Ovarian Cancer Translational Research Initiative Planning Workshop Report

February 10, 2016, 8:00 am – 6:00 pm

Location: OICR | West Tower Boardroom 5-20/21

Invitees:	
Laurie Ailles	Princess Margaret Cancer Centre
Christine Allen	University of Toronto
Marcus Bernardini	Princess Margaret Cancer Centre
David Bowtell	Peter MacCallum
James Brenton	Cancer Research UK Cambridge Institute
Theodore Brown	Lunenfeld-Tanenbaum Research Institute
Julia Burnier	Princess Margaret Cancer Centre
Daniel De Carvalho	Princess Margaret Cancer Centre
John Dick	Princess Margaret Cancer Centre
Gabriel DiMattia	University of Western Ontario
Lynn Douglas	AstraZeneca Canada Inc.
Ronny Drapkin	University Pennsylvania Perelman School of Medicine
Daniel Durocher	The Lunenfeld-Tanenbaum Research Institute
Michael Fung Kee Fung	The Ottawa Hospital
Steven Gallinger	Mount Sinai Hospital
Hal Hirte	Juravinski Cancer Centre
Percy Ivy	National Cancer Institute
Katherine Karakasis	Princess Margaret Cancer Centre
Elise Kohn	National Cancer Institute
Madhuri Koti	Queen's University
Joanne Kotsopoulos	Women's College Hospital
Stephanie Lheureux	Princess Margaret Cancer Centre
Helen MacKay	Sunnybrook Odette Cancer Centre
Ursula Matulonis	Dana-Farber Cancer Institute
Anne-Marie Mes-Masson	Centre de recherche du Centre hospitalier de l'Université de Montréal
Christine Misquitta	Centre for the Commercialization of Antibodies and Biologics
Jason Moffat	University of Toronto
Steven Narod	Women's College Research Institute
Brad Nelson	BC Cancer Agency- Deeley Research
Pamela Ohashi	Princess Margaret Cancer Centre
Amit M. Oza	Princess Margaret Cancer Centre
Jim Petrik	University of Guelph
Trevor Pugh	Princess Margaret Cancer Centre
Robert Rottapel	Princess Margaret Cancer Centre / University Health Network
Patricia Shaw	University Health Network
Trevor Shepherd	Western University
Anil Sood	MD Anderson Cancer Center
Gavin Stuart	University of British Columbia
Shannon Stuart	Princess Margaret Cancer Foundation
Alicia Tone	Princess Margaret Cancer Centre
Barbara Vanderhyden	Ottawa Hospital Research Institute / University of Ottawa
Johanne Weberpals	The Ottawa Hospital
Bradly Wouters	Princess Margaret Cancer Centre
OICR & FACIT	
John Bartlett	Ontario Institute for Cancer Research
Rob Campos	Ontario Institute for Cancer Research
Connie Chen	Fight Against Cancer Innovation Trust
Jeff Courtney	Fight Against Cancer Innovation Trust
Thomas Hudson	Ontario Institute for Cancer Research
Teresa Petrocelli	Ontario Institute for Cancer Research
Juri Reimand	Ontario Institute for Cancer Research
Melanie Spears	Ontario Institute for Cancer Research
Rebecca Tamarchak	Ontario Institute for Cancer Research
Jessica Vaisica	Ontario Institute for Cancer Research

Please note that this is a summary of the workshop. For more details please contact the TRI workshop leaders:

- **Robert Rottapel: rottapel@gmail.com**
- **Amit Oza: Amit.Oza@uhn.ca**
- **Trevor Shepherd: tshephe6@uwo.ca**

1. Background *(Tom Hudson)*

- OICR Strategic Plan 2016-2021: overview
- Translational Research Initiatives

OICR's 5-year strategic plan (2016-2021) was reviewed, including the Institute's mission and goals. Important highlights include the aims to: advance Ontario's best cancer research to improve cancer care and treatment; enhance Ontario's global leadership in cancer research; work in collaboration with partners; and, for economic development (which included a brief introduction to Jeff Courtney Chief Commercial Officer of FACIT).

The Institute's concept of Translational Research Initiatives (TRIs) was discussed, which require expertise, funding, and approaches to move findings and technologies to the clinic. Workshop participants were encouraged to consider leveraging networks supported by OICR (e.g., Global Alliance for Genomics & Health, Ontario Tumour Bank, Canadian Cancer Clinical Trials Network) as well as OICR's Technology Programs which will play a role in providing expertise and access to technologies to the Ontario research community, and in supporting OICR's strategic initiatives.

