SCCOHT Small cell carcinoma of ovary: histopathological fidelity between tissue and organoid

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INTRODUCTION

- The incidence of Small cell carcinoma of ovary hypercalcemic type (SCCOHT) is less than 0.01%. SCCOHT is associated with poor survival outcomes[1].
- Organoids are in –vitro 3D structures grown from stem cells , that self organize through lineage commitment; they recapitulate histological architecture and genetic alterations of original tumour[2].
- We wanted to assess the preservation of key histopathological and molecular features of organoids derived from a patient with SCCOHT.

METHODS

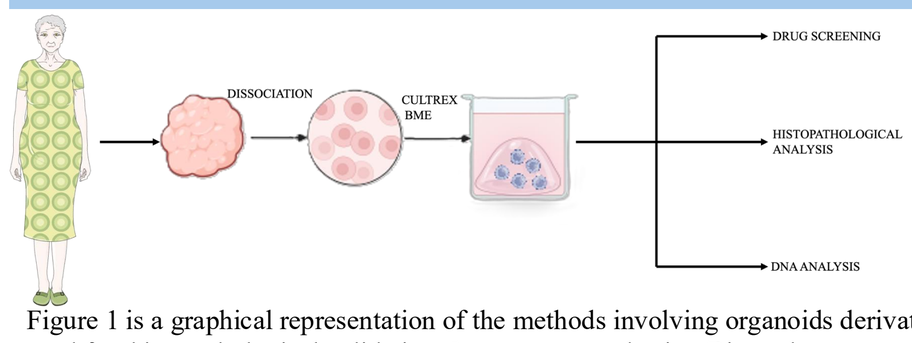

Figure 1 is a graphical representation of the methods involving organoids derivation and the workflow used for histopathological validation. Image generated using Biorender.com

RESULTS- Organoids retain histopathological fidelity to SCCOHT

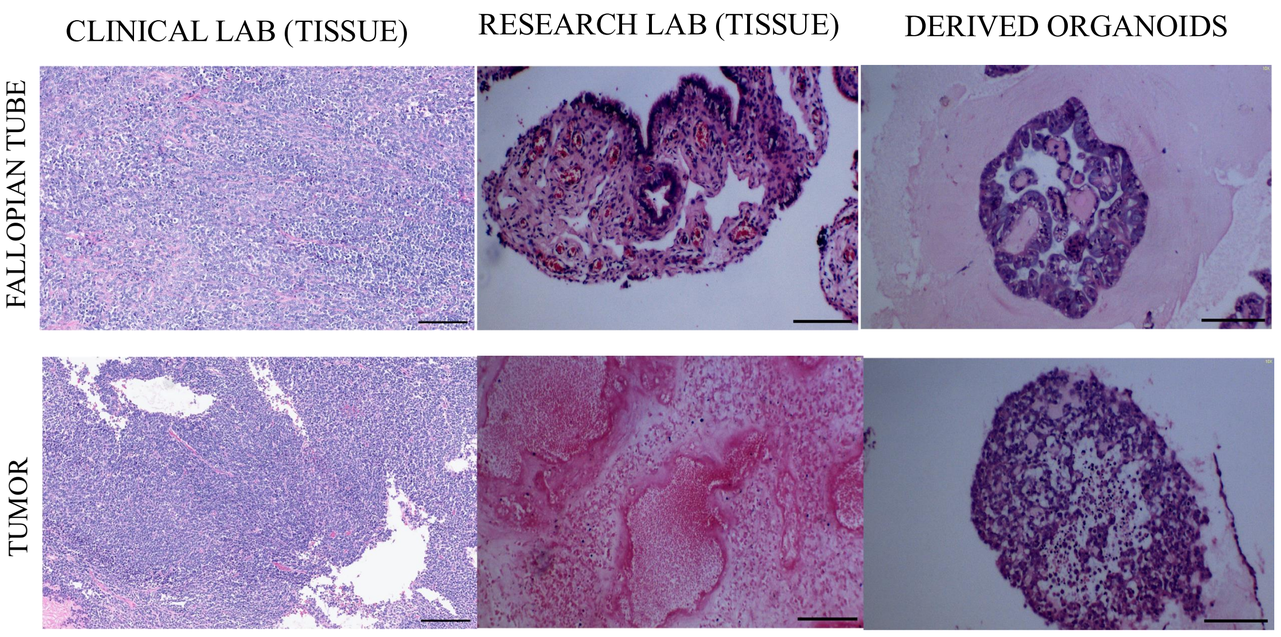

Figure 1 shows the H&E images of clinical diagnostic tissue samples, research lab stained tissue and organoid. All images were captured under 10X with scalebar 150 µm. The H&E stain of fallopian tube in clinical lab and research sample showed patchy areas of abnormal cells . The organoid counterpart showed lakes of glycoprotein surrounded by columnar cells . There were also nests of cells with hyperchromatic nuclei. The H&E stain of tumour in clinical lab and showed discohesive sheets of cells with high mitotic activity. The organoid counterpart (F) formed discohesive sheets of clumped cells with hyperchromatic nuclei. (All images – 10X objective and 150 µm scalebar).

