

Ovarian cancer in Algeria: from epidemiology to potential treatment

1ST International Focus Workshop
on Ovarian and Cervical Cancer

6-7TH APRIL 2018 • MARRAKECH, MOROCCO

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Plan

- Epidemiological Overview of gynecological cancers in Algeria.
- Current therapy in ovarian cancer used in Algeria /challenges.
- Markers used for early Diagnosis for ovarian cancer patients /challenges
- TOC centers in Algeria (Structure and ongoing project)/Challenges.
- Treatment

Introduction

Ovarian Cancer



Epidemiological study:

- **Breast cancer is the most frequent gynecological cancer in young women in Algeria ...**
- **Ovarian cancer is the most lethal gynecological cancer in women in Algeria!!!!**
- **Cervical and endometrial cancers are most frequent in patients post menopause in Algeria,....**

The current treatment for patients with ovarian cancer

Ovarian cancer treatment

Lloyd Healthcare Pvt. Ltd.
[f](#) [t](#) [v](#) /lloydhealthcare



Surgery



Radiation

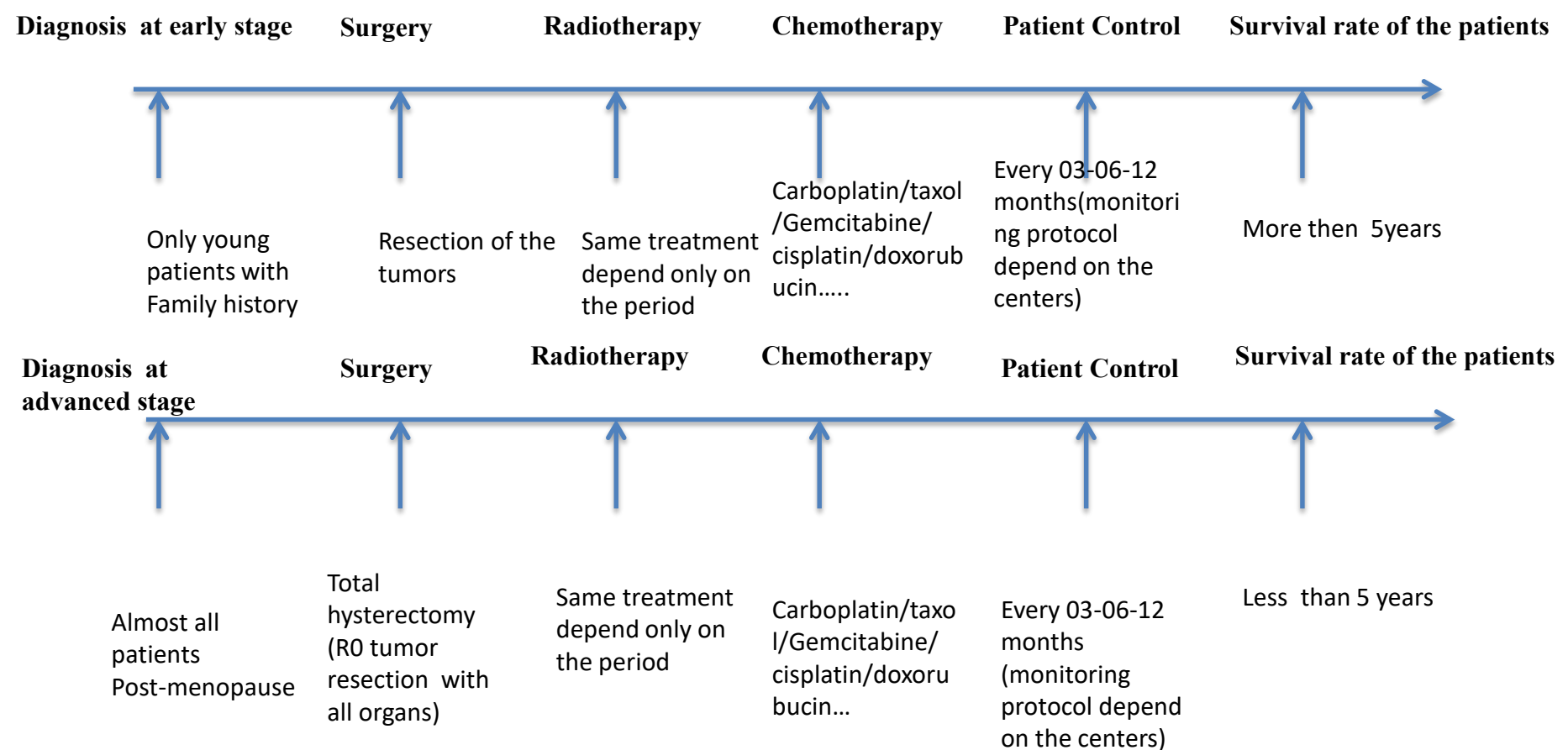


Chemotherapy

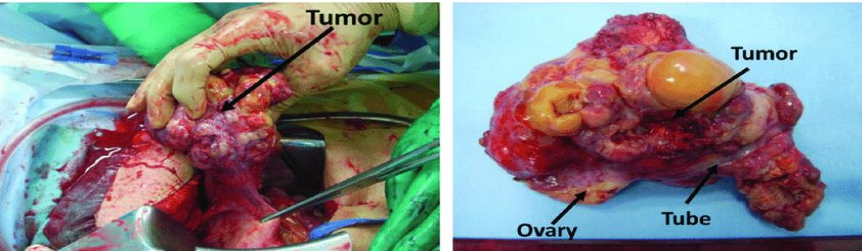
Ovarian cancer Diagnosis/challenges

- Diagnosis at late stage; increased abdominal volume and deterioration of the general conditions.
- Imagery Diagnosis : Duo Ultrasound and IRM
- Tumor markers : CA125 Ca19.9 AFP ACE
- Pre-therapeutic assessment
- The diagnosis of certainty is **histological**

