

# Building your scientific toolbox: OCC's OvCAN Collection of ovarian cancer research models

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\*Information generated/supplied by model providers

### What is the OvCAN Collection?



The OvCAN Collection is a **virtual** collection of highfidelity research models of ovarian cancer whose development and/or characterization has been funded at least in part by Ovarian Cancer Canada (OCC) via the OvCAN research initiative.

The **purpose** of the OvCAN Collection is to facilitate the creation and sharing of these gold standard models among the ovarian cancer research community, to enable and expedite high-quality research focused on improving ovarian cancer outcomes.

#### Types of models/model systems currently available

- ✓ Patient-derived cell lines
- Patient-derived complex culture systems (e.g., organoids)
- ✓ Patient-derived xenografts
- ✓ Syngeneic mouse models
- Richly annotated cohorts of human ovarian cancer biospecimens
- ✓ Fee-for-service platforms (e.g., microfluidics)
- ✓ Technology transfer/protocols

#### How to access models: for now

Please contact the indicated provider lab directly about the models you are interested in accessing. Providers and recipients will be responsible for coordinating the sharing of models and/or data. OCC will reimburse reasonable costs incurred as a direct result of sharing, as funding is available. *See page 20 for additional sharing option in the works*.

#### **Key Acronyms**

**CCC**, clear cell carcinoma **CNV**, copy number variants **EC**, endometrioid carcinoma **GCT**, granulosa cell tumour HGSC, high-grade serous carcinoma LGSC, low-grade serous carcinoma MC, mucinous carcinoma **MDT**, micro-dissected tissue **MMMT**, malignant mixed Müllerian tumor **MMTA**, master material transfer agreement **MS**, mass spectrometry **OC**, ovarian cancer **PDO**, patient-derived organoid **PDX**, patient-derived xenograft **RNA-Seq**, whole transcriptomic sequencing **SCCOHT**, small cell carcinoma hypercalcemic type **TIL**, tumour-infiltrating lymphocytes **WES**, whole exome sequencing **WGS**, whole genome sequencing

Have questions, corrections or updates on available models/ data for the next version of the OvCAN Collection catalogue? Contact Alicia Tone, PhD (Scientific Advisor @OCC) atone@ovariancanada.org

### Patient-derived cell lines: high-grade serous carcinoma (HGSC)

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Lab	ID*	Age	Stage	Chemo	Carboplatin response	Olaparib response	Tumours in Mice (days)	TP53 status**	BRCA1/2 status	High-throughput Data Generated	Key References (PMID)
Mes-	OV866(2)	60	IIIC	post	resistant	resistant	250	missense	wild-type	Clariom S, WES, RNA-Seq, proteomics	<u>26622941; 27374179</u>
Masson / Provencher	TOV1369	EQ	шс	pre	intermediate	resistant	none	missense	wild-type	Clariom S, WES, SNP-Affi, RNA-Seq, proteomics	<u>22931248; 27374179</u>
	OV1369(R2)#	20	inc	post	resistant	resistant	none	missense	wild-type	Clariom S, WES, SNP-Affi, RNA-Seq, proteomics	<u>22931248; 27374179</u>
	TOV1946	75	IIIC	pre	intermediate	sensitive	17	missense	wild-type	Clariom S, WES	<u>18507860; 27374179; 22931248</u>
	OV1946			pre	intermediate	sensitive	none	missense	wild-type	Clariom S, WES, RNA-Seq, proteomics	<u>18507860; 27374179</u>
	OV2085	62		post	N/A	N/A	57	missense	wild-type	Clariom S, WES, RNA-Seq, proteomics	<u>32784519</u>
	OV2085(3)	05	IIIC	post	N/A	N/A	N/A	missense	wild-type		
	TOV2223G	89	IIIC	pre	intermediate	intermediate	none	nonsense	wild-type	Clariom S, WES	<u>18507860; 27374179</u>
	OV2295			pre	sensitive	sensitive	none	missense	wild-type	Clariom S, WES, SNP-Affi, RNA-Seq, proteomics	<u>22931248; 27374179</u>
	OV2295(R2)	59	IIIC	post	sensitive	intermediate	none	missense	wild-type	Clariom S, WES, SNP-Affi, RNA-Seq, proteomics	<u>22931248; 27374179</u>
	TOV2295(R)			post	sensitive	intermediate	none	missense	wild-type	Clariom S, WES, RNA-Seq, SNP-Affi	<u>22931248; 27374179</u>
	TOV2835EP	62	IIIC	post	sensitive	N/A	none	missense	wild-type	Clariom S, WES	<u>32784519</u>
	TOV2881EP	56	IIIC	post	sensitive	N/A	none	missense	wild-type	Clariom S, WES	32784519
	TOV2929D	77	IIIC	pre	intermediate	N/A	none	missense	wild-type	Clariom S, WES	32784519
	TOV2978G	62		pre	sensitive	intermediate	none	splice	wild-type	Clariom S, WES	<u>26622941; 27374179</u>
	OV2978	63	63 IIIC	pre	sensitive	N/A	none	splice	wild-type	Clariom S, WES	
TOV30	TOV3041G	61	IVA	post	sensitive	sensitive	none	wild-type	wild-type	Clariom S, WES, RNA-Seq, proteomics	<u>26622941; 27374179</u>