Structure-wise, TRIs represent large-scale, multi-disciplinary collaborations between laboratory and clinical scientists, to advance Ontario assets and improve cancer patient outcomes. They should be focused on a clinical need that builds on assets or innovations in an area of leadership for Ontario. TRIs will include 2-5 projects, with at least one mandatory clinical trial which must be started in the first 2 years of a TRI. A budget of up to $10 M over 4 years may be requested for a TRI, with the clinical trial budget comprising at least $2 M over the 4 years (if less than $2 M, then the total budget will be reduced accordingly). Additional supplemental funding should be sought at the start of the TRI and continued throughout the course of the TRI

TRI workshops are intended to support development of Letters of Intent (LOIs) for TRIs. TRIs will be led by two co-leaders (preferably not from the same institution), one scientific and one clinical. They are intended to build consensus around the TRI priorities, discuss potential projects, identify collaborations among Ontario scientists, consider how to best leverage OICR Technology Programs, and identify potential sources of co-funding. A workshop report will be generated to inform the community about the workshop and to facilitate LOI applications.

There was a reminder that all guidelines about the TRI process are available by contacting OICR's Scientific Secretariat at scientificsecretariat@oicr.on.ca.

2. Opening remarks *(workshop co-leaders: Amit Oza, Trevor Shepherd, and Rob Rottapel)*

Dr. Oza welcomed the attendees to the day's session and introduced ovarian cancer (OC) as a site priority. He stated that OC is the most lethal gynecologic malignancy in Ontario with >1000 cases per year, and hope that the workshop's discussions would be candid and frank to allow the group to foster thoughtful ideas that can be developed into a successful TRI Letter of Intent (LOI) and proposal. The resulting proposal should define populations and will have impact in terms of research and clinical trials moving forward. The aim is to leverage the existing expertise in Ontario

and internationally in order to glean a better understanding of the biology of the disease; ultimately to develop mechanisms that will benefit treatment. He introduced some of the existing capacity in Ontario/Canada: the Terry Fox Research Institute Canadian Ovarian Experimental Unified Resource (COEUR), The Society of Gynecologic Oncology of Canada (GOC), the Canadian Cancer Trials Group, Princess Margaret Consortium, and OICR Programs.

Trevor Shepherd reiterated the goals of the workshop and described that the co-leaders had assembled a group of nationally- and internationally-recognized OC experts. He noted that the workshop should not be viewed as simply an information session, but rather a dynamic workshop and brainstorming session. He wanted attendees to focus on what the group has already achieved in order to develop next steps to expand upon this success. He also reminded the group that they should be considering the existing networks and collaborations that can be connected to develop a successful TRI and the workshop presents an opportunity to raise serious questions and start developing an action plan.

Robert Rottapel provided an overview of the Innovation in Target Validation (ITV) Program. The Program combines aspects from the groups of Dev Sidhu (ubiquitin tools), Jason Moffat (new target validation tools), and Rottapel (whole kinome monitoring). He noted that cisplatin-resistant and -sensitive cells show distinct kinome profiles; this property is not only true for cisplatin compounds but can be expanded to other agents. The expansion of these genetic tools can be of use to the wider cancer community.

Discussion Topic 1: Platinum Resistance in Ovarian Cancer

The Clinical Conundrum (Stephanie Lheureux)

Dr. Lheureux noted that she often sees patients at advanced stages (III or IV), but that at an early stage, patients tend to have a much better prognosis. The issue here is that we don't currently have a very robust screening strategy that would allow these patients to be identified and treated earlier. In order to develop such a strategy, we need to better understand the various risk factors. She noted that the origin of OC depends on the type. High-Grade Serous Ovarian Cancer (HGSOC) tends to originate in the fallopian tubes, whereas low-grade cancers tend to originate from a benign cystadenoma. Currently, patients are diagnosed via pathology and CT scan, but she wondered if better methods can be developed (perhaps laparoscopic investigation?). Current treatment regimens involve debulking surgery with the goal to remove all disease. This is then followed by chemotherapy and surveillance, but this often leads to disease recurrence. Disease is classified as platinum-resistant if it recurs in less than 6 months. Patients classified as platinum-resistant will receive mono chemotherapy followed by maintenance while those who are platinum-sensitive will receive platinum based chemotherapy and maintenance. Within the platinum-sensitive group there is a specific BRCA-mutant subpopulation who benefit from treatment with Olaparib during the post-platinum chemotherapy maintenance period. There are currently two ongoing clinical trials investigating this (EVOLVE and OLALA). We need to better understand what differentiates the short- and long-term responders.