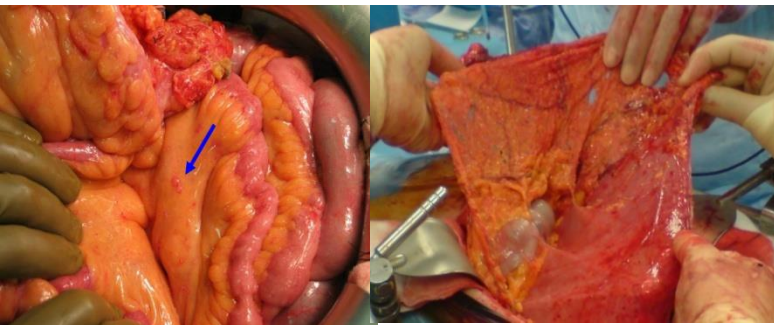
Ovarian cancer clinic



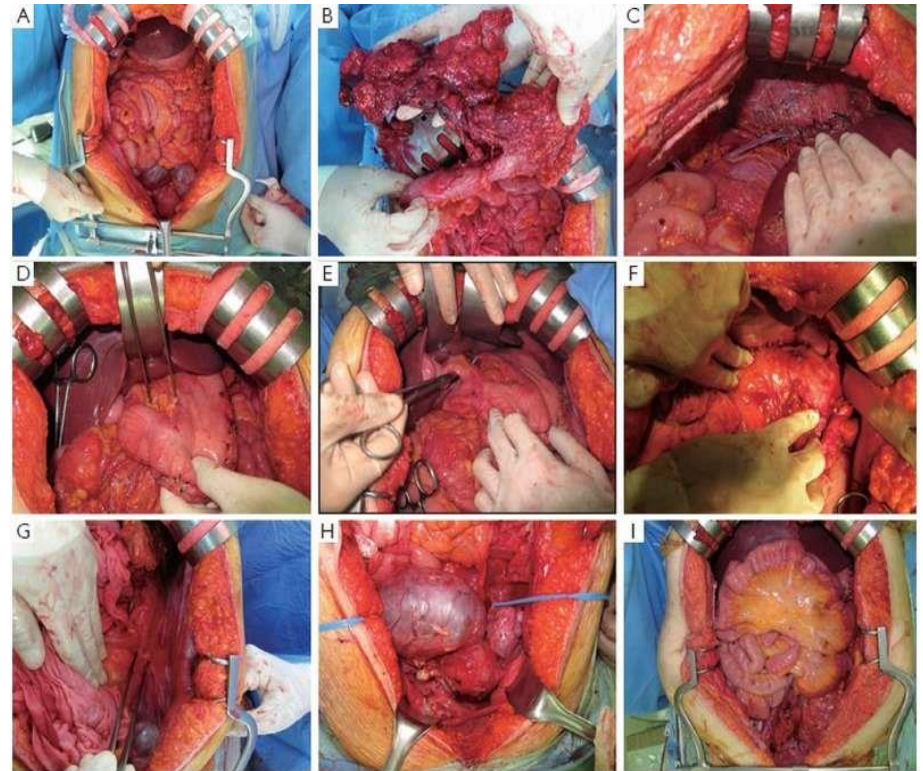
Surgery before/ after relapse in ovarian cancer patients



