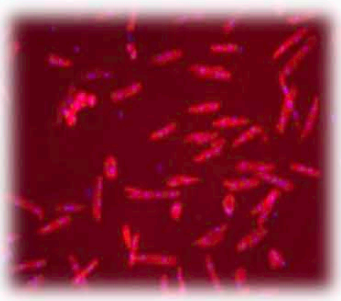
Oleocanthal Combined with Lapatinib Treatment synergized against HER-2 Positive Breast Cancer in vitro and in vivo

Khalid A. El Sayed et al. 2019 Nutrients

WHBA Presentation 23-05-2019
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Overview

- Introduction
- Results
- Discussion
- Future Perspectives

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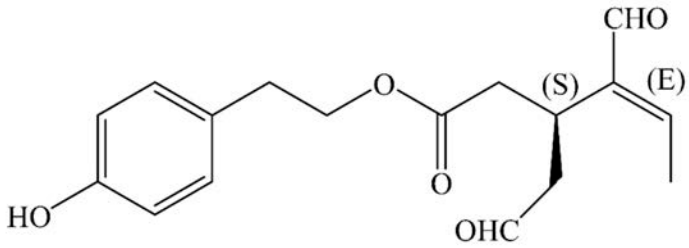
(-)-Oleocanthal (OC)



- Olive oil compound
- Involved in multiple mechanisms: anti-oxidant, anti-inflammatory, anti-diabetic, anti-bacterial, anti cancer (*Kok-Yong chin et al. 2018, nutrients*)
- most potent phenol amongst the olive oil polyphenols
- OC showed promising results in lung cancer-, prostate-, multiple myeloma-, hepatocellular-, melanoma- and leukemia studies
- Anti cancer effect with minimal cytotoxicity effect in normal cell lines depending on the dose

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Breast Cancer (BC)

- Leading cause of cancer in women (25%)
- ~20% of BC cases are HER2-amplified
- Disregulation is associated with poor prognosis, aggressive phenotype profile, poor disease outcome, reduced overall survival

Treatment options of HER2+ BC

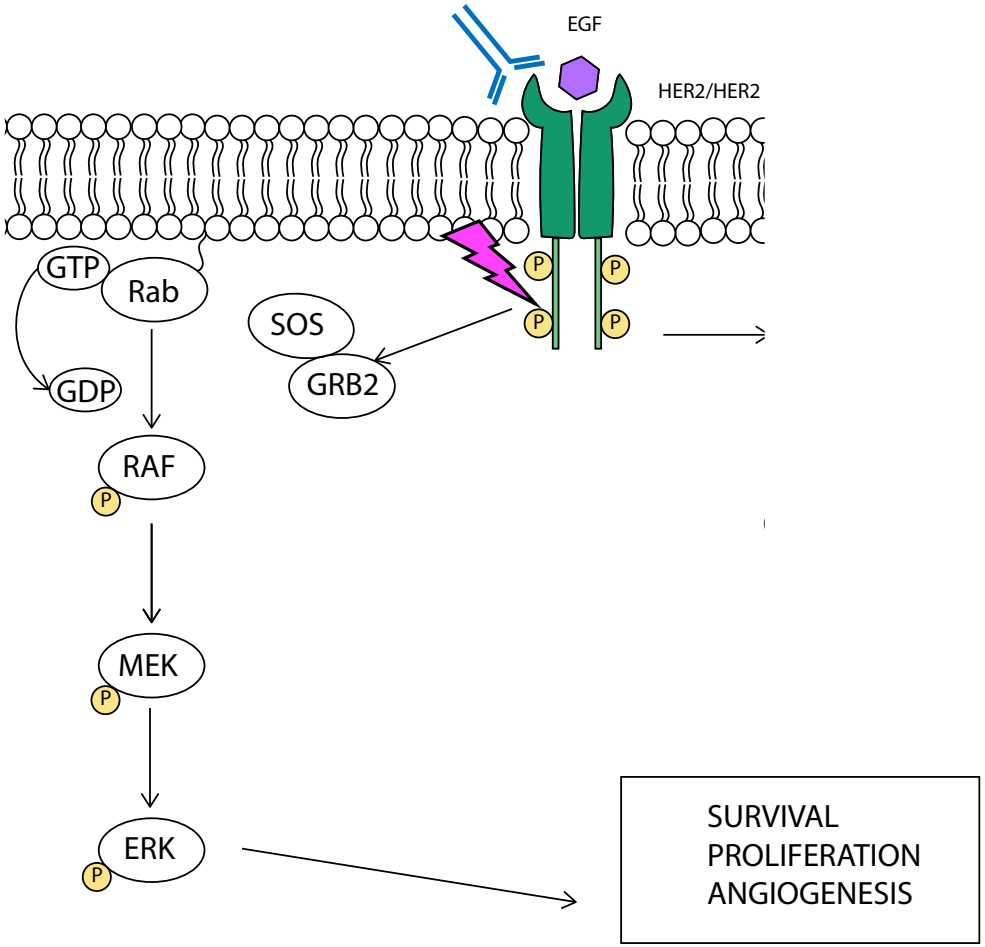
Herceptin (Trastuzumab)