The Bench Conundrum (Anil Sood)

Dr. Sood provided an overview of an approach being employed at MD Anderson. It's known that patients with zero residual disease (R0) do well. If you operate on all patients upfront (standard treatment), at best, R0 will range from 15-30%, meaning that 70% of patients will not derive the greatest benefit. At MD Anderson, patients with expected advanced OC undergo laparoscopic investigation. Independent review by at least two gyne-oncologists classifies patients into the R0 "feasible" (undergo surgery), or "not feasible" (undergo neo-adjuvant chemotherapy prior to surgery)

categories. Post implementation, surgical outcomes have increased dramatically. Next, Dr. Sood presented work using functional screens to discover targets. These screens aim to specifically reduce the viability of cancer cells. miR-517 and GRAMD1B have been identified as high value. MD Anderson is currently investigating RNAi therapy in trials (EPHARNA trial; phase 1). This trial investigates siRNA delivery for recurrent or "incurable" solid tumours. To summarize, Dr. Sood reiterated that functional screening allows for rapid identification and validation of therapeutic vulnerabilities, and noted that careful pre-clinical biological evaluation is needed. He also noted co-extinction strategies with multiple siRNAs offer unique therapeutic opportunities.

Bridging Laboratory and Clinical Resistance (James Brenton)

Data from ongoing, yet to be published, trials in the UK were discussed. Study suggests that patients can be stratified based on the analysis of a number of data points; however, it's difficult to sufficiently power these studies. Dr. Brenton suggested that these studies benefit from the collection of biopsy tissues, liquid biopsies, imaging, and highly annotated records. He also provided an overview of the UK mandated Genomic England (GeL) Pilot study. In this study, WGS is to be performed on 100,000 participant samples, but, he indicated, the real question is: what do you do with all this data? Dr. Brenton noted that this study will likely result in improved classification and new areas of interest: real-time integration of emerging data into translational programs, new trial designs to test biomarker-drug combinations, the absence of functional data from clinical trials, and population-based strategies for detection of minimal residual disease.

Key Discussion Points of the Session:

- There is a gap at multiple phases in terms of OC management, lots of variability in patient management – leads to downstream consequences;
- One of the major goals should perhaps be an improved and empirically determined definition of platinum-resistance (6 months may be outdated);
- Need more molecular stratifications to define treatment sensitivity. Ideally, markers would be utilized at the time of diagnosis;
- International efforts to define biomarkers would be useful;
- As we look at developing biomarkers, these could be implemented and tested to inform strategies for clinical trial development;
- Circulating markers (ctDNA) is indeed feasible and other makers are now coming forward – these can be used for monitoring response;
- Improve and implement new clinical trial designs to allow for information rich output.

Discussion Topic 2: DNA Damage & DNA Repair

Homologous recombination and ovarian cancer: basic biology to translation opportunities (Daniel Durocher)

Dr. Durocher introduced HGSOC as, essentially, a disease of genomic instability. One goal of his lab is to understand the basic biology of BRCA1/2 in the DNA damage response, specifically during homologous recombination (HR). He noted that loss of HR creates a vulnerability to PARP inhibitors. He described his group's work using the Toronto Knock Out (TKO) lentiviral sgRNA library and CRISPR to conduct PARP inhibitor sensitivity screens. He noted that a number of HGSOC vulnerability genes have been identified in the CRISPR screens and are in various stages of follow-up.

Active Areas of Clinical Trial Investigation – Academic Opportunities (Elise Kohn)

Dr. Kohn noted that DNA repair processes should provide a number of opportunities for treatment and management of OC, however, only a few validated targets, and even fewer biomarkers, have been identified. She suggested that we dissect the

pathways to look for the unexpected; thinking seriously about combinations as a "one-two-punch" which often provides greater effect. For example, we should consider drugs + mutational status + checkpoint inhibitors for greatest effect.

Exceptional response and end-stage high-grade serous cancer. Two ends of the clinical spectrum (David Bowtell)

An overview of the Australian Ovarian Cancer Study (AOCS) was provided by Dr. Bowtell. He noted the presence of "exceptional responders" (patients with complete response despite sub-optimal debulking), and "multiple responders" (patients who sustain multiple complete responses to platinum-based chemotherapy). It's important to understand the biology behind these groups, as within the exceptional responders group, there was frequent inactivation of HR genes.