Annexectomy

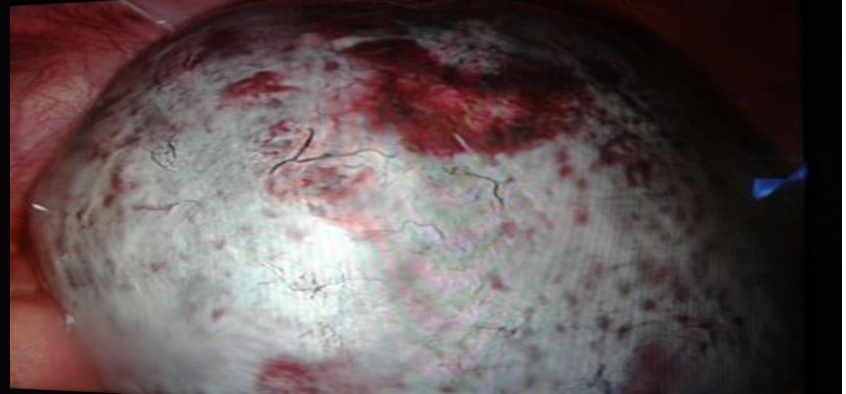


**Advanced stage
(metastasis) epiploic
nodule**

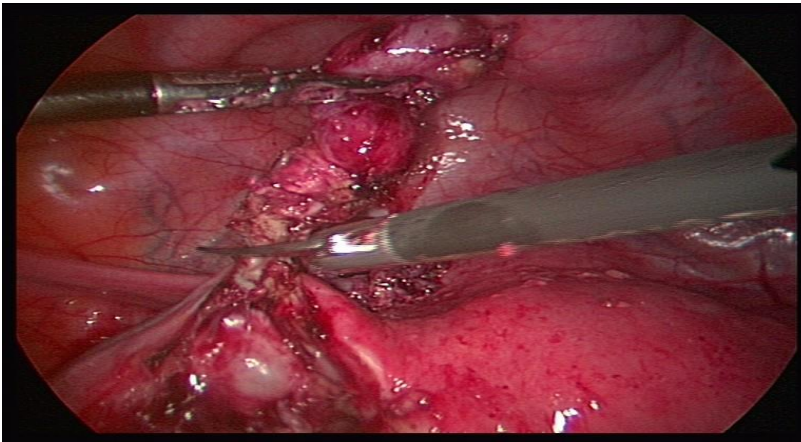


**Primary ovarian tumors (seen
from laparotomy, classic)**

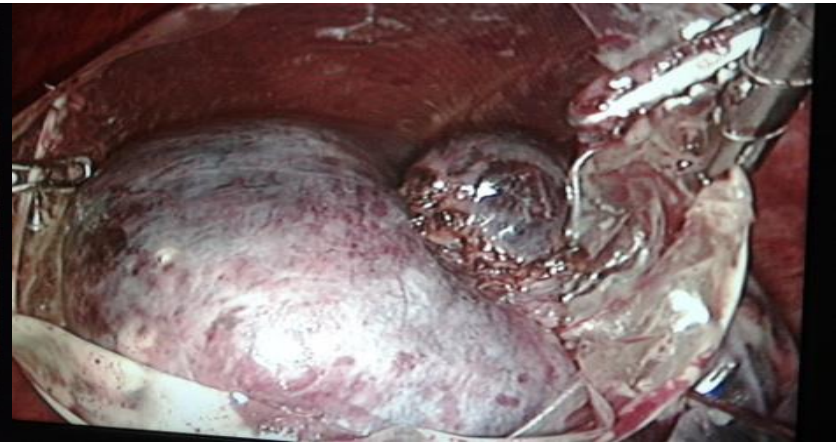
Surgery in patients with ovarian cancer



Ovarian tumors, laparoscopic view

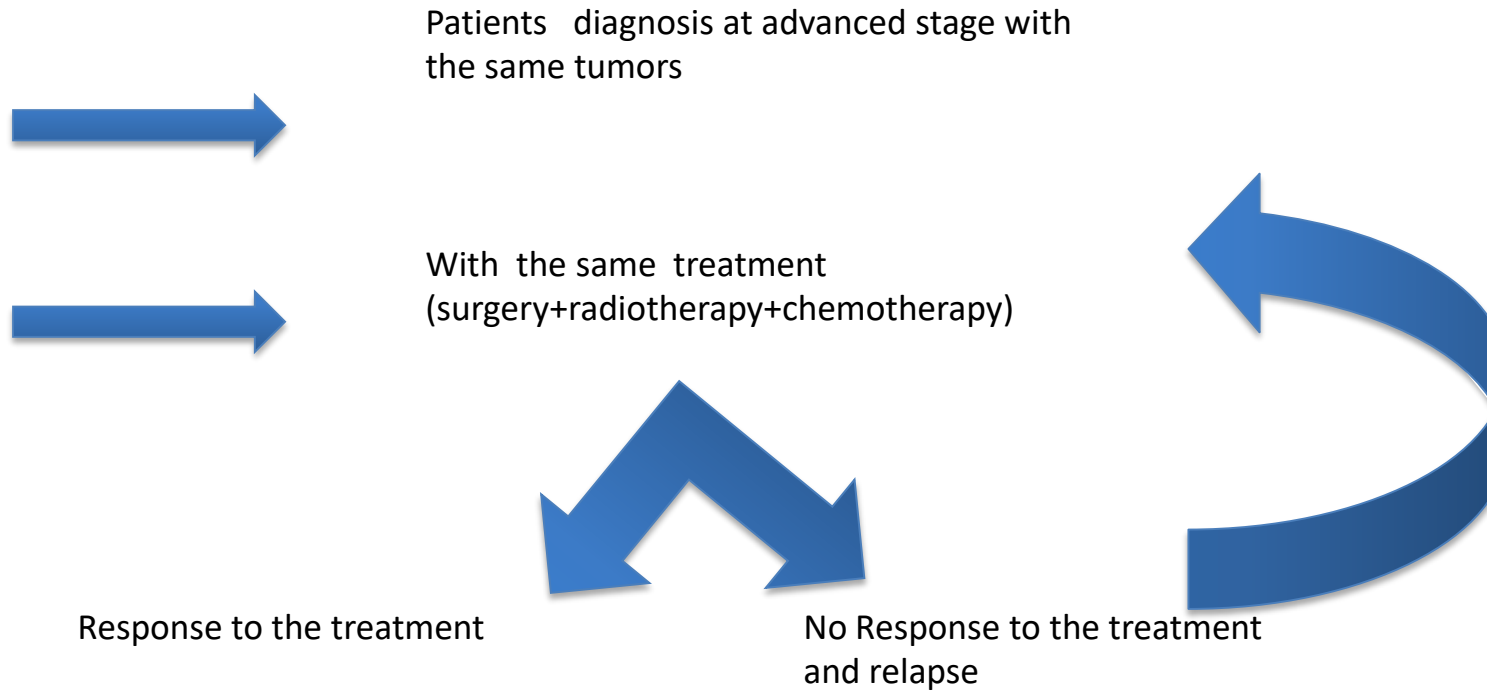


**Annexectomy,
laparoscopic view**



**Remove protected annexe by
endobag**

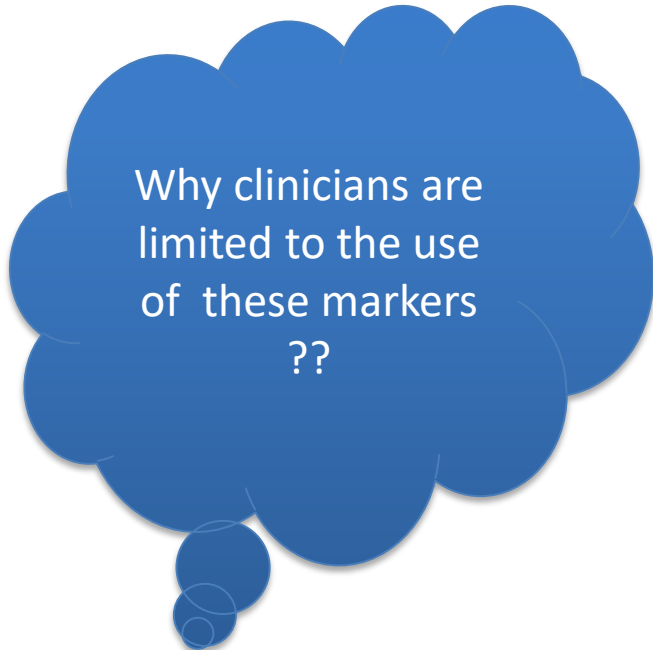
Challenges on ovarian cancer treatment



challenges for clinician in ovarian cancer treatment

Markers used for patients with ovarian cancer in Algeria /challenges

- **CA125- Cancer- Antigen 125.**
- **CA19-9 Cancer Antigen 19-9**
- **CEA Carcino Embryo Antigen**
 - **AFP Alpha Foeto Protein**



Why clinicians are limited to the use of these markers ??