### Patient-derived cell lines: HGSC, continued



Lab	ID*	Age	Stage	Chemo	Carboplatin response	Olaparib response	Tumours in Mice (days)	TP53 status**	BRCA1/2 status	High-throughput Data Generated	Key References (PMID)
Mes-Masson	TOV3121D	62	шс	post	N/A	N/A	N/A	frameshift	wild-type	Clariom S, WES	
/ Provencier	TOV3121EP	02	IIIC	post	intermediate	N/A	none	frameshift	wild-type	Clariom S, WES	<u>32784519</u>
	TOV3133G			pre	sensitive	intermediate	none	nonsense	wild-type	Clariom S, WES, SNP-Affi, RNA-Seq, proteomics	<u>22931248; 27374179</u>
	TOV3133D	БЭ	шс	post	sensitive	intermediate	none	nonsense	wild-type	Clariom S, WES, RNA-Seq, SNP-Affi	<u>22931248; 27374179</u>
	OV3133(R)	JZ	52 1110	post	sensitive	intermediate	55	nonsense	wild-type	Clariom S, WES, SNP-Affi, RNA-Seq, proteomics	<u>22931248; 27374179</u>
	OV3133(R2)			post	intermediate	N/A	none	nonsense	wild-type	Clariom S, WES, RNA-Seq, SNP-Affi	22931248
	TOV3291G	FO		pre	intermediate	intermediate	none	missense	wild-type	Clariom S, WES, RNA-Seq, proteomics	<u>26622941; 27374179</u>
	OV3291		IIIC	pre	intermediate	N/A	none	missense	wild-type	Clariom S, WES	32784519
	OV4453	70	IIIC	pre	sensitive	sensitive	138	splice	BRCA2 G6085T	Clariom S, WES, SNP-Illu, RNA-Seq, proteomics	<u>26622941; 27374179</u>
	OV4485	55	IIIC	post	intermediate	intermediate	98	missense	BRCA1 IVS 14-1 G>T	Clariom S, WES, SNP-Illu, RNA-Seq, proteomics	<u>26622941; 27374179</u>

N/A: data not available

\*IDs starting with "OV" were derived from the cellular fraction of ascites collected through centrifugation; IDs starting with "TOV" were derived from solid tumour

<sup>#</sup>IDs ending in "(R)" were obtained at the time of disease relapse

\*\*all HGSC from Mes-Masson/Provencher lab are KRAS + BRAF wildtype, with exception of OV2085(3) with no data available