Key Discussion Points of the Session:

- DDR and DNA repair inhibitors need to be rich, as the process is blossoming and is ready to yield many new opportunities; the application of genomic editing technologies can lead to the identification of vulnerabilities within and across OC;
- In the short-term, this would lead to new therapeutic directions;
- In the mid-term, genomic editing technologies could lead to better understanding and prediction of targets – leading to patient-centred decisions;
- Interaction of the cell cycle is important for knowledge of therapeutics;
- Microenvironment is contextually important.

Discussion Topic 3: Protein Homeostasis & The Proteotoxic Stress Response

Overview of general problem – What we know (Brad Wouters)

Dr. Wouters introduced the notion that diseases are characterized by defects in the DNA damage response and other cellular pathways, and that cancer cells are able to adapt to this stress. Proteotoxic stress arises as a consequence of the microenvironment and hypoxia, which is a common feature of tumours. One of the key proteotoxic stressors is endoplasmic reticulum (ER) stress. Cells respond to ER stress via the Unfolded Protein Response (UPR). Hypoxia is associated with aggressive disease and thus has been a clinical target for many years. As one example, when PERK signaling is blocked in mice, rates of hypoxia are halved. When these mice are then treated, tumours have enhanced sensitivity to radiation.

Maintenance of Protein Homeostasis as a Potential Therapeutic Vulnerability (Robert Rottapel)

We have a lot to learn about the basic biology of the ovarian tumour. We know that this is a disease of copy number variation and DNA damage response deficiencies. The transition from a normal cell to a transformed cell involves new fitness properties being acquired and the ability of the cell to tolerate physiological stresses. The Rottapel group has used RNAi and CRISPR to investigate disease pathways. They have found that the genes which tend to be overexpressed in OC assort themselves into biosynthetic pathways (proteasome subunits, initiation, ribosomal subunits, etc.). Thus, protein homeostasis functions are important for sustaining tumour viability. Future studies should be aimed to uncover proteasome and stress response pathway components that could represent a potential clinically relevant therapeutic pathway.

Key Discussion Points of the Session:

- We will need additional new therapeutic targets (have looked at DNA repair and cisplatin for many years already);
- Idea is to take some of the work that's gone on for the past several years to look at new avenues (i.e. stress response pathways);
- Exploit some of the unique biology of OC (secretory epithelial cell of origin, tubo-ovarian and peritoneal microenvironment, etc.);
- Two approaches to target this new vulnerability: (1) augment the stress to take advantage to this feature (2) augment pathways that mediate tolerance;

- Some opportunities for early translational work – preclinical models or window of opportunity clinical trials with the goal to introduce new therapies;
- Finally, appreciate that responses are likely also occurring in normal, tumour-associated cells. There may be some interaction and overlap.

Discussion Topic 4: Immuno-Oncology

Introduction to Immunotherapies (Ursula Matulonis)

Dr. Matulonis reviewed that, currently, there aren't any approved immuno-oncology (IO) strategies approved for OC. There are, however, several therapies currently underway as trials (IO agents alone, IO agents and chemotherapy, IO agents and other biologics) – a discussion of some of these trials was presented. In BRCA1/2 mutated OCs there is a higher neoantigen load, higher numbers of CD3+ and CD8+ TILs, and higher intra-tumoral expression of PD-1 and PD-L1 expression compared to OCs without alterations in HR genes.

Novel areas of immune research in ovarian cancer – lessons learned from other disease settings (Marcus Butler)

Dr. Butler presented data from studies of melanoma as possible "lessons learned" for the OC group. Combination therapy using Ipilimumab can lead to better progression free survival in the melanoma test patients. The question is, how do we select patients who will best respond to these treatment? He discussed the various adoptive T cell strategies currently under investigation: antigen-specific T cells, gene-engineered T cells, tumour infiltrating lymphocytes (TIL). Princess Margaret Hospital (PMH) is in the planning stages for a clinical trial called Adoptive Cell Therapy InVigorated to Augment Tumour Eradication (ACTIVATE) – this study will enroll a recurrent OC cohort in addition to a metastatic melanoma cohort. Patients will receive TIL infusion, treatment with IL-2 and anti-PD-1, and biopsy/CT assessment. Another study, Cell therapY to augmeNt oncolytic viRus Generated immunitY (CYNRGY) is also in the planning stages at PMH. As it was found that less activated/differentiated cells are better able to be grafted and induce memory, this study will infuse central memory T cells which can be expanded by Maraba oncolytic vaccination.