- Monoclonal antibody against HER2/Neu
- Several side effects (e.g: Cardiomyopathy, neutropenia…)
- Resistance
- ~70 000 $ /year

Lapatinib (LP)

- Signal transduction inhibitor
- Several side effects (e.g: Cardiovascular, severe diarrhea…)
- Resistance
- ~3 500 $ /year

HER2/c-Met axis



Hypothesis

Multi-targeted combination therapy using c-Met inhibitor, Oleocanthal (OC), could be appealing to enhance treatment effects of anti-HER2 targeted therapies and chemosensitize HER2-positive Breast Cancer (BC) such as lapatinib (LP).

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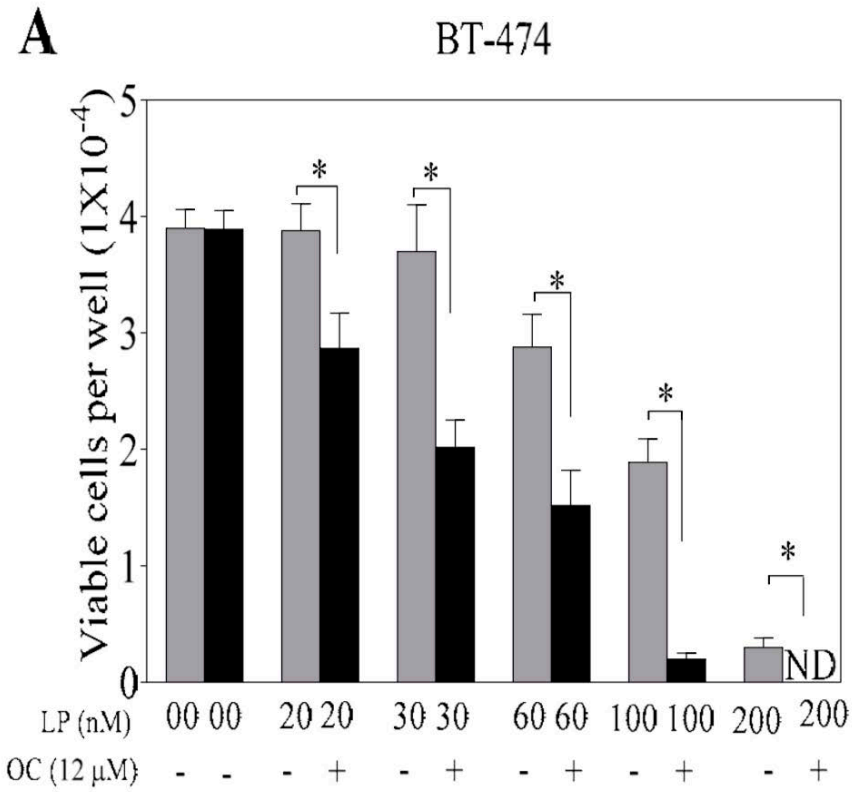
BT-474:

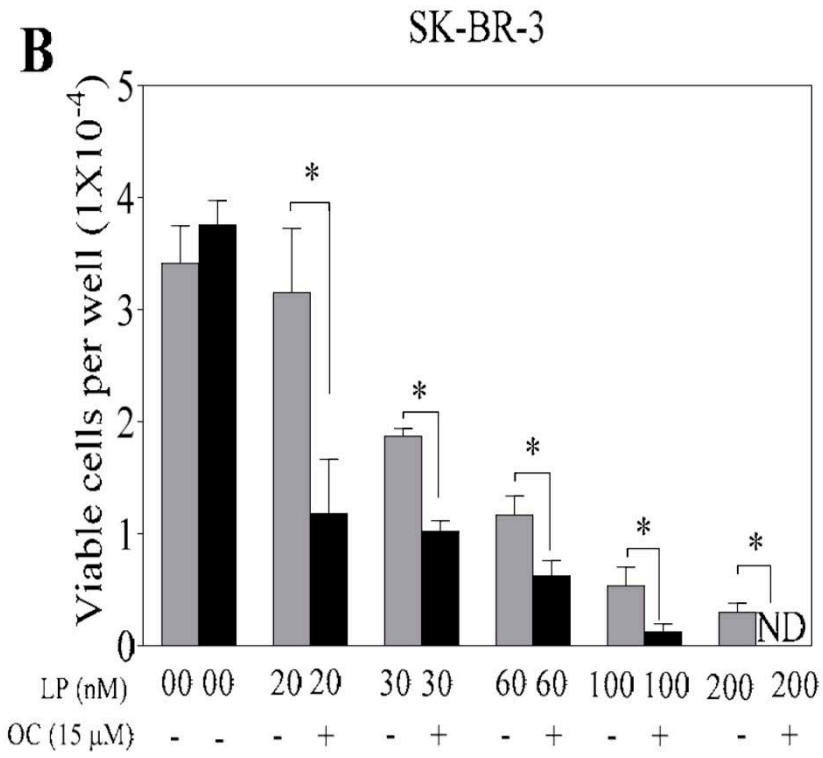
- Estrogen receptor (+)
- Progesteron receptor (+)
- HER2 (+)
- C-Met (+)
- EGFR (+)

SK-BR-3:

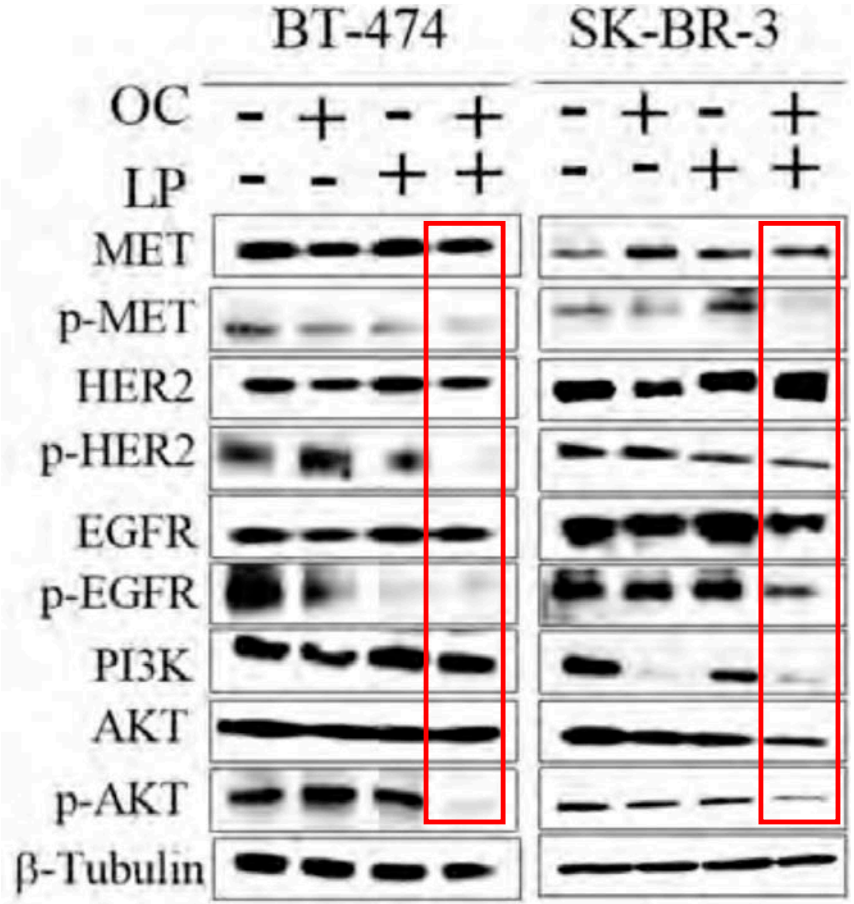
- Estrogen receptor (-)
- Progesteron receptor (-)
- HER2 (+)
- C-Met (+)
- EGFR (+)