### Patient-derived cell lines: Low-grade serous carcinoma (LGSC)



Lab	ID	Age *	Stage *	Chemo	Trametinib sensitivity <sup>%</sup>	Tumours in Mice (days) <sup>&amp;</sup>	TP53 status	KRAS status	NRAS status	BRAF status	High-throughput Data Generated	Key References (PMID)
Carey/ Lee	VOA-1312 <sup>r,a</sup>	64		none	sensitive	N/A	wild-type	G12V	wild-type	wild-type	WES, CNV, RNA-Seq, RPPA, MS	<u>27822414; 28545687; 30636931</u>
	VOA-1056 <sup>p,t</sup>	62	IIIC	none	resistant	N/A	wild-type	wild-type	Q61R	wild-type	WES, CNV, RNA-Seq, RPPA	<u>27822414; 28545687; 30636931</u>
	VOA-3993 <sup>r,t</sup>	67		post-AHT	resistant	N/A	wild-type	wild-type	Q61R	wild-type	WES, CNV, RPPA, proteomics	<u>27822414; 30636931</u>
	VOA-2962 <sup>r,a</sup>	45			N/A	N/A	N/A	N/A	N/A	N/A	-	-
	VOA-3448 <sup>r,a</sup>	45		post-chemo +	resistant	N/A	wild-type	wild-type	wild-type	wild-type	WES, CNV, RPPA	<u>27822414; 30636931</u>
-	VOA-3723 <sup>r,a</sup>	46		AHT	resistant	N/A	wild-type	wild-type	wild-type	wild-type	WES, CNV, RNA-Seq, RPPA, MS	<u>27822414; 30636931</u>
	VOA-4627 <sup>r,a</sup>			nost-	resistant	N/A	R273H	wild-type	wild-type	wild-type	WES, CNV, RNA-Seq, RPPA, MS	<u>27822414; 30636931; 26076164</u>
	VOA-4698 <sup>r,a</sup>	44		chemo/AHT/	resistant	N/A	R273H	wild-type	wild-type	wild-type	WES, CNV, RPPA	27822414; 30636931
	VOA-4881 <sup>r,a</sup>	]			N/A	N/A	R273H	wild-type	wild-type	wild-type	Hotspot, RPPA	
	VOA-5646 <sup>r,a</sup>				N/A	N/A	R273H	wild-type	wild-type	wild-type	Hotspot, RPPA	28545687
	VOA-6406 <sup>r,t</sup>	56		post-chemo	resistant	70 (1 <sup>st</sup> gen); 30 (2 <sup>nd</sup> gen)	wild-type	wild-type	Q61R	wild-type	WES, CNV, RNA-Seq, MS	<u>30636931</u>
	VOA-7608 <sup>p,t</sup>	60	N/A	none	N/A	N/A	N/A	N/A	N/A	N/A	WES, RNA-Seq, proteomics	
	VOA-7681 <sup>p,t</sup>	59	IV	none	N/A	N/A	wild-type	wild-type	wild-type	wild-type	WES, RNA-Seq, proteomics	
	VOA-8862 <sup>p,a/t</sup>	76	IIIA	none	sensitive	N/A	wild-type	G12D	C118Y	wild-type	WES, CNV, RNA-Seq, MS	30636931
	VOA-9164 <sup>r,t</sup>	71		post-AHT	sensitive	N/A	wild-type	G12V	wild-type	wild-type	WES, CNV, RNA-Seq, MS	<u>30636931</u>
	VOA-10841 <sup>p,t</sup>	71	IIIB	none	N/A	N/A	wild-type	wild-type	Q61K	wild-type	WES, CNV, <i>RNA-Seq</i> , proteomics	

### Patient-derived cell lines: Low-grade serous carcinoma (LGSC)



Lab	ID	Age *	Stage*	Chemo	Trametinib sensitivity <sup>%</sup>	Tumours in Mice (days) <sup>&amp;</sup>	TP53 status	KRAS status	NRAS status	BRAF status	High-throughput Data Generated	Key References
Carey/ Lee	VOA-6857 <sup>r,#</sup>	42		post- chemo/AHT/ targeted tx	resistant	365 (1 <sup>st</sup> gen) 240 (2 <sup>nd</sup> gen)	N/A	N/A	N/A	N/A	WES, CNV (patient tumor)	<u>30636931</u>
	VOA-11865 <sup>r,t,#</sup>	33		post-AHT	N/A	330 (1 <sup>st</sup> gen) 150 (2 <sup>nd</sup> gen)	N/A	N/A	N/A	N/A	WES, CNV (patient tumor)	
	VOA-12512 <sup>r,t,#</sup>	52			N/A	330 (1 <sup>st</sup> gen)	N/A	N/A	N/A	N/A		
	iOv241Ca <sup>p,a</sup>	51	IIIA	post-chemo	sensitive	N/A	wild-type	G12D	wild-type	wild-type	WES, CNV, RNA-Seq, RPPA, MS	<u>27822414</u>
	VOA-14202	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	WES, RNA-Seq, proteomics	
Mes- Masson	TOV81D	66	IIIC	pre-chemo	N/A	none	wild-type	wild-type	N/A	wild-type	Clariom S, WES	<u>10949993</u>

AHT: anti-hormone therapy; CNV: copy number variant; MS: mass spectrometry; N/A: data not available; RPPA: reverse-phase protein arrays; WES: whole exome sequencing <sup>P</sup>obtained at primary diagnosis; <sup>r</sup>obtained at time of recurrence; <sup>a</sup>derived from ascites; <sup>t</sup>derived from tumour tissue; <sup>#</sup>PDX only

\*Age and tumour stage at the time of sample collection for research development.

<sup>%</sup>Trametinib sensitivities are based on cell proliferation experiments (100nM, 5 days). LGSC cell lines are much slower than commercial or HGSC lines, thus IC50 experiments are not ideal. Data not availability on sensitivity to carboplatin.