Current initiatives in Immuno-Oncology of Ovarian Cancer: Partnering in Ontario and Canada (Pamela Ohashi)

Dr. Ohashi discussed how TILs from OC specimens show variable rates of expansion. In OC, you get a spectrum (fast – medium – slow growing in culture). It has been noted that the presence of NK cells is associated with slow growth of TILs. When looking at patient samples, those patients with NK cells exhibit a quicker relapse than those who do not. Dr. Ohashi discussed the Investigator-initiated Phase II Study of Pembrolizumab Immunological Response Evaluation (INSPIRE) trial which looks to evaluate the changes in genomic and immune landscapes in patients during pembrolizumab treatment. The study will also perform a thorough immunological response evaluation. Other consortia that also support these initiatives include BioCanRx, Terry Fox immunotherapy Network, and the OICR-TRIs.

Engineering modularity for immune-therapeutics (Jason Moffat)

Dr. Moffat provided an overview of the Toronto Recombinant Antibody Centre (TRAC) which has been developing a number of humanized antibody libraries. TRAC produces bi-specific antibodies; two bi-specific antibodies have been approved for therapy (Removab and Blincyto) and more than 30 additional bi-specific antibodies are currently in development. TRAC is currently developing a set of antibodies against all human receptor tyrosine kinases (RTKs); Ephrin receptor is expressed in glioblastomas and EPHA2 might be a good model for OC. Dr. Moffat discussed the use of Bispecific T-cell engagers (BiTEs) to induce cell death in glioblastomas and hopes that this approach might also have impact for OC.

Key Discussion Points of the Session:

- Use of immune therapy is an open field for ovarian cancer;
- Several approaches – but these have low response rate;
- OC is a "cold" tumour'
- Adoptive T cell treatment clinical trial;
- Strengths of the oncolytic virus group may impact the work (Maraba);
- NK cells and how they inhibit the expansion of TILs;
- Personalization of dendritic cell vaccines;
- Discussed various initiatives in Canada;
- Bi-specific antibodies – work in GBM – has the capability to be translated into OC;
- Formation of CD133 BiTEs – may have applicability to OC therapeutics.

Discussion Topic 5: Model Systems

Experimental Model Systems for Ovarian Cancer (Ronny Drapkin)

Dr. Drapkin presented an introduction to the various models available for studying OC including genetically engineered mouse (GEM) models and a discussion of the pros and cons of each model system. Some concerns were raised: the fact that PDX models are not immune-competent, and that you must be aware of the genetic alterations that are important for your disease in GEM models. Future directions/ items for consideration for expanding the use of GEM models - what are the contributions of other alleles? Can they be used for prevention studies? Should they be used as preclinical immunotherapy models? For implementation in drug development and drug resistance to complement PDX models?

Preclinical Model Systems (Trevor Shepherd)

Dr. Shepherd reviewed that the primary therapy for OC is surgery – thus, we are afforded an opportunity to obtain cells from tumours (and/or ascites). A further advantage is that samples can be collected pre- and post-chemotherapy. It was noted that when you start to culture cells, or establish cell lines, you lose the heterogeneity of the tumour. The idea that some more recently generated but less characterized cell lines might provide a better option for maintaining original tumour biology, and the group was encouraged to start incorporating the use of these new lines. The idea of raising cells in spheroid cultures was also discussed to better mimic the natural tumour environment as models of metastasis and 3D tumour biology.

Key Discussion Points of the Session:

- Deriving new patient-derived lines and best type(s) of media to maintain genotype and phenotype;
- In vivo application of CRISPR technology using GEM models;
- Consideration of metastatic disease in animal models.

Next Steps/Wrap Up

Attendees were thanked for their time and input. Meeting notes will be shared with attendees and will be contacted for input as the LOI is developed.