Synergistic inhibition of growth in BT-474 and SK-BR-3 cancer cell lines





Effect of combination treatment on HER2- and c-Met signalling cascade



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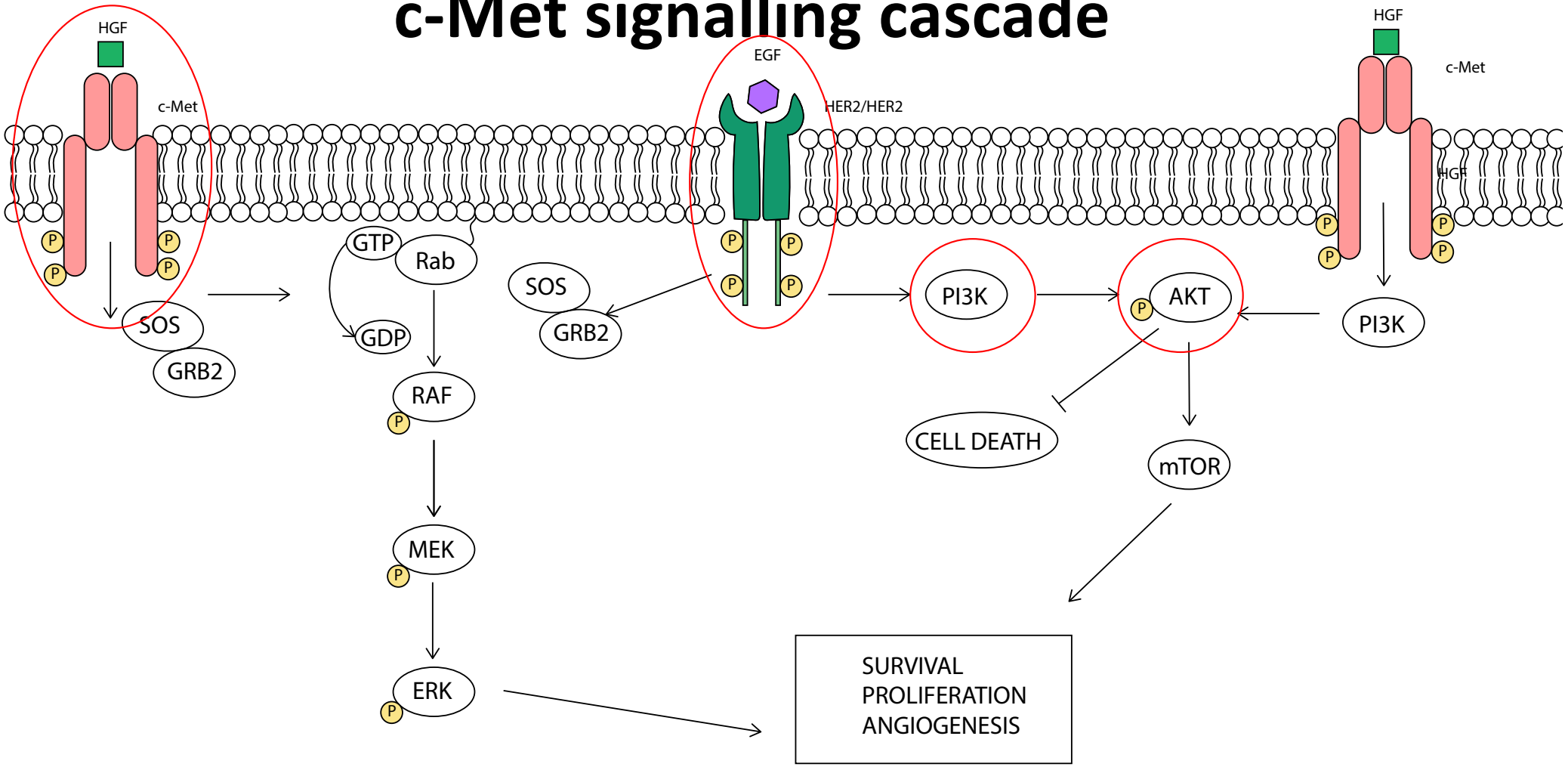
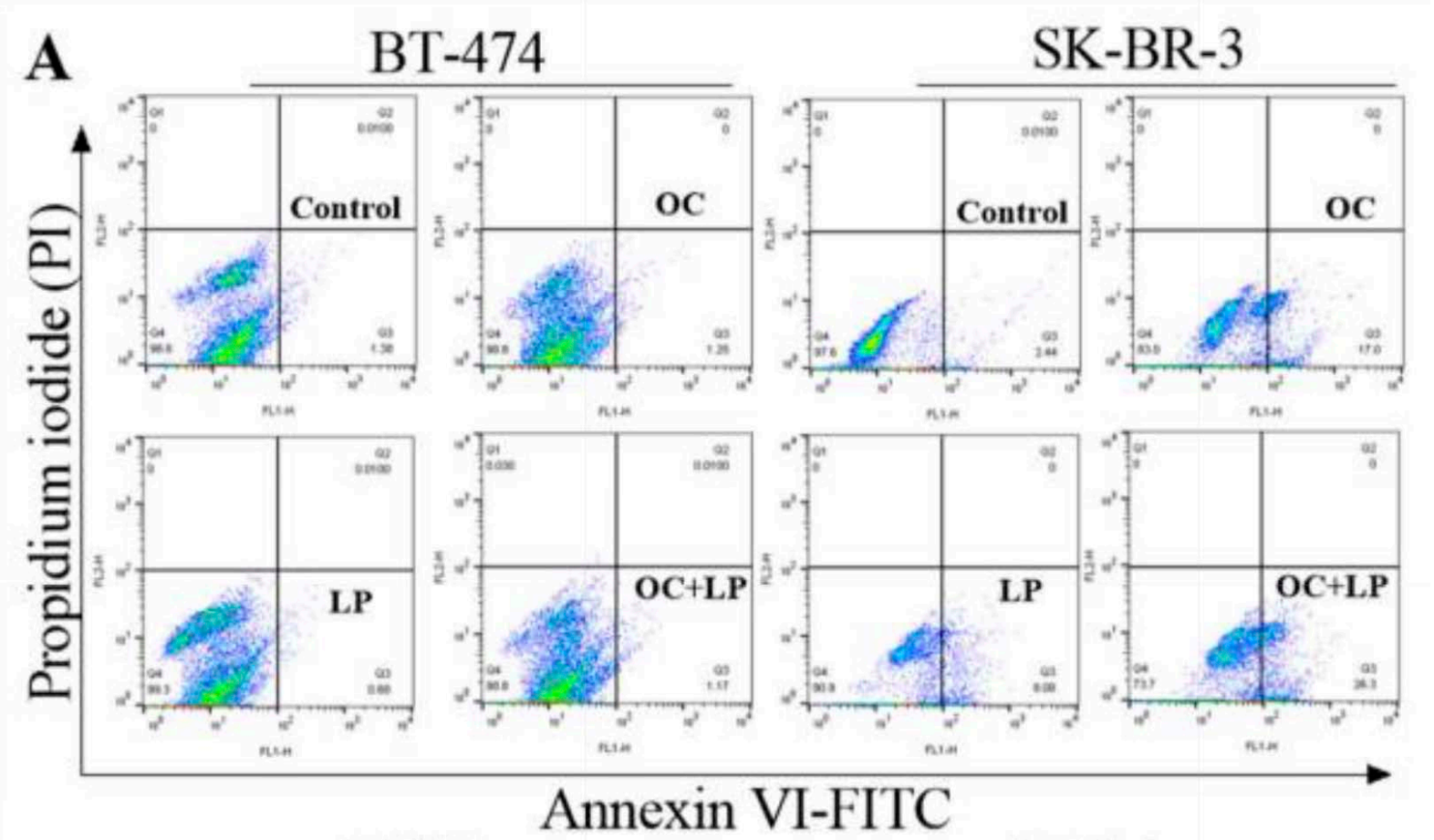
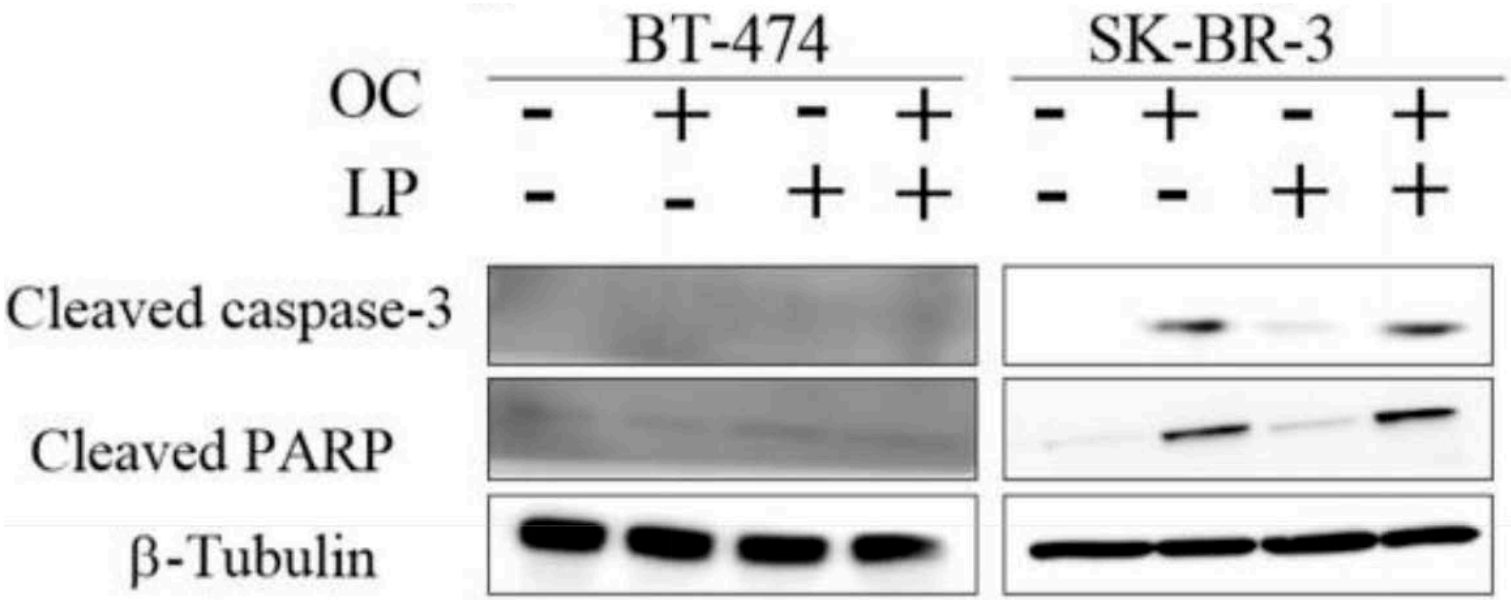
Effect of combination treatment on HER2- and c-Met signalling cascade



