

Efficacy of carboplatin against Clear Cell Ovarian Carcinoma is improved by inhibition of glycogen utilisation



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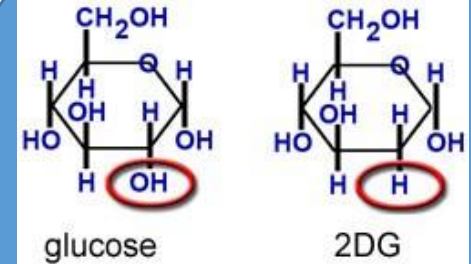
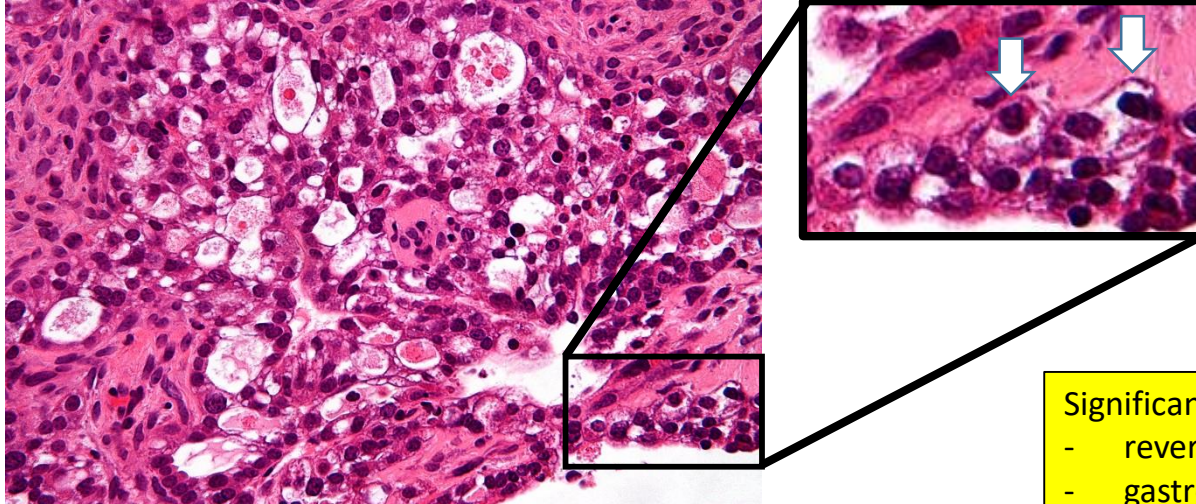
³Mater Health Services, Brisbane

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Clear Cell Ovarian Cancer



**2-Deoxy-D-glucose
(2-DG)**

- “clear” cell histology may promote resistance

- Store of Glycogen (glucose polymer)
- Can be mobilised to provide an alternate energy source during periods of stress; including treatment with chemotherapy

Significant adverse effects at 63-88 mg/kg/day

- reversible hyperglycemia (100%)
- gastrointestinal bleeding (6%)
- reversible grade 3 QTc prolongation (22 %).

Targeting glycogen in Clear Cell Ovarian Cancer:



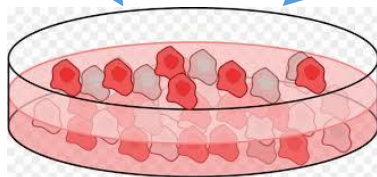
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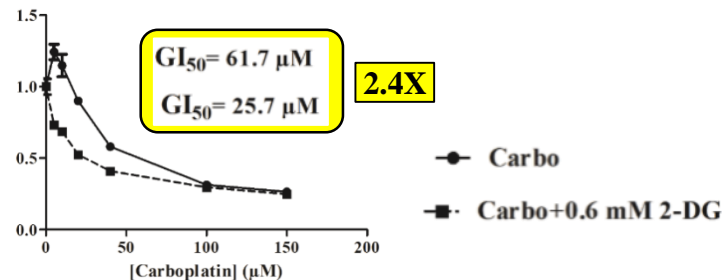
In Vitro Data

Increasing
Carboplatin
Concentration
0 to 200 μM

Constant **2-DG**
MTD = 63
mg/kg/day
($C_{\text{max}} \sim 0.6 \text{ mM}$)

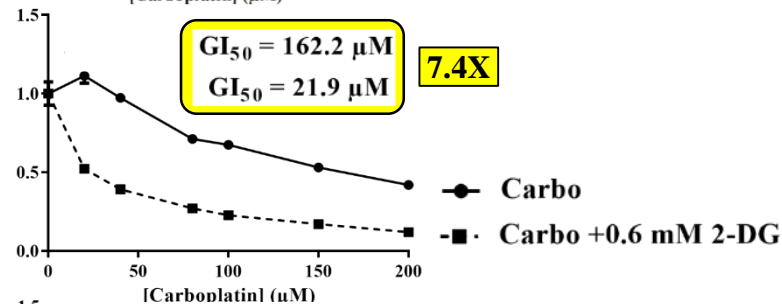


TOV21G
(chemo-
sensitive)