RESULTS

- A 42year old lady with a background of endometriosis presented with rectal pain and rectal bleeding. An MRI pelvis and abdomen with contrast showed 16cm right adnexal mass, with ascites and peritoneal carcinomatosis.
- CA 125 level was 335kU/L and serum calcium level was 2.49mmol/L.
- Laparotomy and right salpingo-oophorectomy, omentectomy and peritoneal biopsy was performed (fertility conserving procedure).
- Research samples were taken from fimbrial end of the fallopian tube and the tumour.
- Figure 1 demonstrates the H&E stain of diagnostic tissue lab in clinical histopathological lab and in the research lab compared with the derived organoids.
- Table 1 and Figure 2 show the immunohistochemical diagnostic stains performed clinically.
- Comparative histological assessment demonstrated close concordance between primary tumour and organoid architecture, supported by PAX8 immunohistochemistry.
- Figure 3 is the PAX8 IHC mages of tissue and the organoids stained in the research lab.

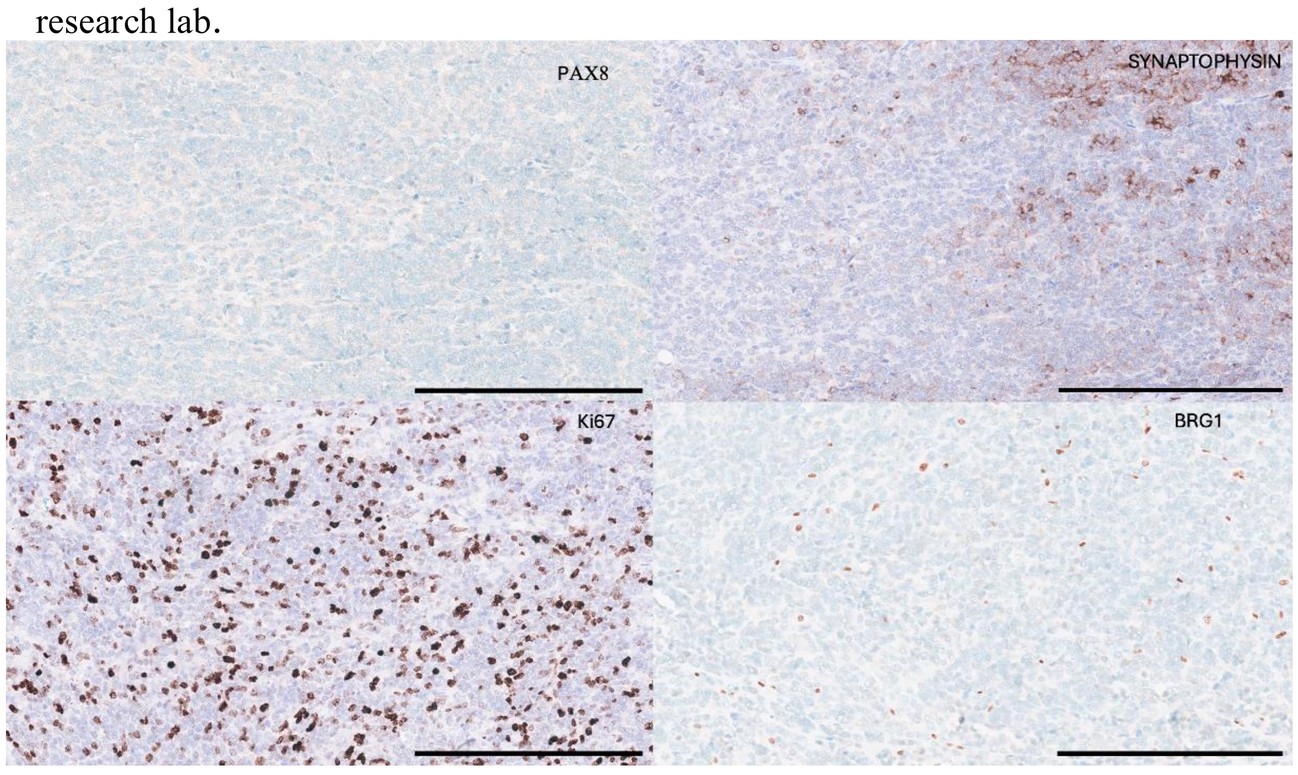

Figure 2 shows the clinical diagnostic immunohistochemical workflow of the tumour. This high grade malignant neoplasm stained negative for tumour of Mullerian origin (PAX8) ,with positive focal neuroendocrine marker (Synaptophysin) and positive proliferative marker (Ki67) (proliferation index 70-90%). The subsequent loss of SMARCA4 (BRG1) expression confirmed the diagnosis. All images – 20X Objective , 150 µm scalebar.