TOC Centers in Algeria



TOC Centers in Algeria

- TOC center in Bejaia city

- Faculty of Medicine, University of Bejaia
- Gynecology Oncology Department, Khellil Amrane University Hospital, Bejaia

- TOC center in Algiers:

- Gynecology Obstetrics and Pathology Departments, Mustapha Pacha University Hospital, Algiers
- Anti Cancer Center, Pierre Marie Curie CPMC Algiers

TOC Centre in Algeria/ structure

Head of Gynecology Obstetric Departement Mustapha Pacha H/U

Prof. MD.Dr.ADDAD Bouzid

Head of Pathology Departement Mustapha Pacha H/U

Prof.MD.Dr.Amir

Head of Oncology Department CPMC Center Algiers

Prof.Kamel Bouzid

Deen of Faculty of Science in Bejaia Prof.Dr. Djebbar Atmani

**TOC-Coordinator
Imane CHARID**

Projects

Tumor bank

Data bank

Tech. support

Statistics

**Dr.GHIDOUCHE
Abderrazak
CHARID IMANE
PhD**



**CHARID IMANE
PhD
Dr.KhHIREDDINE Malek**

Data bank manager

**Electr. Data base/
Monitoring**

**PhD students
Researchers**

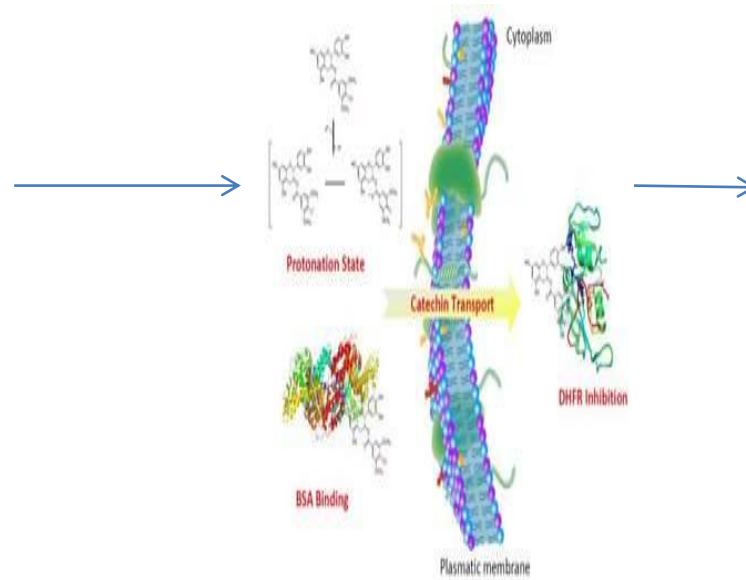
Documentation

Specimen Quality Control

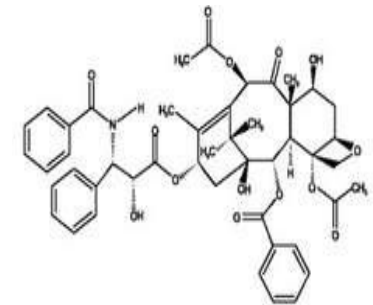
Research and ongoing project



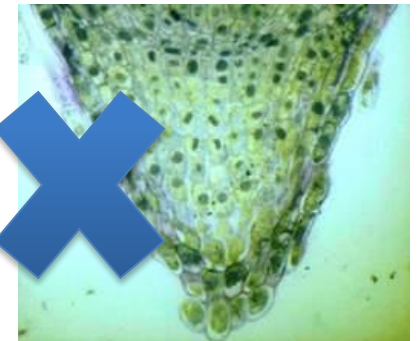
Medicinal plants



Phenolic compounds



Paclitaxel
Pure molecule



Cancer proliferation

From plants to molecules to stop cancer proliferation

Research and projects



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Kaempferol inhibits VEGF expression and *in vitro* angiogenesis through a novel ERK-NFκB-cMyc-p21 pathway

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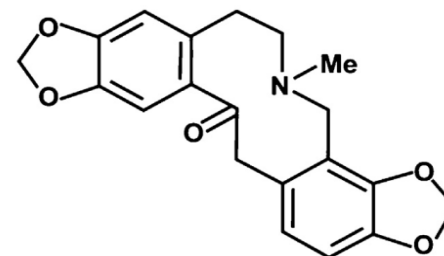
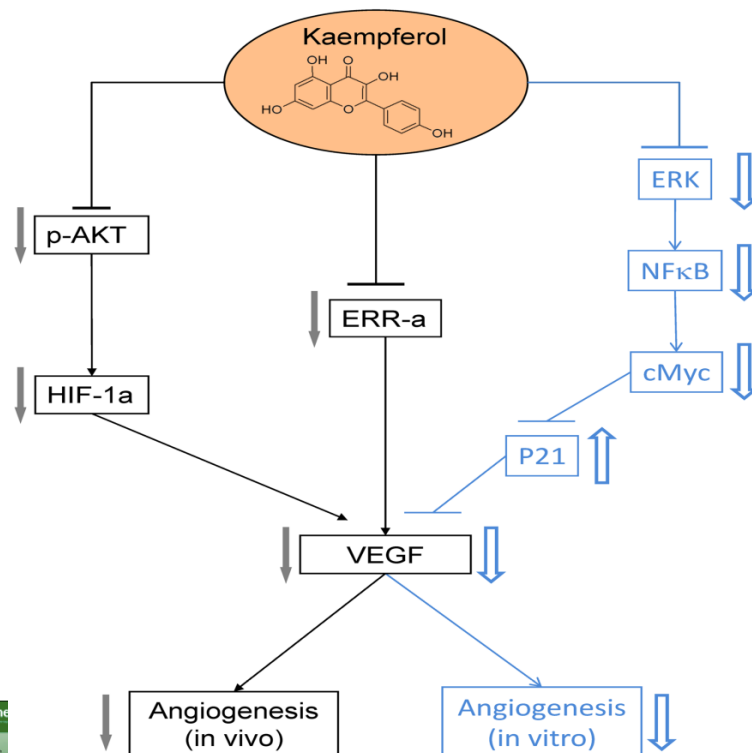
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journal homepage: www.elsevier.de/phytmed



ELSEVIER



1. Protopine

Revealing the anti-tumoral effect of Algerian *Glaucium flavum* roots against human cancer cells

Lamine Bournine^{a,b,c}, Sihem Bensalem^a, Paul Peixoto^b, Arnaud Gonzalez^b, Fadila Maiza-Benabdesselam^a, Fatiha Bedjou^a, Jean-Noël Wauters^c, Monique Tits^c, Michel Frédérick^c, Vincent Castronovo^b, Akeila Bellahcène^{b,*}

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^c Laboratory of Biochemistry, CIBM, University of Liège, Liège, Belgium



Research and ongoing projects

EBV reactivation as a target of luteolin to repress NPC tumorigenesis

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²National Institute of Infectious Diseases and Vaccinology, National Health Research Institutes, Tainan, Taiwan

