

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

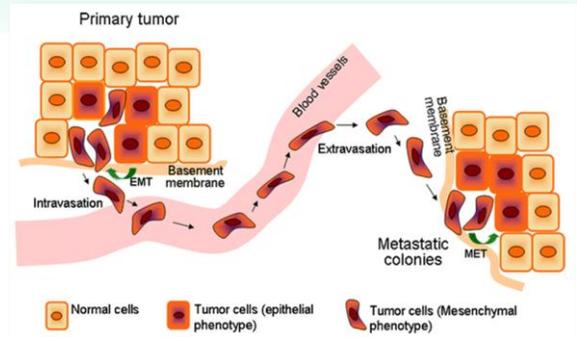
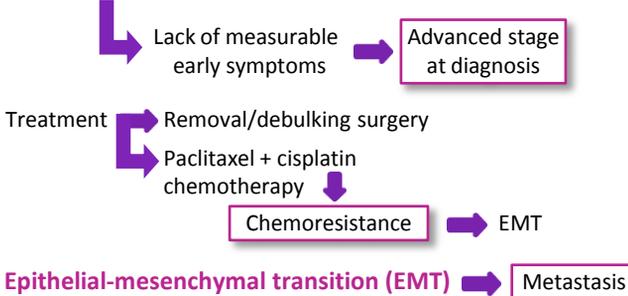


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## Introduction

**Ovarian cancer** 140.000 deaths/year worldwide 45% of survival



**Fig. 1** Epithelial-mesenchymal transition process in cancer: from a primary tumor epithelial cell to a motile mesenchymal cell. Meng F et al.

## 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  $\rightarrow$   $\uparrow$  Snail, Slug, Twist1, Zeb1 and Zeb2  $\rightarrow$   $\downarrow$  E-cadherin  $\rightarrow$  EMT

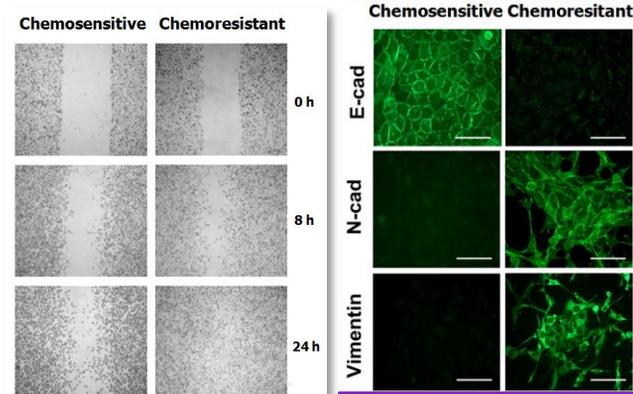
- Analyze paclitaxel resistant ovarian carcinoma cells: phenotype, migration, proliferation, gene expression.
- Determine if there is a relation between the activation of the transcription factors and the acquisition of paclitaxel chemoresistance.
- Compare the results of the different tumor types.

## 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
- Invasion: Boyden chamber assay
- Migration: Wound-healing assay
- Immunofluorescence
- Western Blot
- Statistical analysis

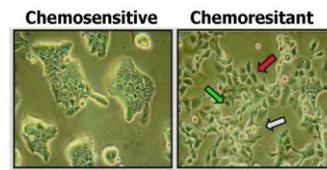
## Expected results

	Chemosensitive cells	Chemoresistant cells
Chemosensitivity	$\downarrow$ IC50	$\uparrow$ IC50
Proliferation	$\uparrow$ Cell number	$\downarrow$ Cell number
Anchorage-independent growth	$\downarrow$ Colonies	$\uparrow$ Colonies
Invasion	$\downarrow$ Cell invasion	$\uparrow$ Cell invasion
Migration	$\downarrow$ Cell migration	$\uparrow$ Cell migration
Immunofluorescence	$\uparrow$ E-cadherin, $\downarrow$ N-cadherin, $\downarrow$ Vimentin	$\downarrow$ E-cadherin, $\uparrow$ N-cadherin, $\uparrow$ Vimentin
Western Blot	$\downarrow$ Gene expression	$\uparrow$ Gene expression

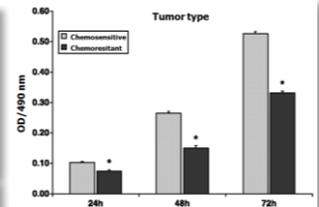


**Fig. 5** Wound healing assay. Modified from Yang YC et al.

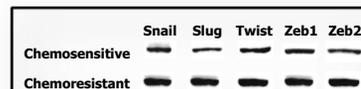
**Fig. 6** Immunofluorescence staining. Scale bars, 100  $\mu$ m. Modified from Evdokimova et al.



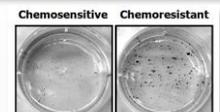
**Fig. 2** Morphologic changes. Spindle-cell shaped cells with loss of polarity (red), intercellular separation (green), and pseudopodia (white). x20 magnifications. Modified from Yang AD et al.



**Fig. 3** Proliferation assay. Modified from Yang AD et al.



**Fig. 7** Western Blot.



**Fig. 4** Soft Agar assay. Modified from Dallas et al.

## 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.

## References

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