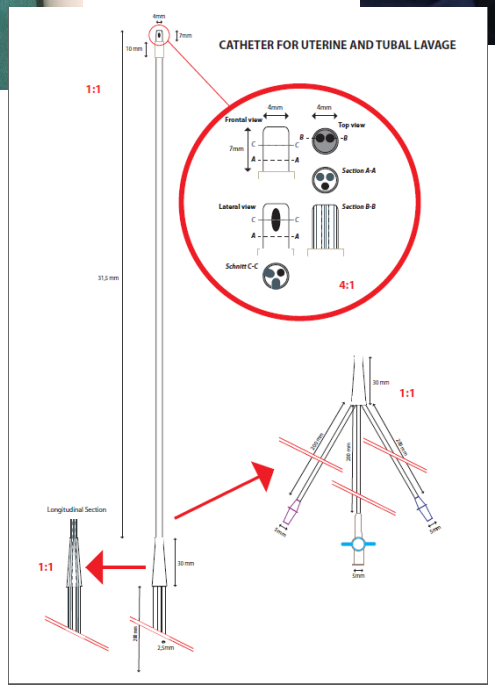
Digital droplet PCR for sensitive detection of ovarian cancer from lavage of the uterine cavity

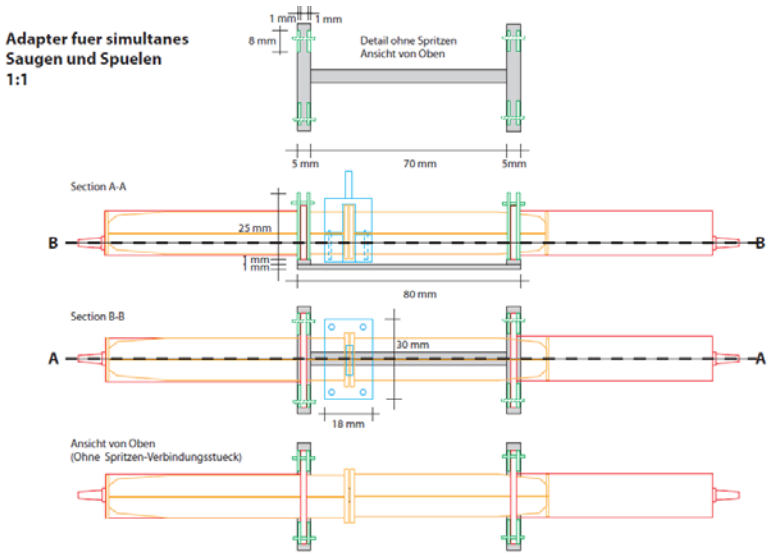
Gynecologic Cancer Intergroup
GCIG 2013 Spring Meeting
Chicago, IL
May 30th

Paul Speiser
Medical University Vienna
Department Gynecologic Oncology
Comprehensive Cancer Center Vienna