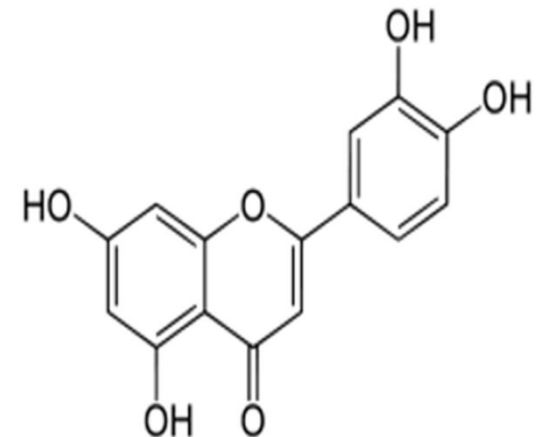
³Department of Microbiology, College of Medicine, National Taiwan University, Taipei, Taiwan

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Keywords: nasopharyngeal carcinoma, relapse, Epstein-Barr virus, reactivation, luteolin

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PLoS one

Acetonic Extract of *Buxus sempervirens* Induces Cell Cycle Arrest, Apoptosis and Autophagy in Breast Cancer Cells

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Sample collection and phenolic compounds extraction



Fraxinus angustifolia



Leaves of Fraxinus angustifolia



Pistacia lentiscus



Leaves of Pistacia lentiscus

**Extraction using organics solvents
Ethanol, Methanol, and Acetone**



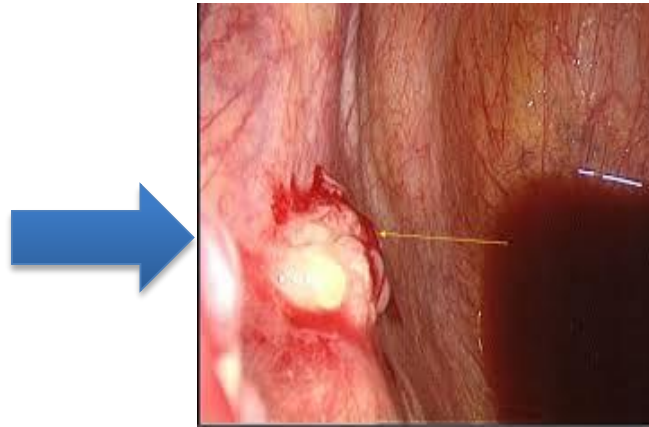
**Ethanolic, methanolic
and acetic
crude extracts**

(Atmani et al., 2009)

Establishment and characterization of primary ovarian cancer cells lines



Collect of tumors samples at the surgery

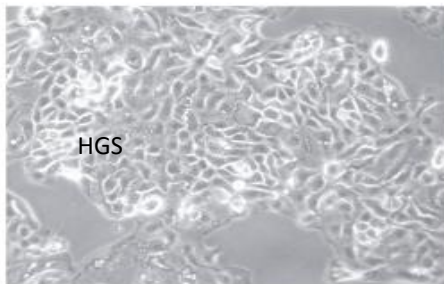


Collect fresh ascites from peritoneum of the patients With ovarian cancer

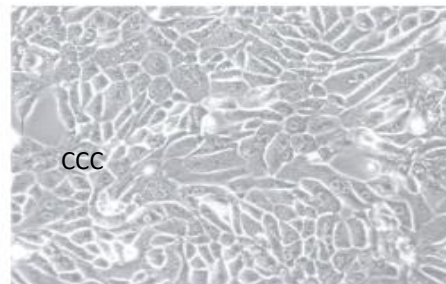


In vitro cancer cells lines

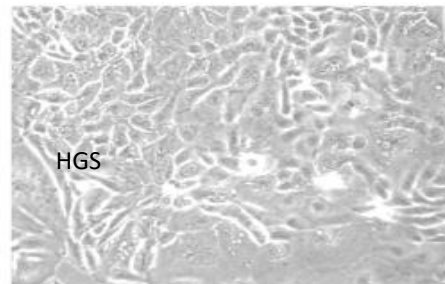
OCC48



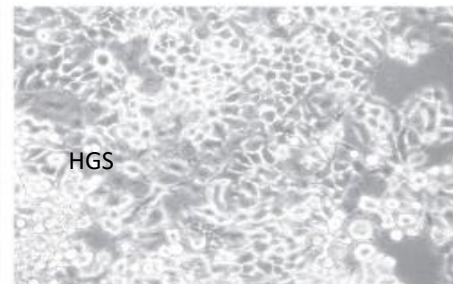
O2342



O2385

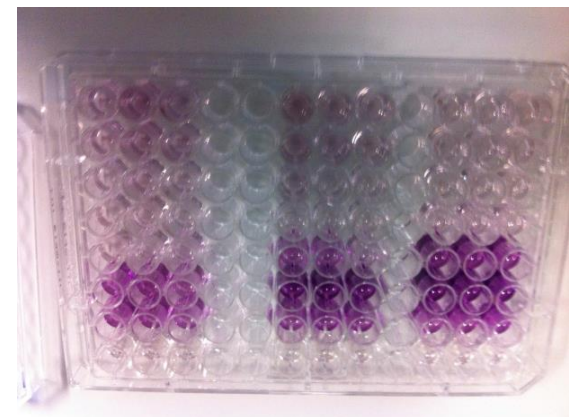
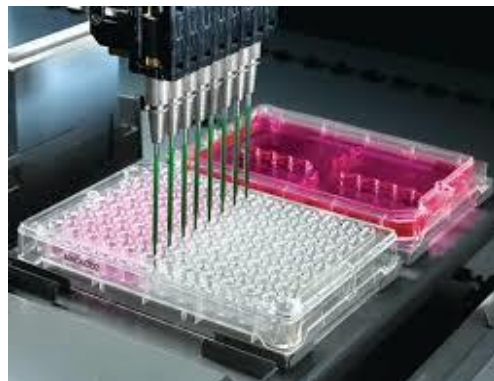
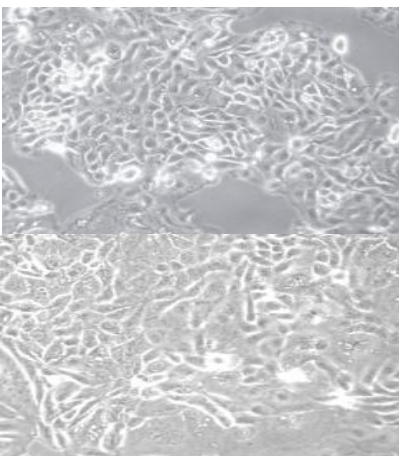


