Chemoresistance to paclitaxel induces EMT in different types of ovarian carcinoma tumors

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Introduction
Ovarian cancer 140,000 deaths/year worldwide 45% of survival
Lack of measurable early symptoms Advanced stage at diagnosis

Treatment Removal/debulking surgery Paclitaxel + cisplatin chemotherapy
Chemoresistance EMT
Epithelial-mesenchymal transition (EMT) Metastasis

Hypothesis and Objectives
The chemoresistance to paclitaxel promotes the epithelial-mesenchymal transition in the four main epithelial ovarian tumor types by the upregulation of the transcription factors that repress E-cadherin.

Chemoresistance to paclitaxel ↑ Snail, Slug, Twist1, Zeb1 and Zeb2 ↓ E-cadherin EMT

Material and methods
• Human cell lines Serous ovarian adenocarcinoma from ascites (OV17R)
Mucinous ovarian carcinoma (COV644)
Endometrioid ovarian carcinoma (COV362)
Clear cell ovarian carcinoma (ES-2)
• Establishment of paclitaxel resistance and chemosensitivity assay: IC50
• Proliferation: MTT assay
• Anchorage-independent growth: Soft agar assay Immunofluorescence
• Invasion: Boyden chamber assay Western Blot
• Migration: Wound-healing assay Statistical analysis

Expected results
<table>
<thead>
<tr>
<th>Chemosensitive cells</th>
<th>Chemosensitive cells</th>
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</thead>
<tbody>
<tr>
<td>Chemosensitivity</td>
<td>↓ IC50 ↑ IC50</td>
</tr>
<tr>
<td>Proliferation</td>
<td>↑ Cell number ↓ Cell number</td>
</tr>
<tr>
<td>Anchorage-independent growth</td>
<td>↓ Colonies ↑ Colonies</td>
</tr>
<tr>
<td>Invasion</td>
<td>↓ Cell invasion ↑ Cell invasion</td>
</tr>
<tr>
<td>Migration</td>
<td>↓ Cell migration ↑ Cell migration</td>
</tr>
<tr>
<td>Immunofluorescence</td>
<td>↓ E-cadherin, ↓ N-cadherin, ↓ Vimentin ↑ E-cadherin, ↑ N-cadherin, ↑ Vimentin</td>
</tr>
<tr>
<td>Western Blot</td>
<td>↓ Gene expression ↑ Gene expression</td>
</tr>
</tbody>
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Reference

Benefits
A better understanding of the mechanisms that underlie the chemoresistance by which tumor cells survive treatment could lead to the identification of novel therapeutic targets and development of an appropriate therapy for certain cancers, like ovarian carcinoma, for which the early detection is still a barrier.