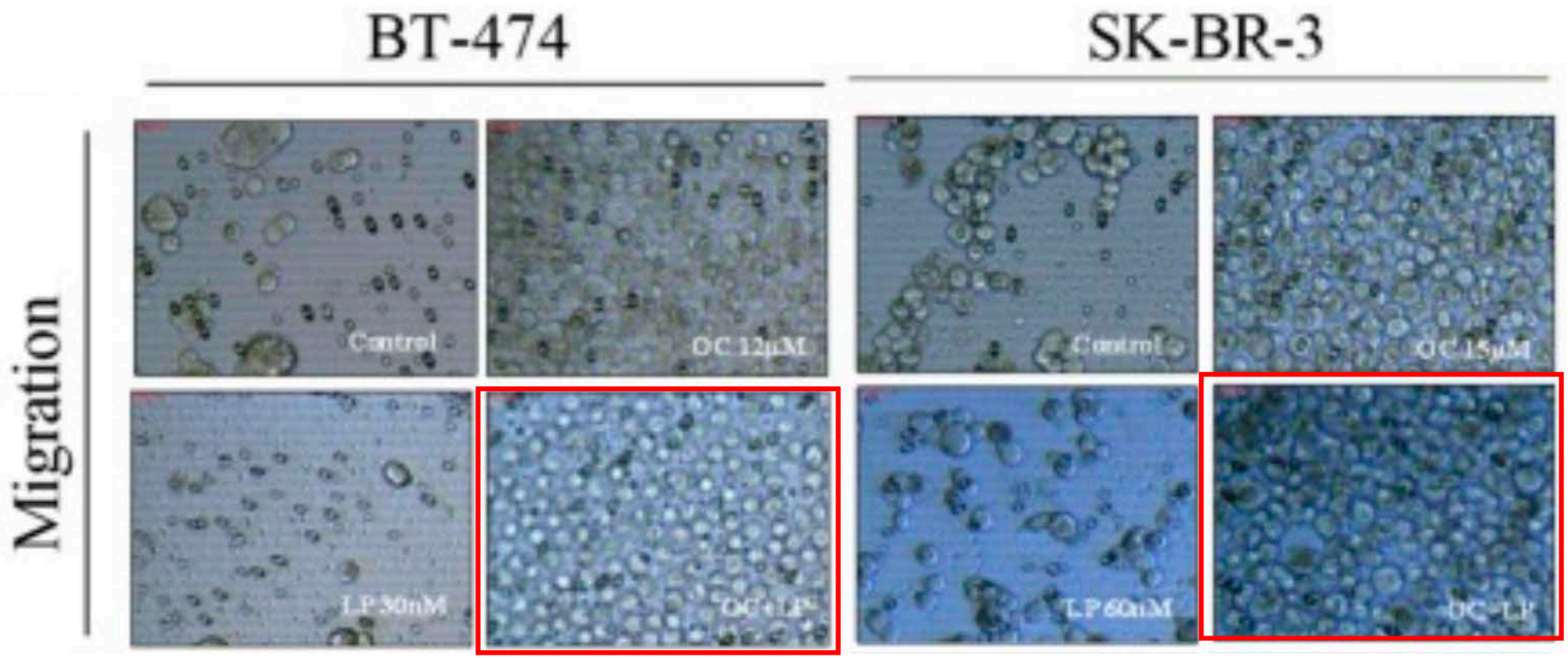
Pro-apoptotic effect of combined treatment in HER2+ Breast cancer