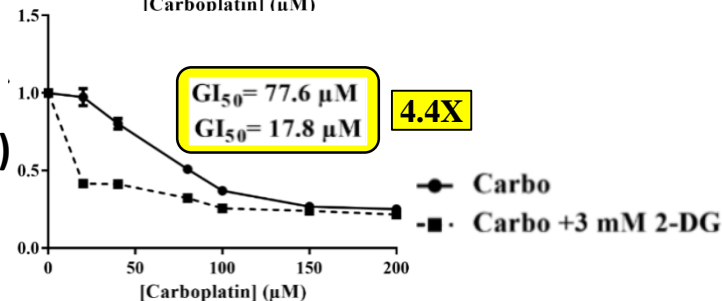


72 h

OVTOKO
(chemo-
resistant)



KOC7C
(chemo-
refractory)



Targeting glycogen in Clear Cell Ovarian Cancer:

In Vivo Data



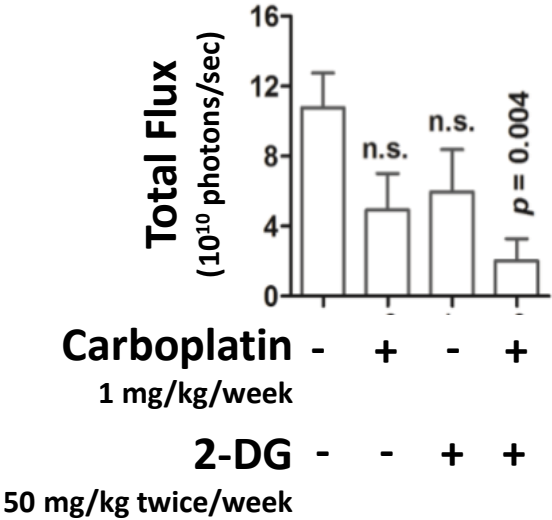
Intraperitoneal injection of cells
Treatments start 2 weeks later

2-DG MTD

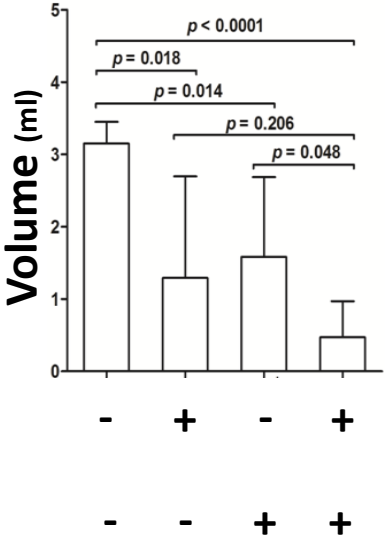
63 mg/kg/day
= ~800 mg/kg/day in mice

TOV21G (chemo-sensitive)

TUMOUR BURDEN



ASCITES



KOC7C
(chemo-refractory)

PH250
Recurrent
Grade 3

PH138
Stage 1C
Grade 3



Conclusions:

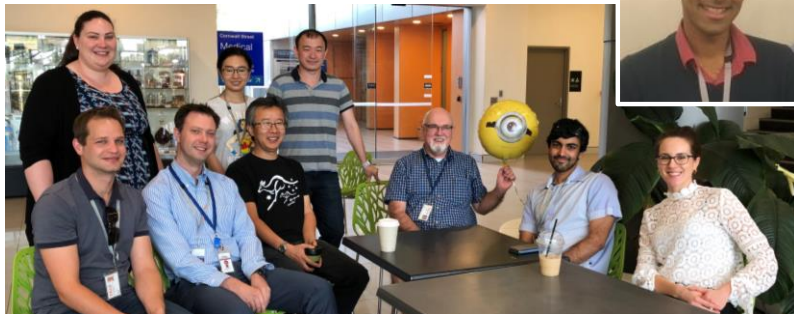
- Clear Cell OvCa is often resistant to platinum-based chemotherapies (especially recurrent and late-stage disease)
- *Our data suggest that combining carbo with an inhibitor of glycogen utilisation (such as 2-DG) could benefit patients*

ACKNOWLEDGEMENTS



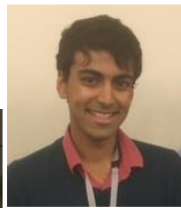
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Hooper Laboratory

Dr Paul Haluska & Dr John
Weroha, Mayo Clinic



Mater Ovarian Cancer Research Collaborative
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Faculty Disclosure

| | |
|---|-------------------------|
| | No, nothing to disclose |
| X | Yes, please specify: |

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|--------------|--------------------------------|---|----------------------------|------------------------------|--------------------------|--|-----------------|-----------------------------------|
| Astra Zeneca | | | X | | | | | |
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