<sup>&</sup>Days to reach 100 mm<sup>3</sup> tumor volume

### Patient-derived cell lines: other histologies



Lab	ID	Histology	Age	Stage	Chemo	Carboplatin response	Olaparib response	Tumours in Mice (days)	TP53* status	KRAS status	High-throughput Data Generated	Key References (PMID)
Mes-Masson / Provencher	OV90	AC	64	IIIC	pre	resistant	resistant	21-84	missense	wild-type	Clariom S, WES, RNA-Seq, proteomics	<u>10949993;</u> 27374179
	OV3331	AC	72	IIIC	post	intermediate	N/A	163	frameshift	wild-type	Clariom S, WES, RNA-Seq, proteomics	<u>32784519</u>
	TOV21G	CCC	62	Ш	pre	sensitive	N/A	21-84	wild-type	G13C	Clariom S, WES, RNA-Seq, proteomics	<u>10949993</u>
	TOV3392D	CCC	42	IIIC	pre	resistant	N/A	33	wild-type	G12S	Clariom S, WES, RNA-Seq, proteomics	<u>32784519</u>
Huntsman	VOA4841ª	CCC	42	IC	pre	N/A	N/A		N/A	N/A	WES, RNA-Seq, proteomics	
	VOA6861ª	CCC	53	IC	N/A	N/A	N/A		wild-type	N/A	WES, RNA-Seq, proteomics	
	VOA10816 <sup>t</sup>	CCC	62	IA	N/A	N/A	N/A		wild-type	N/A	WES, RNA-Seq, proteomics	
	XVOA295 <sup>p</sup>	ССС	42	IIIC	pre	N/A	N/A	Yes	N/A	N/A	WES, RNA-Seq, proteomics	
	XVOA867 <sup>p</sup>	ССС	55	IV	pre	N/A	N/A	Yes	wild-type	N/A	To be completed/shared	
	VOA12539 <sup>t</sup>	ССС	63	IC1	N/A	N/A	N/A		wild-type	N/A	WES, RNA-Seq, proteomics	
	VOA4395 <sup>t</sup>	EC	41	IIIB	N/A	N/A	N/A		N/A	N/A	WES, RNA-Seq, proteomics	
	VOA5596ª	EC	78	IB	pre	N/A	N/A		wild-type	N/A	To be completed/shared	
Mes-Masson/ Provencher	TOV112D	EC	42	IIIC	pre	resistant	N/A	<10	missense	wild-type	Clariom S, WES, RNA-Seq, proteomics	<u>10949993;</u> 22931248
	TOV2414	MC	63	IIIC	post	resistant	N/A	123	wild-type	G12A	Clariom S, WES, RNA-Seq, proteomics	<u>32784519</u>
Huntsman	VOA8762 <sup>a</sup>	MC	55	IV	pre	N/A	N/A		wild-type	N/A	WES, RNA-Seq, proteomics	
	VOA8771ª	MC	55	IV	pre	N/A	N/A		wild-type	N/A	WES, RNA-Seq, proteomics	

### **Patient-derived cell lines: other histologies**



Lab	ID	Histology	Age	Stage	Chemo	Carboplatin response	Olaparib response	Tumours in Mice (days)	TP53* status	KRAS status	High-throughput Data Generated	Key References (PMID)
Huntsman	VOA5217 <sup>a</sup>	MMMT	E 1		post	refractory	N/A		wild-type	N/A	WES, RNA-Seq, proteomics	
	VOA5436 <sup>a</sup>	MMMT	21		post	refractory	N/A		wild-type	N/A	WES, RNA-Seq, proteomics	
	VOA12721 <sup>p</sup>	SCCOHT	33	IC	pre	N/A	N/A	Yes	wild-type	N/A	WES, RNA-Seq	
	COV434	SCCOHT	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	RNA-Seq, proteomics	
Vanderhyden	BIN67	SCCOHT	N/A	N/A	N/A	resistant	N/A	82 (IP)	wild-type	wild-type	SNP array; RNA-Seq, proteomics, WES and WGS available through Huntsman lab	23433318

AC: adenocarcinoma; CCC: clear cell carcinoma; EC: endometrioid carcinoma; IP: intraperitoneal; MC: mucinous carcinoma; MMMT: malignant mixed Müllerian tumor; N/A: data not available; SCCOHT: small cell carcinoma hypercalcemic type; WES: whole exome sequencing; WGS: whole genome sequencing <sup>a</sup>derived from ascites; <sup>t</sup>derived from solid tumour; <sup>p</sup>derived from PDX <sup>\*</sup>non-serous cell lines in Mes-Masson/Provencher lab are wild-type for *BRAF* and *BRCA1/2* 