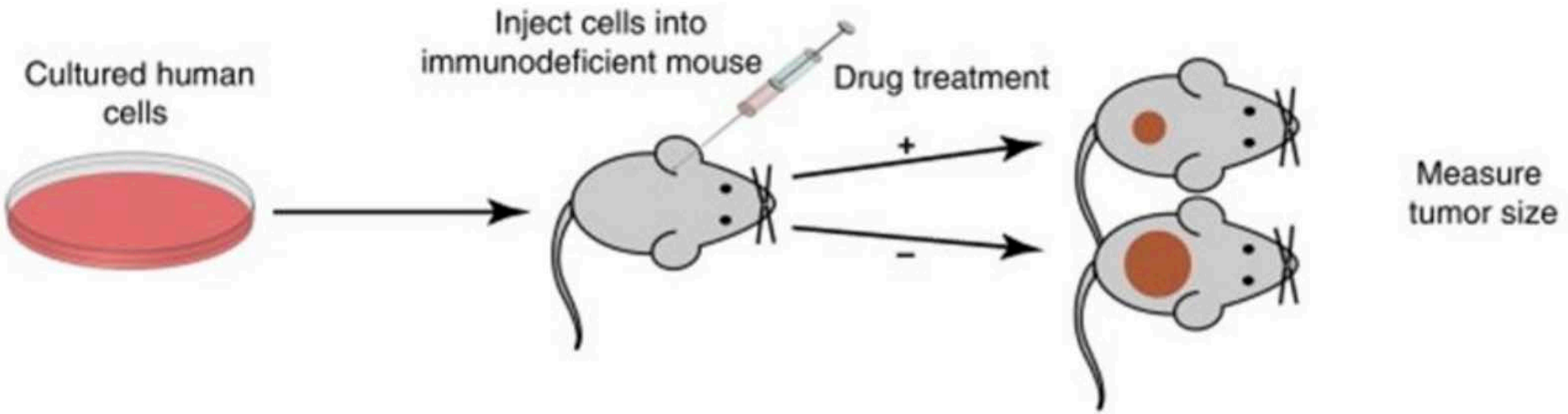
Pro-apoptotic effect of combined treatment in HER2+ SK-BR-3 cells