O2418



Four newly established and well characterized primary ovarian cancer cell lines

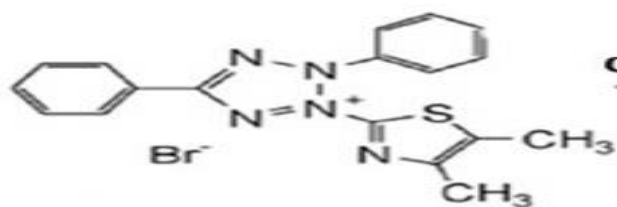
Cancer Cells Treatment



Primary ovarian
cancer cells
lines

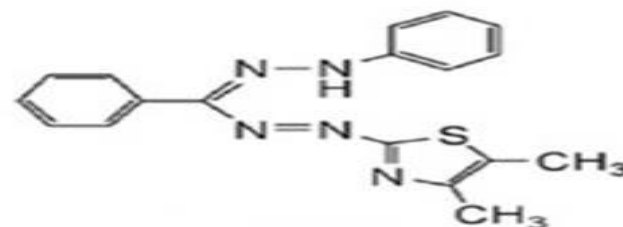
Treated with different
concentrations of extracts
alone or/ in combination
with Taxol/Carboplatin

Effect of the crude
extracts on ovarian
cancer cell lines



MTT

Succinate
dehydrogenase



MTT Formazan

Results

Primary ovarian cancer cell lines	OCC48	O2385	O2342	O2418
IC50 (µg/ml)	45	50	>100	>100

Table01: Proliferative activity in four primary ovarian cancer cell lines was determined after 72 hours treatment with MEPL using the WST-1 assay.

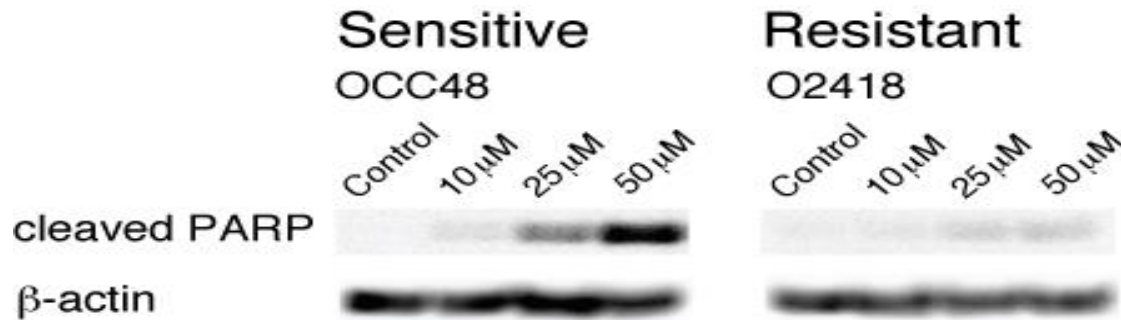


Figure 01: Apoptotic activity was assessed using cleaved-PARP as a marker of apoptosis by Western blot analysis in two representative HGS ovarian cancer cell lines after 48 hours treatment.

Effect in combination with carboplatin

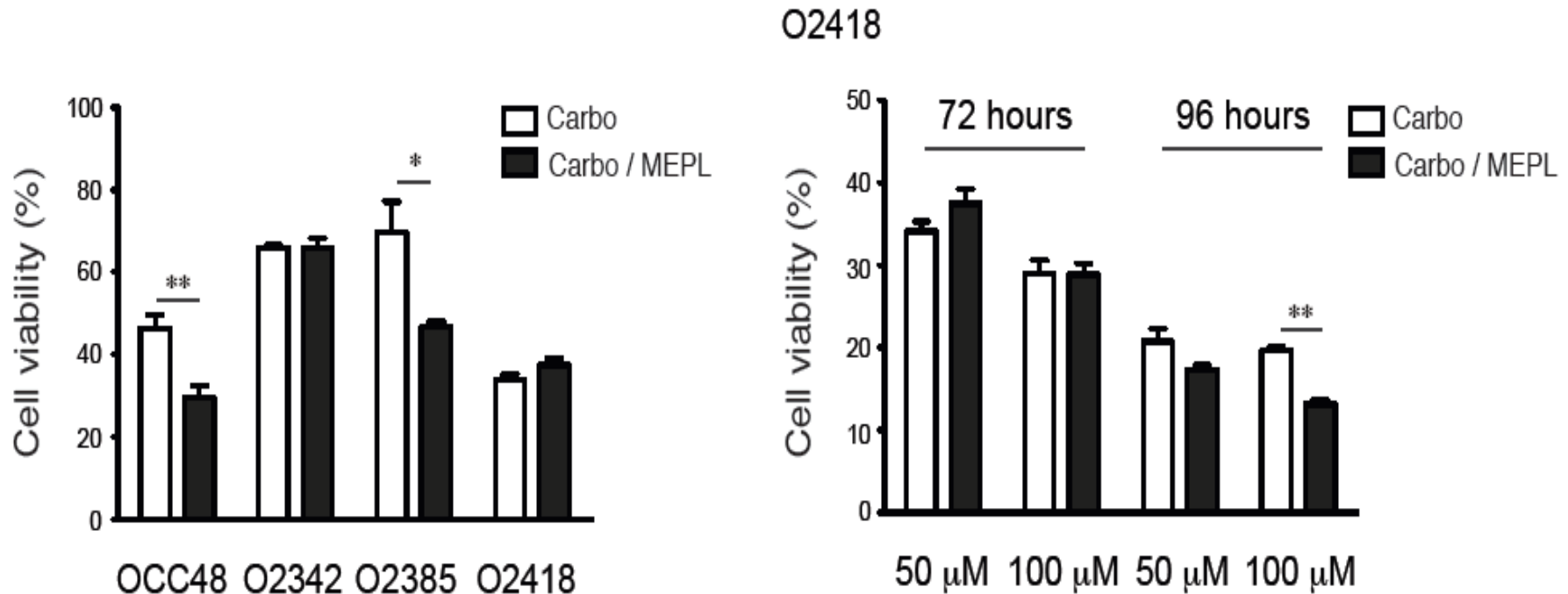


Figure 02: Effect of MEPL on chemosensitivity to carboplatin after pre-treatment with 50 μ g / ml of MEPL for 48 hours followed by 50 μ M incubation with carboplatin. Cell viability was assessed by cell counts after 72 or 96 hours treatment, respectively (mean $\pm$ SEM, **, $P < 0.01$, *, $P < 0.05$).