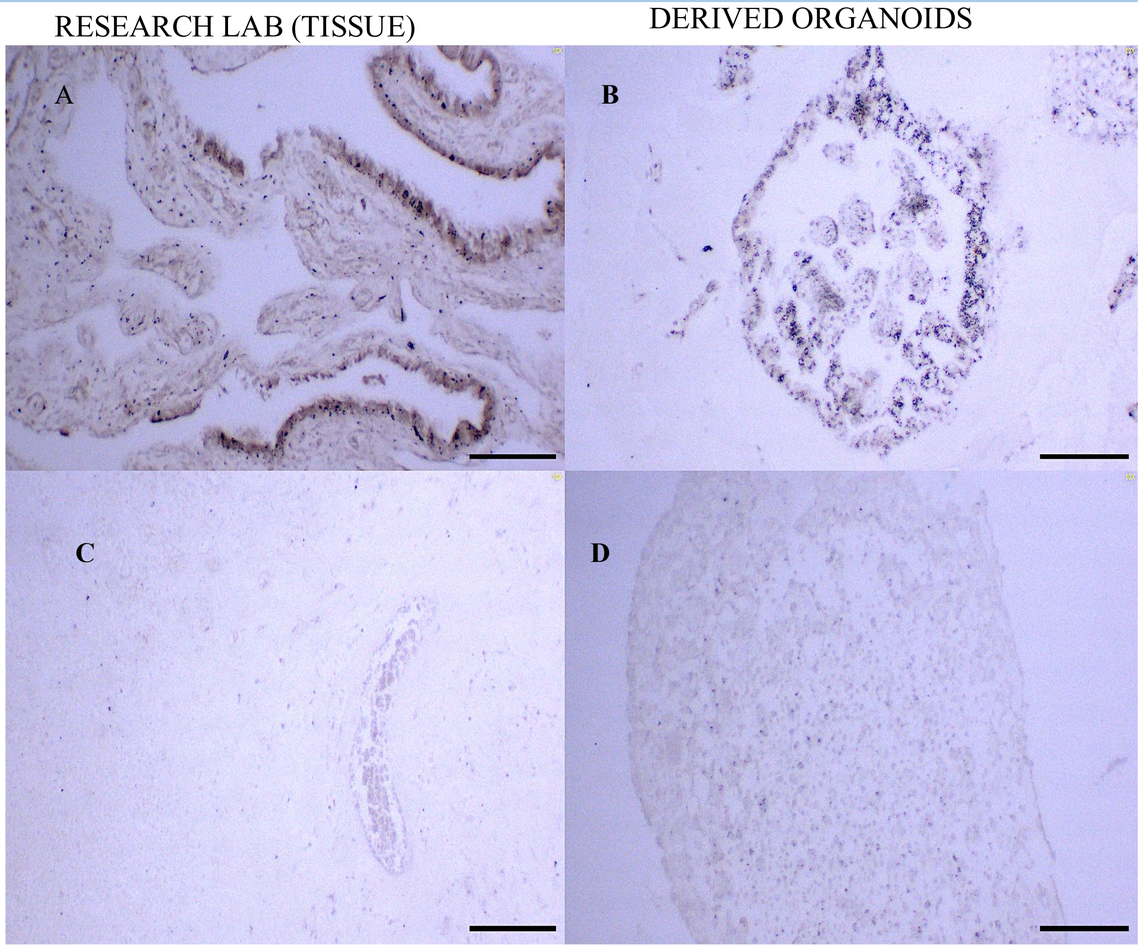

Figure 3 shows the PAX8 immunohistochemical staining results in our research lab and organoids. The images A (Tissue) and B (Organoid) represent the PAX8 staining of Fallopian tube . The images C (Tissue) and D (Organoid) represent the PAX8 staining of tumour tissue. All images – 10X objective , 150 µm scalebar.

Table 1 shows the immunohistochemical clinical diagnostic staining profile of the donor

Immunochemical stain type	Staining expression and distribution	Marker
Lineage markers	Strong diffuse	WT1
	Positive focal	EMA, MNF116
	Negative	PAX8, CK7, CK20
Proliferation marker	Strong positive	Ki67
Hormonal markers	Negative	ER, PR
Tumor suppressor marker	Wild type	p53
Neuroendocrine markers	Positive focal	Synaptophysin
	Negative	Chromograffin
Molecular markers	Positive	MMR Proficient
	Negative	SMARCA4
Germ cell markers	Negative	OCT 3/ 4, PLAP, AFP, HCG

CONCLUSIONS

- SCCOHT remains an aggressive tumour with diagnostic and management challenges.
- Rare and aggressive ovarian malignancy can be modelled ex vivo while retaining defining pathological and molecular features.
- In vitro research models which use small sample cells can be used to study rare cancer types , where disease scarcity has limited biological

REFERENCES

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