### Complex culture systems: 3D spheroid culture system & patientderived organoids (PDO)



### 3D spheroid culture – *available through the Shepherd laboratory* (PMID: <u>31744879</u>)

- 1) Technology transfer: all protocols for performing 3D spheroid experiments using the ULA cultureware system and assays for cell viability with drug treatments
- 2) Collaboration: as study co-authors, will perform 3D spheroid culture experiments for drug treatment assays of cell viability (compared with standard 2D adherent cells)
  - Multiple established/new cell lines for HGSC, LGSC, CCC, EC
  - IncuCyte ZOOM and numerous fluorescent cells for direct visualization of spheroid growth and viability
- Fee-for-service: will perform assays as described above, with compensation for tech time, consumables and use of infrastructure

### PDO collaborations – *available through the Shepherd laboratory*

As study co-authors, will perform viability assays for drug treatments:

- Initiated work in November 2019 with primary cultures
- Apply three-component viability z-score used by Soragni group (PMID:<u>30820473</u>) - quantify organoid size, number and CellTiter-Glo readings

#### PDOs available for sharing

Lab	ID	Type of OC	Procedure	Split Ratio	Passage interval (d)	High- throughput Data Generated
Princess	OCAD.96	HGSC	Paracentesis	1:04	14	Genomics,
Margaret Living	OCAD.97	HGSC	Paracentesis	1:06	14	epigenomics in
Biobank /	OCAD.36.G1	HGSC	Xenograft	1:03	14	progress
Radulovich / Shepherd	OPTO.112	HGSC	Surgical Resection	1:03	18	
/ Shepheru	OCAD.93	HGSC	Paracentesis	1:03	14	
	OPTO.98	HGSC	Surgical Resection	1:04	10-11	
	OCAD.36.G1	HGSC	Paracentesis	1:03	14	
	OPTO.138	HGSC	Surgical Resection	1:06	7	
	OCAD.106	HGSC	Paracentesis	1:03	14	
	XDO.OPTO.112	HGSC	Xenograft	1:02	14-21	
	XDO.BD.55	HGSC	Xenograft	1:04	14-21	
	XDO.OV.2345	HGSC	Xenograft	1:04	14	

### **Complex culture systems: T-SLICE, tissue cell fate**



T-SLICE: Tumor Spheroids Layered in an Imageable Cancer Environment – *Boudreau laboratory* 





To enable high-throughput imageable studies within a complex simulated tumour microenvironment (bioRxiv; <u>https://doi.org/10.1101/2022.1</u> 0.08.511443)

# Tissue cell fate (TCFate) manipulation and detection tool – *Rodier laboratory*

Various fluorescence versions of cell fate reporter system have been validated and are now sharable:

- Destination lentivector for p21SEN reporter activity (contains the p21SEN promoter followed by a Gateway destination cassette to receive additional novel reporter via gateway recombination)
- Lenti p21SEN-tGPF (green fluorescence reporter)
- Lenti p21SEN-3MR (multimodality reporter red fluorescence, renilla Luc and inducible killing via ganciclovir)
- Lenti p21SEN-fLuc (Firefly luciferase reporter)

A dual vector system allowing fully automated cell number quantification is also available for sharing:

✓ Lenti H2B-GFP (PMID: <u>31186408</u>)

### Complex culture systems - microfluidics platform for *ex vivo* drug testing

#### Fee-for-service platform at the CRCHUM

Microfluidic culture devices (also called Lab-on-a-Chip devices) offer an excellent spatiotemporal control of a biological sample and its environment. They allow the preservation, in the appropriate culture conditions, of the viability and architecture of the tissue. In oncology, the Lab-on-Chip approach can be used to observe the effects of radiotherapy and chemotherapy treatments on cancer tumor samples and biopsies.

We have developed a novel 3D *ex vivo* culture model, called micro-dissected tissue (MDT), which gives tissue spheres of 350-450 $\mu$ m in diameter. MDTs (Fig 1), prepared from primary tumour samples or biopsies, can be cultured in the static (non-perfused) microfluidic model with a viability of >75% after 8 days without suffering hypoxia.

We have also designed microfluidic devices in polydimethylsiloxane (PDMS) optimised for the culture of 3D biological structures such as MDTs or spheroids. In these microfluidic devices, we can treat our 3D samples with diverse chemotherapy agents or culture conditions. Each device has wells capable of trapping 25 to 70 MDTs divided amongst 4 - 7 channels. Pictured (Fig 2) is a device that can hold 32 MDTs or spheroids; 8 samples in each of 4 channels. This device was custom designed to treat samples in a tissue microarray format that is then used for paraffin embedding (Fig 3) or the samples can be collected and digested for flow cytometry analysis (FACS). Response monitoring can be performed through analysis of the culture medium (about 70  $\mu$ L), by FACS or histopathology.