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Ovarian Cancer Translational Research Initiative Planning Workshop

Wednesday February 10, 2016
8:00 a.m. – 6:00 p.m.
Light breakfast will be served at 8:00 a.m.
Location: OICR | West Tower Boardroom 5-20/21

TIME	AGENDA ITEM	PRESENTER/ MODERATOR
8 a.m.	**Arrivals and light breakfast**	
8:30 a.m.	**Background** • OICR Strategic Plan 2016-2021: overview • Translational Research Initiatives	*Tom Hudson*
8:50 a.m.	**Introduction & Opening remarks** • Workshop goals and deliverables/outcomes • Funding opportunities and timeline • Existing activities from OICR Programs and Ontario	*Rob Rottapel, Amit Oza & Trevor Shepherd*
9:15 a.m.	**DISCUSSION TOPIC 1** **Platinum Resistance in Ovarian Cancer** **Clinical Presenter: Stephanie Lheureux** *Time: 15 minutes* Title: The Clinical Conundrum **Scientific Presenter: Anil Sood** *Time: 15 Minutes* Presentation Title: The Bench Conundrum – Disease Evolution **Translational Presenter: James Brenton** *Time: 15 minutes* Presentation Title: Bridging Laboratory and Clinical Resistance Characteristics	*Moderator: Anil Sood*
10:00 a.m.	**DISCUSSION PANEL – Topic 1** *Questions & Answers*	
10:30 a.m.	**Break**	

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10:45 a.m.	**DISCUSSION TOPIC 2** **DNA Damage & DNA Repair** **Scientific Presenter: Daniel Durocher** *Time: 15 minutes* Presentation Title: "Homologous recombination and ovarian cancer: basic biology to translation opportunities" **Clinical Presenter: Elise Kohn** *Time: 15 minutes* Presentation Title: Active Areas of Clinical Trial Investigation – Academic Opportunities **Translational Presenter: David Bowtell** *Time: 15 minutes* Presentation Title: 'Exceptional response and end-stage high grade serous cancer. Two ends of the clinical spectrum'	*Moderator:* *Daniel Durocher*
11:30 a.m.	**DISCUSSION PANEL – Topic 2** *Questions & Answers*	
12:00 p.m.	**Lunch**	
1:00 p.m.	**DISCUSSION TOPIC 3** **Protein Homeostasis & The Proteotoxic Stress Response** **Scientific Presenter: Brad Wouters** *Time: 15 minutes* Presentation Title: Overview of general problem – What we know **Scientific Presenter: Robert Rottapel** *Time: 15 minutes* Presentation Title: "Maintenance of Protein Homeostasis as a Potential Therapeutic Vulnerability"	*Moderator:* *Brad Wouters*
1:30 p.m.	**DISCUSSION PANEL – Topic 3** *Questions & Answers*	
2:00 p.m.	**Break**	

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2:15 p.m.	**DISCUSSION TOPIC 4** **Immuno-Oncology** **Introduction to Immunotherapies: Ursula Matulonis** *Time: 15 minutes* **Clinical Presenter: Marcus Butler** *Time: 15 minutes* Presentation Title: Novel areas of immune research in ovarian cancer – lessons learned from other disease settings **Scientific Presenter: Pamela Ohashi** *Time: 15 minutes* Presentation Title: Current initiatives in Immuno-Oncology of Ovarian Cancer: Partnering in Ontario and Canada. **Translational Presenter: Jason Moffat** *Time: 15 minutes* Presentation Title: "Engineering modularity for immuno-therapeutics"	*Moderator:* *Ursula Matulonis*
3:15 p.m.	**DISCUSSION PANEL – Topic 4** *Questions & Answers*	
3:45 p.m.	**DISCUSSION TOPIC 5** **Model Systems** **Scientific Presenter: Ronny Drapkin** *Time: 15 minutes* Presentation Title: “Experimental Model Systems for Ovarian Cancer” **Scientific Presenter: Trevor Shepherd** *Time: 15 minutes* Presentation Title: Preclinical Model Systems	
4:15 p.m.	**DISCUSSION PANEL** *Questions & Answers*	

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4:45p.m.	**MODERATOR SUMMARIES** **Topic 1: Platinum Resistance in Ovarian Cancer** Summary of Major Discussion Topics *Time: 5 minutes* **Topic 2: DNA Damage & DNA Repair** Summary of Major Discussion Topics *Time: 5 minutes* **Topic 3: Protein Homeostasis & The Proteotoxic Stress Response** Summary of Major Discussion Topics *Time: 5 minutes* **Topic 4: Immuno Oncology** Summary of Major Discussion Topics *Time: 5 minutes*	
5:15 p.m.	• **Potential collaborations** • **Next steps** o **Workshop report** o **Declaration of interest** o **Letter of intent**	*Facilitated by Workshop Leaders*
6:00 p.m.	**Adjourn**	