Combined treatment inhibits migration



Generation of human tumor xenograft model



Co-administration of OC and LP results in greatest tumor growth inhibition

Combination treatment OC + LP in contrast to LP alone showed…..

- Growth inhibition
- EMT decrease
- Reduction in multiple cascade mediators
- Cytostatic and apoptotic effect

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Future Perspectives

- Potential therapeutic strategy in HER2 Breast cancer
- Potential decrease in resistance due to targeting multiple downstream mediators of the HER2/c-Met axis.
- Reduction in cost
- Genetic stability
- Unravelling the mechanism of action to benefit from its whole potential and prevent for possible side effects
- Human studies (Dose-dependent toxicity)

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Take home some greek olive oil….

Acknowledgements

- **WHBA**
- **A. Paola Rojas-Gil**
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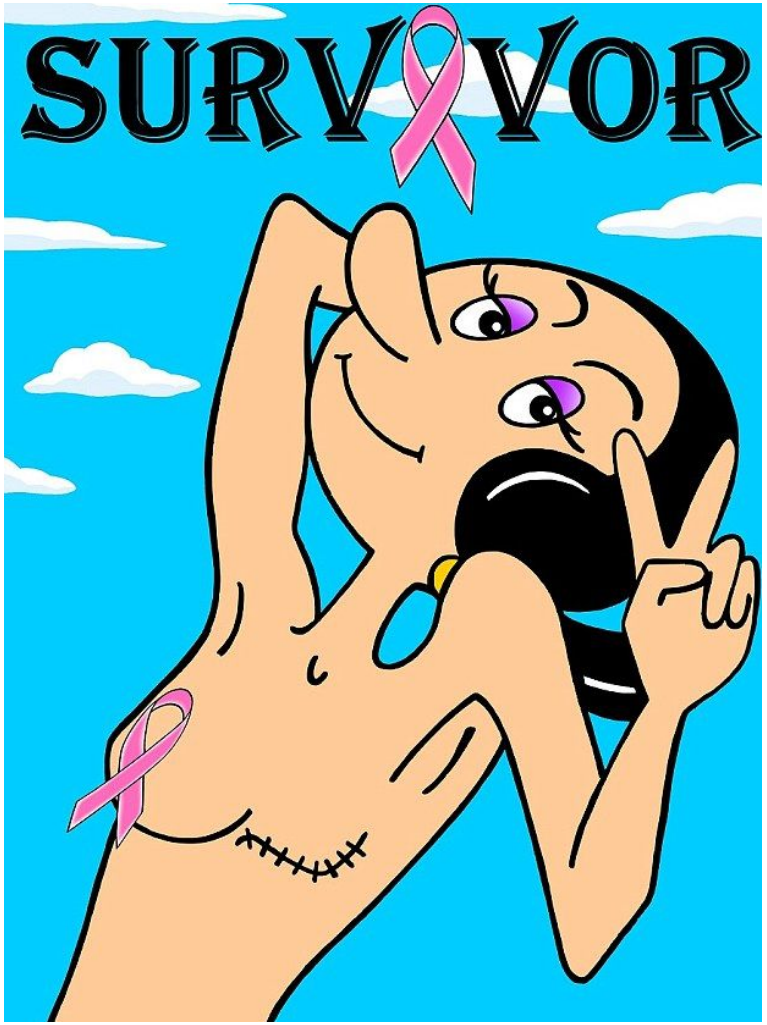
Questions & Suggestions



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