We have adapted paraffinization techniques from the pathology department to generate microdissected tissue microarrays (MDTMA) allowing the molecular analysis of the MDTs. Using this method, we can perform H&E staining to see the heterogeneity of the samples and follow the effects of different treatments on various markers. We have also been testing methods of freezing chopped tissue samples for future analysis.

For more info: PMID 26659477; PMID 30671574. Contact Microfluidic.cr.chum@ssss.gouv.qc.ca



**Fig 1.** a) Primary tumor or biopsy, b) chopped tissue, c) punching of chopped tissue and d) MDTs in HBSS ready for loading.



**Fig 3.** Paraffin embedding procedure for MDTMA and finished paraffin block.

### Human Ovarian Cancer Biospecimens & Clinical Data: The Pan-Canadian COEUR Repository



**Overview:** COEUR is a pan-Canadian cohort whose assembly was supported by the Terry Fox Research Institute; ongoing funding is being provided by OCC. COEUR has been created to promote access, ensure quality, and provide standardization of biological material and data resources for biomarker research in OC. The central research platform is based on a retrospective collection of human epithelial OC biological material (described at right).

**To Access:** To access the repository, researchers should complete an application form, including a study description. Study projects must meet management and study committee scientific criteria and applicants will need to provide an REB approval letter. COEUR is set up on the principle that biospecimens will be openly shared, so applicants must be willing to deposit results and data in the COEUR repository at the end of the study.

#### **Key Publications:**

- Characteristics and outcome of the COEUR Canadian validation cohort for ovarian cancer biomarkers. BMC Cancer. 2018 Mar 27;18(1):347. PMID: 29587661
- Specimen quality evaluation in Canadian biobanks participating in the COEUR repository. *Biopreserv Biobank.* 2013 Apr;11(2):83-93. PMID: <u>24845429</u>

To submit your application, or for more information, please contact <u>biobanque.cr.chum@ssss.gouv.qc.ca</u>

#### **COEUR Repository Snapshot**

#### *Includes different types of OC:*

- ✓ High-grade serous carcinoma
- ✓ Low-grade serous carcinoma
- ✓ Endometrioid carcinoma
- ✓ Clear cell carcinoma
- Mucinous carcinoma

# Includes different biological materials:

- ✓ Formalin-fixed paraffinembedded (FFPE) tissue
- ✓ Frozen tissue
- ✓ Blood DNA
- ✓ Serum
- ✓ Plasma
- ✓ Ascites fluid
- Tissue microarrays (TMA)

### **Patient-derived xenografts (PDX)**



Lab	Description	N	Origin	Take Rates	Tumour Growth Kinetics	Characterization to date	Clinical Outcomes
Ailles/ Princess Margaret Living Biobank	HGSC PDX models (established)	49	Princess Margaret Cancer Centre, surgical patients	100%	3-6 months to reach 1.5 cm	Targeted DNA panel, copy number and transcriptome (microarray) on 39 models	Known
Postovit	HGSC PDX	4	Oncotest and ACRB	68- 80%	3-6 months to reach 1.5 cm	RNA and DNA sequencing, hypoxia	Known
Rodier/ Stagg	HGSC PDX-TILs (matched TILs, peripheral PBMC + tissue)	6	CHUM, surgical patients	100% fresh tissue	3-6 months to reach 150mm <sup>2</sup>	Clinical genetic panels, BRCA1/2 mutation status available, pathology confirmation in progress	Known

PBMC: peripheral blood mononuclear cell; TILs: tumour-infiltrating lymphocytes.

Snapshot of mutations in Princess Margaret Living Biobank PDX

Total by		Co-Mutations							
gene*	TP53	BRCA1	BRCA2						
<i>TP53</i> (N=30)	n=21 <i>TP53</i> only	n=4	n=5						
<i>BRCA1</i> (N=5)	n=4	n=1 <i>BRCA1</i> only	n=0						
<i>BRCA2</i> (N=7)	n=5	n=0	n=2 <i>BRCA2</i> only						

Additional PDX available through Mes-Masson/Provencher lab (HGSC, pg 4-5) and Carey/Lee lab (LGSC, pg 6-7)