Targeting STICS – Uterine lavage

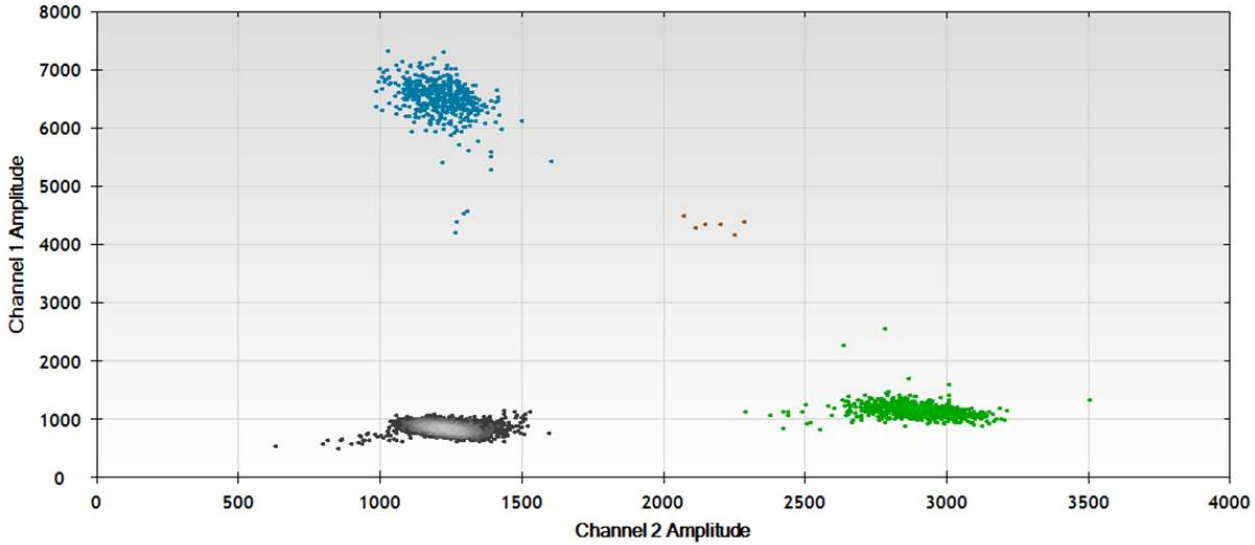




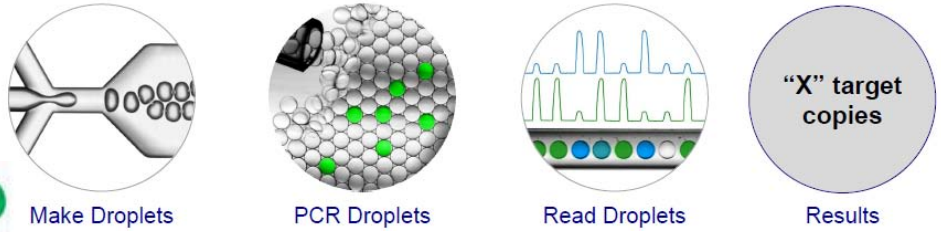


Digital droplet PCR (ddPCR)

- 20,000 droplets per sample
- 2 colour optical detection using FAM/VIC labeled probes
- Absolute quantification of target molecules
- Single molecule sensitivity



- KRAS_G12D
- P53_cd234
- P53_cd248
- P53_cd282



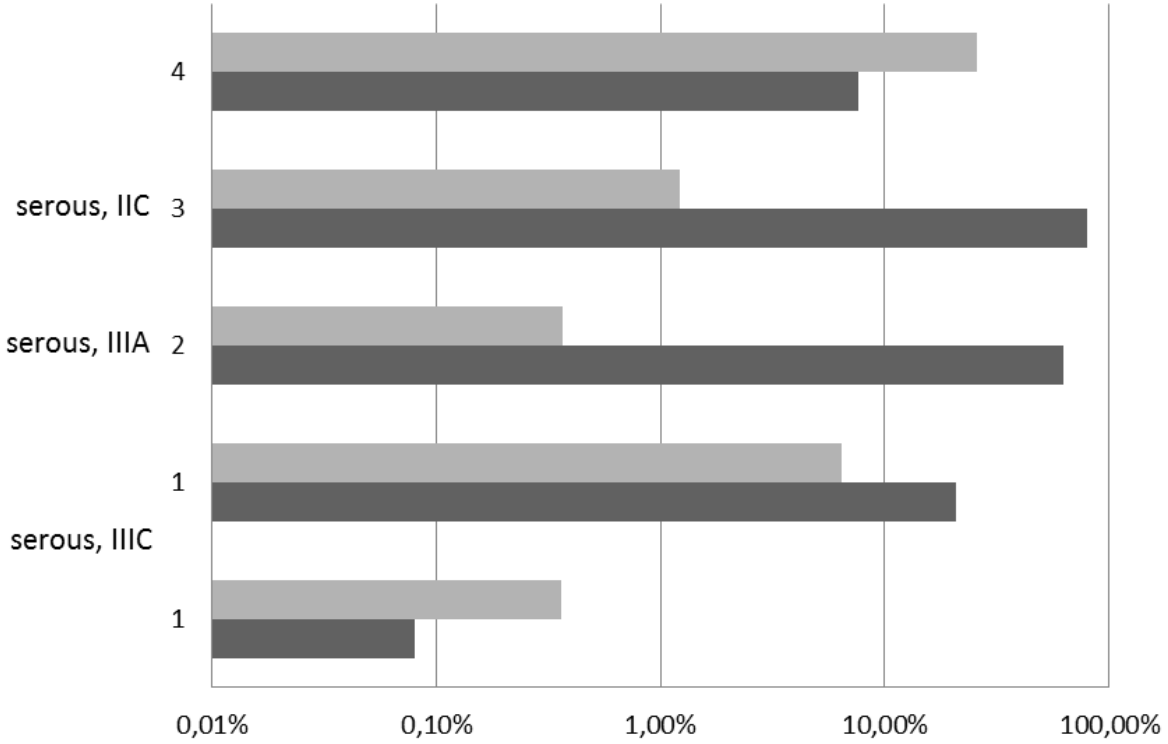
BIO-RAD

Proof of principle **(n=5)**

Uterine lavage, matched tumor tissue

↓

Digital droplet PCR (ddPCR)



	KRAS_G12D	p53_cd282	KRAS_G12D	p53_248	p53_282
	1	1	2	3	4
lavage	0,36%	6,42%	0,37%	1,22%	25,55%
tissue	0,08%	20,80%	62,48%	80,17%	7,60%

Co-ordinating complex translational sample collection across multiple sites and multiple countries

Iain McNeish
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Sample Collection Challenges

1. Cost

    NiCCC sample collection alone = £91,000

        24 tumour biopsies = £20,000

        Courier costs = £47,000

2. Infrastructure

    -80 freezers and centrifuges

3. Quality

    Plasma processing across 8 countries…

4. Getting hold of the archival samples

Harmonisation committee input

1. GCIG standards for translational research
2. Ownership of samples after completion of clinical trial
3. The boring bit – Standard Operating Procedures