Effect on anti-inflammatory cytokine profiles

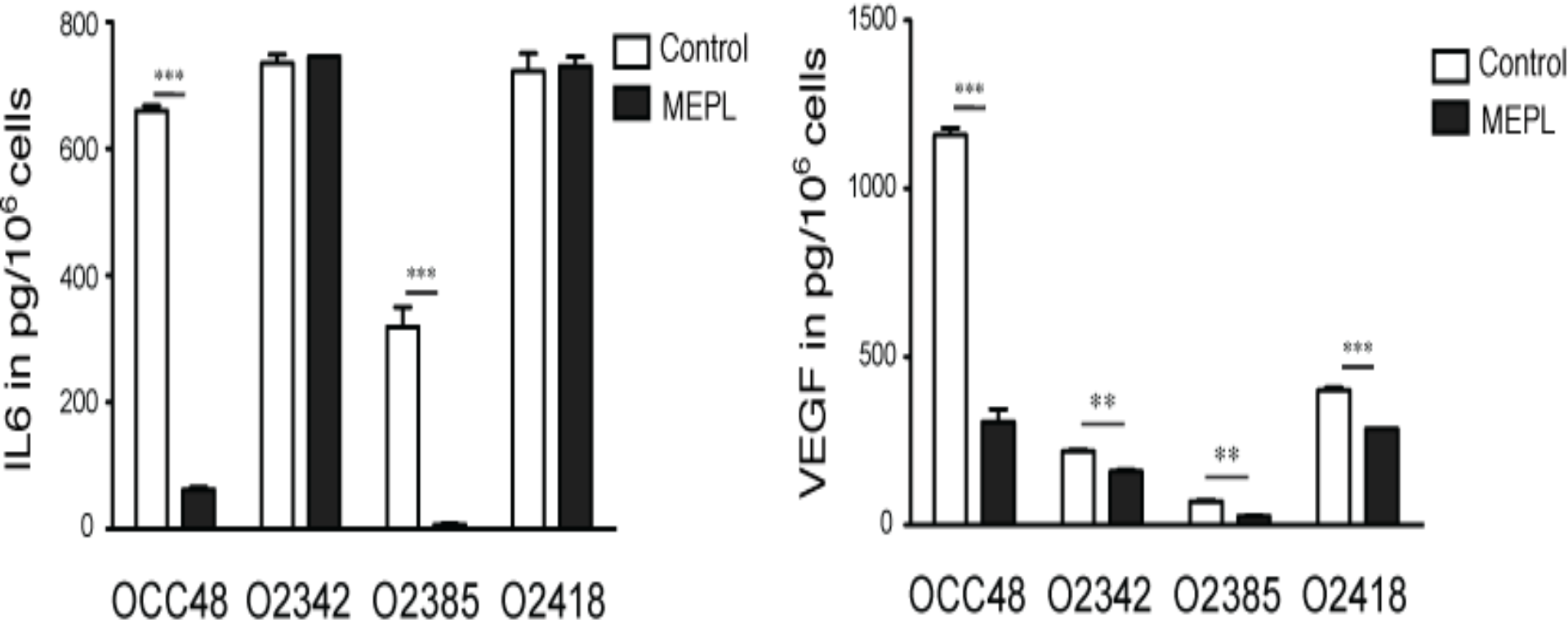


Figure 03: Interleukin 6 and growth factor expression levels were measured in cell culture supernatants after 48 hours treatment with 50 mg / ml of MEPL (mean $\pm$ SEM, ***, $P < 0.001$, **, $P < 0.01$)