### Syngeneic mouse models: High-grade serous cancer (HGSC)



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Lab	Name	Mouse Strain	Known Mutations	Origin	Tumorigenicity (Median Survival)	Charact	erization	References (PMID)
Vanderhyden <sup>#</sup> (+ collaborations	*ID8-C3 (control)	C57BL/6	Wild-type	Ovarian surface epithelium	N/A (101 days)	Sensitivity to platinum, PARP	Multiplexed flow cytometry for	<u>27530326; 36311166;</u> <u>37957414</u>
with Petrik lab)	ID8-F3	C57BL/6	Trp53-/-		IP/IB (46 days)	L1, VSV-d51	(tumour, ascites); cytokine profiling	<u>27530326; 36311166;</u> <u>37957414</u>
	ID8	C57BL/6	Trp53-/-; Brca2-/-		IP (80 days)		(ascites); RNA-Seq (lines, IB tumours, ascites): multi-	<u>27530326; 36311166;</u> <u>37957414</u>
	ID8 C57BL/6   ID8 C57BL/6   ID8 C57BL/6	C57BL/6	Trp53-/-; Brca1-/-		IP (47 days)	Sensitivity to platinum and PARP	plexed IF (tumours)	<u>29203787; 36311166;</u> <u>37957414</u>
		C57BL/6	Trp53-/-; Nf1-/-		IP (36.5 days)	inhibition		<u>29203787; 37957414</u>
		C57BL/6	Trp53-/-; Pten-/-		IP (34 days)			<u>29203787; 37957414</u>
	ID8	C57BL/6	Trp53-/-; Brca2-/-; Pten-/-		IP (40 days)			<u>29203787</u>
Petrik	ID8	C57BL/6	Trp53R273H	ID8 ascites	IB (??)	Genomic analysis		<u>27329838</u>
Vanderhyden	STOSE	FVB/N	None known (no Trp53 mutations)	Ovarian surface epithelium	IP/IB (70 days)	Cytokine profiling (ascites); RNA-Seq (lines, IB tumours, ascites); multi- plexed IF (tumours)	Single-cell RNA-Seq data on orthotopic tumours; WES; sensitivity to platinum, PARP inhibition, anti-PD- L1, VSV-d51	<u>24672774; 36311166;</u> <u>37957414</u>
				STOSE ascites (A12-2)	N/A			<u>37957414</u>
				STOSE ascites (A12-3)	IP (45 days)			
			S	STOSE ascites (1506)	IP (36 days)	RNA-Seq (lines)		
				STOSE ascites (1508)	IP (36 days)	RNA-Seq (lines)		

### Syngeneic mouse models: HGSC, continued



Lab	Name	Mouse Strain	Known Mutations	Origin	Tumorigenicity (Median Survival)	Characterization	References (PMID)
Stanford	MOSE line**	HHD (HLA- A2 transgenic) on C57BL/6	none	Ovarian surface epithelium	SC and IB (40 days)	Data on efficacy of immunotherapy and imaging studies	
Vanderhyden	Vanderhyden MOE-PTEN		Pten shRNA	Oviductal	N/A	N/A	<u>36311166; 37957414</u>
MOE-PTEN/p53		FVB/N	Pten shRNA; Trp53 <sup>R273H</sup>	epithelium	N/A	Sensitivity to platinum, PARP inhibition,	<u>36311166; 37957414</u>
	MOE-PTEN/ KRAS	FVB/N	Pten shRNA; KRAS <sup>G12D</sup>		N/A	anti-PD-L1, VSV-d51	<u>36311166; 37957414</u>
Vanderhyden	OVE4/16	FVB/N		Oviductal		WES, RNA-Seq	<u>37957414</u>
	OVE	FVB/N	Pten shRNA; KRAS <sup>G12D</sup>	epithelium	Yes	Immunohistochemistry, Cytokine	<u>37957414</u>
	OVE4-Trp53 <sup>R273H</sup> OVE16-Trp53 <sup>R273H</sup>	FVB/N	Pten shRNA; Trp53 <sup>R273H</sup>		Yes	profiling (ascites); RNA-Seq (lines, IB tumours, ascites); multiplexed IF (tumours)	<u>37957414</u>
Petrik OVE4-Trp53-/- OVE16-Trp53-/-		FVB/N	Trp53-/-		Yes		<u>37957414; 37986175</u>
	OVE4-Trp53 <sup>R175H</sup> OVE16-Trp53 <sup>R175H</sup>	FVB/N	Trp53 <sup>R175H</sup>		Yes		

DC: dendritic cell; IB: intrabursal; IF: immunofluorescence; IP: intraperitoneal; N/A: data not available; OVA: ovalbumin; SC: subcutaneous; WES

<sup>#</sup>Vanderhyden lab has also created an ID8 line with stable ovalbumin (OVA) expression similar to that previously described by the Coukos lab (<u>23838316</u>); these have been tested *in vitro* and are able to activate OT-1 cells after 24-48 hours in co-culture.