Effect on signaling oncogenic pathways PI3k/AKT and MAPK/ERK

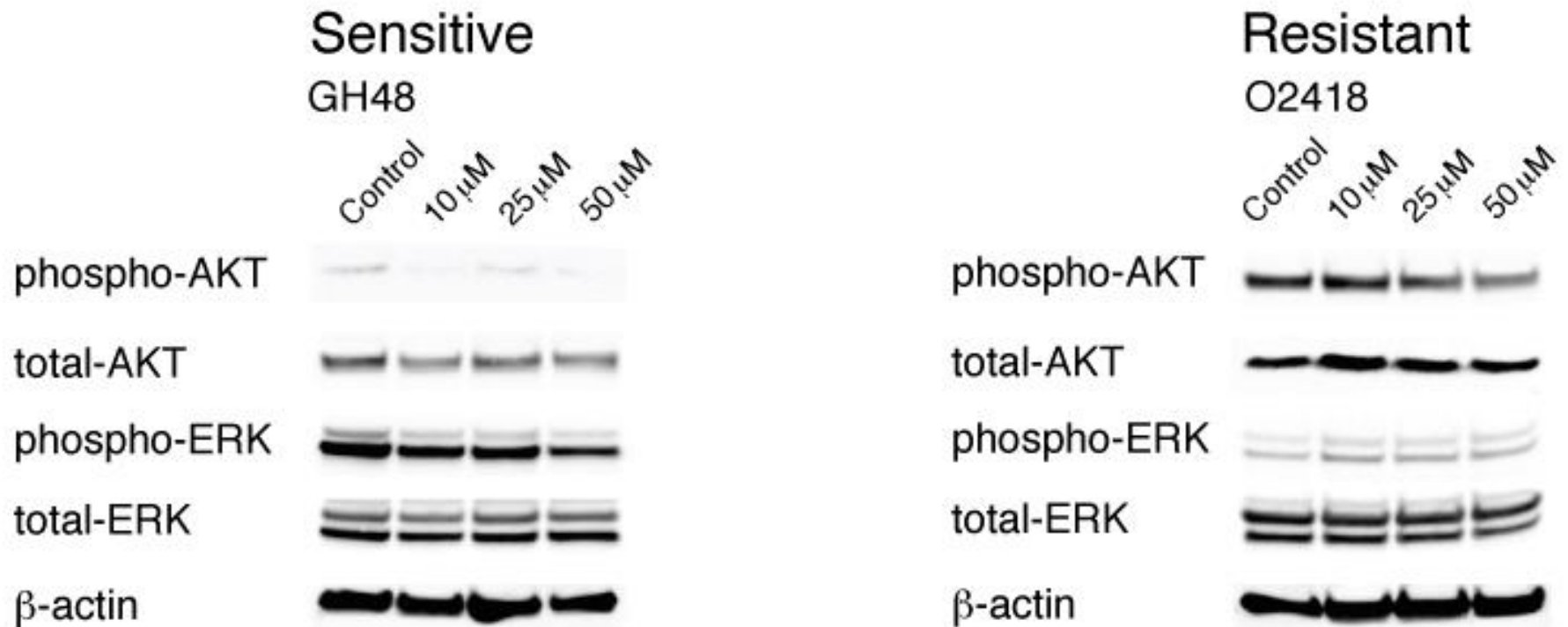
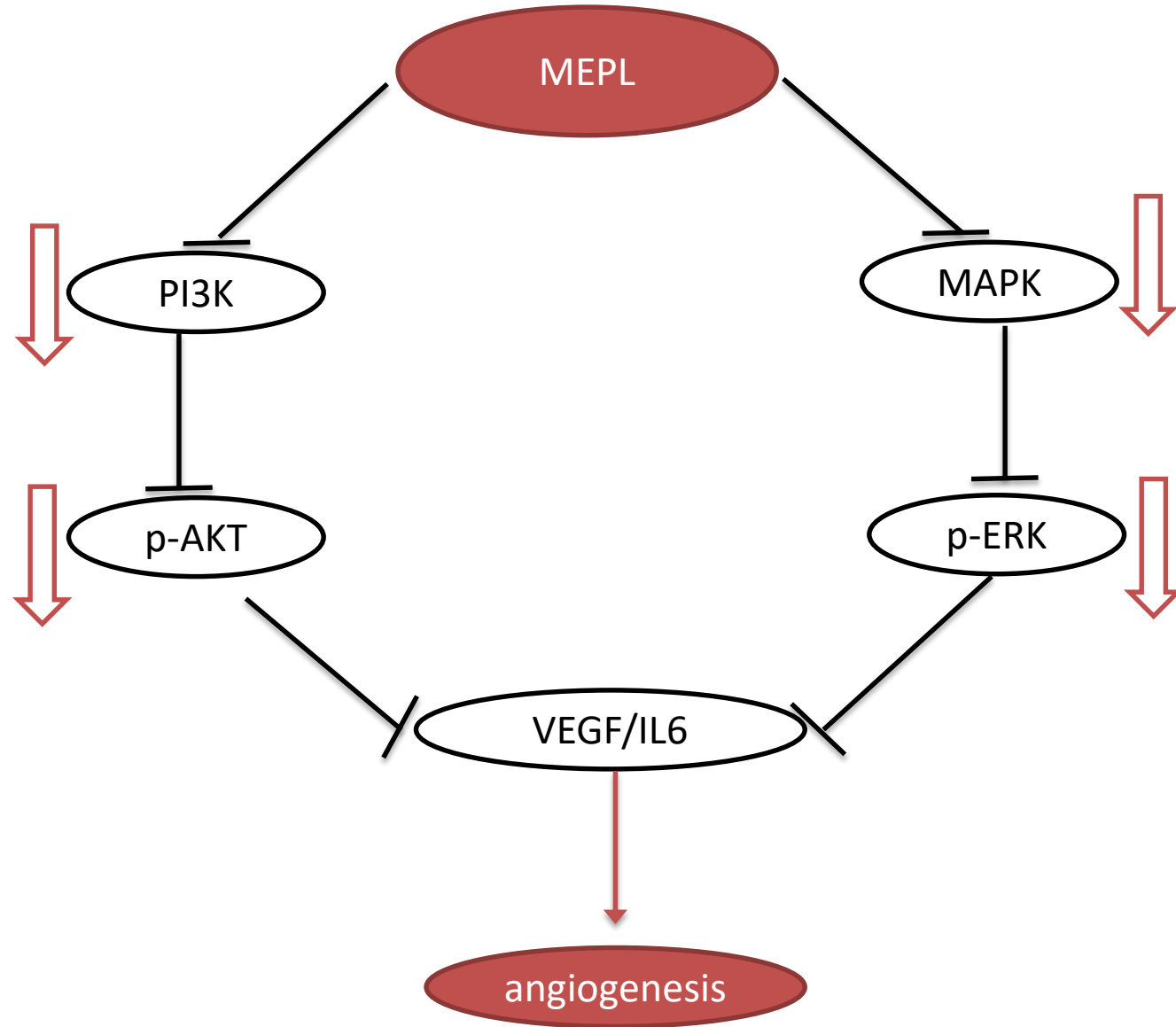


Figure 04: Western blot analysis of PI3K/AKT and MAPK signaling pathways by monitoring phospho-AKT and phospho-ERK activity after 48 hours treatment with MEPL in two representative primary HGS cell lines.

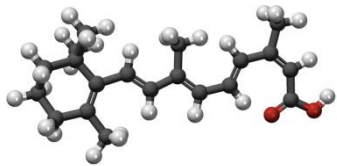
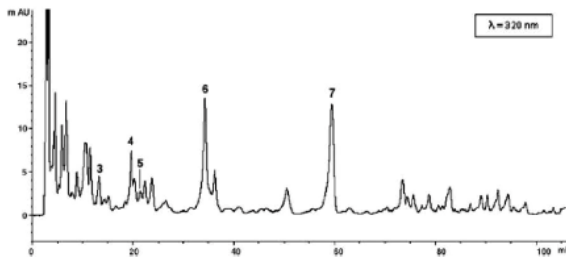
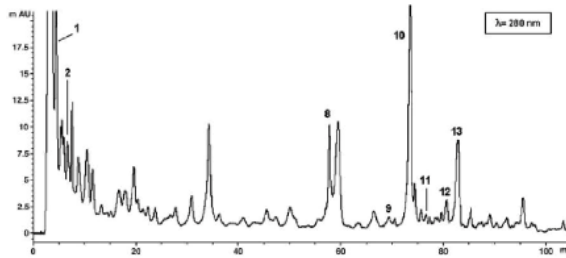
Mecanisme of action of MEPL



Conclusion

- A better understanding of the ultrastructure of the genetics and the immunology of tumors will improve the therapeutic management of patients.
- MEPL increases sensitivity to chemotherapy in human primary ovarian cancer cells through dual blocked PI3k/AKT and MAPK/ERK oncogenic signaling pathways.

Perspectives



PDX modèles



Extraction and
identification of
the active
compounds in the
MEPL extract

Active anti-
cancer effect
of natural
compounds in
vivo

Clinical trials