\*ID8 lines originally from Iain McNeish lab. ID8 lines expressing reporter genes (Firefly and Gaussian Iuciferase, GFP, and mCherry) are also available from both the Vanderhyden and Koti labs <sup>&</sup>Originally from Joanna Burdette lab

\*\*derived cell line: MOSEHHD\_SVV MOSEHHD cell line transduced with mouse BIRC5 cDNA; tumorigenicity: SC, IB, and IP

### In the works



#### 2D and 3D culture

- ✓ New patient-derived LGSC lines (Carey)
- ✓ In vitro co-culture system to evaluate responses to immune checkpoint blockade (Stagg)
- ✓ 3D culture models of LGSC from patient specimens and established PDX (Carey/Shepherd)

#### **Patient-derived xenografts**

- Development and molecular characterization of SCCOHT and CCC PDXs (Huntsman)
- ✓ PDO-X models of OC (Petrik/Shepherd)
- ✓ Additional paired PDX + tumourinfiltrating lymphocytes (TILs) (Stagg, Rodier)

#### **Mouse models**

- Endometriosis-associated ovarian carcinomas: mouse model for premalignant lesion establishment and progress (Anglesio)
- Humanized natural killer cell competent mouse model for ovarian cancer (Boudreau)
- ✓ CCC and EC Metastasis Model (Huntsman)

#### **Resource papers**

- Histopathological characterization of the orthometastatic tumors formed by ovarian cancer cell lines of the OvCAN initiative (Telleria, QC)
- ✓ Multi-omics analysis of patient-derived cell lines in OvCAN Collection (Cook, Mes-Masson, Vanderhyden, Huntsman, Carey, Morin)

### Choosing the right model system





Recreated by Dr. Anne-Marie Mes-Masson from Boussommier-Calleja et al., *Trends in Cancer*, 2017

#### **Resource Papers**

- Le Page et al. Characteristics and outcome of the COEUR Canadian validation cohort for ovarian cancer biomarkers. PMID: <u>29587661</u>
- Sauriol et al. Modeling the Diversity of Epithelial Ovarian Cancer through Ten Novel Well Characterized Cell Lines Covering Multiple Subtypes of the Disease. PMID: <u>32784519</u>
- Yee et al. Three-Dimensional Modelling of Ovarian Cancer: From Cell Lines to Organoids for Discovery and Personalized Medicine. PMID: <u>35223797</u>
- Cook et al. Comparative analysis of syngeneic mouse models of high-grade serous ovarian cancer. PMID: <u>37957414</u>
- Pereira et al. Mutant p53 murine oviductal epithelial cells induce progression of high-grade serous carcinoma and are most sensitive to simvastatin therapy in vitro and in vivo. PMID: 37986175
- McCloskey et al. Ovarian Cancer Immunotherapy: Preclinical Models and Emerging Therapeutics. PMID: <u>30049987</u>
- Rodriguez et al. The Tumor Immune Profile of Murine Ovarian Cancer Models: An Essential Tool for Ovarian Cancer Immunotherapy Research. PMID: <u>36311166</u>

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# FYI coming soon: OvCAN Collection MMTA to facilitate sharing of ovarian cancer research models\*



# Upon signing of the master agreement at your institution, OCC will:

- Compile, share and update relevant information on Material and types of Model Data available in the OvCAN Collection, and contact information for Provider Scientist(s), as provided by Provider Scientist(s) to OCC on an annual basis
- Receive and review Material & Data Request Forms submitted by prospective Recipient(s) in a timely manner, sharing requests with Scientific Leaders and Provider(s) as appropriate, and ensuring that requests are in accordance with the Purpose and Permitted Use;
- Send all Implementing Email(s) to Provider(s) and Recipient(s) upon approval of requests;
- Solicit and compile annual progress reports from Recipient(s) on presentations and/or publications resulting from the use of transferred Material and Model Data, and updated information on Material and Model Data available for sharing from Provider(s);
- Reimburse reasonable costs incurred as a direct result of sharing Material and Model Data, as funding is available.

#### Providers of Material and Model Data shall:

- Provide Material and Model Data to Recipients in accordance with details provided in Implementing Email(s);
- Ensure Model Data is complete and accurate, to the best of their knowledge/ ability;
- Clearly indicate which Model Data is considered Confidential Information;
- Provide OCC with annual updates on Material and types of Model Data available for sharing.

#### **Recipients of Material and Model Data shall:**

- ✓ Provide proof of Research Ethics Board approval;
- ✓ Use Material and Model Data from Provider(s) in accordance with details provided in Implementing Email(s);
- ✓ Ensure that Confidential Information from Provider(s) is handled in accordance with Section 5 of this Agreement;
- Provide OCC with annual progress report on presentations and/or publications resulting from the use of transferred Material and Model Data, for the duration of the project.