UNIWERSYTET MEDYCZNY W ŁODZI

International Doctoral School
Medical University of Lodz

Marta Kozieł

Alternariol induces DNA damage in ovarian cancer cells- the role of G protein coupled receptor 1

Marta Justyna Kozieł, Karolina Kowalska, Agnieszka Wanda Piastowska-Ciesielska

Department of Cell Cultures and Genomic Analysis, Medical University of Lodz

Introduction

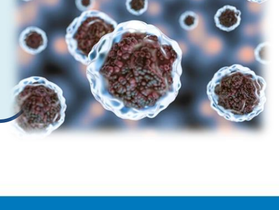
Mycotoxins are toxic secondary metabolites of fungi produced mainly by *Fusarium, Alternaria, Aspergillus and Penicillium* species. It is generally known that mycotoxins might trigger a negative impact both on human and animal health but their detailed impact on human health is still under investigation. Due to structural similarity to naturally occurring estrogen, mycotoxins might affect the human endocrine system via binding to the estrogen receptors (ERs). Recent research indicates that AOH is an estrogenic mycotoxin. AOH was also previously reported to induce DNA damage as a topoisomerase inhibitor. However, the effect of AOH in ovarian cancer cells as well as the role of non-classical estrogen receptor (GPER1) in this process was not evaluated yet.

The study aimed to evaluate the ability of AOH to induce DNA damage in ovarian cancer cells and evaluate the possible involvement of GPER1 in this process.

Methods

Desinged by FreePik

Flow cytometry

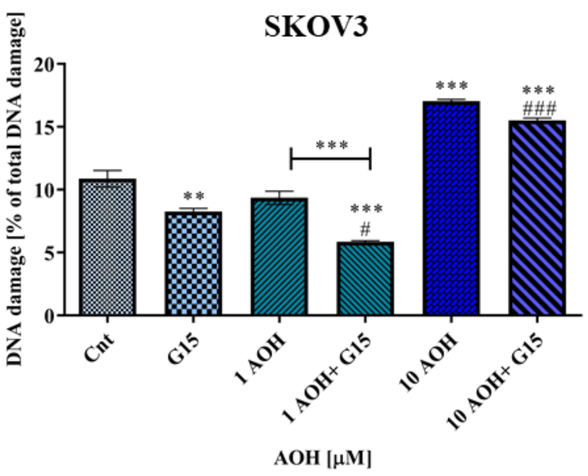


Confocal microscopy

RTqPCR

Statistic Analysis

Results & Conclusions



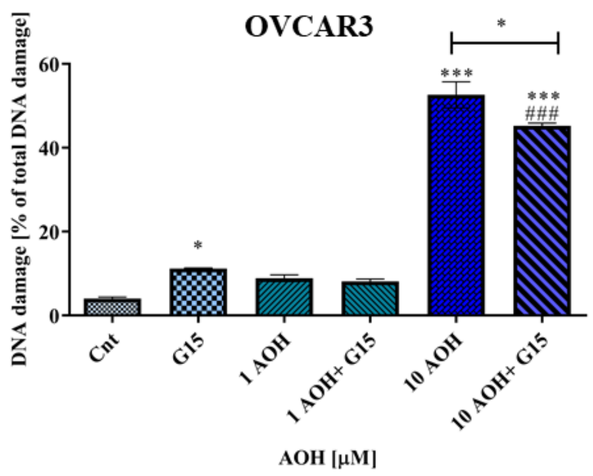


Figure 1. Alternariol induces DNA damage in ovarian cancer cells. A- DNA damage in the SKOV3 cell line. B- DNA damage in the OVCAR3 cell line. Results from flow cytometry, expressed as mean±SE, **p<0.05*, ***p<0.01*, ****p<0.001* as compared to control. * refers to non-treated cells, # to positive control. AOH- alternariol, Cnt- control, G15- GPER1 inhibitor.

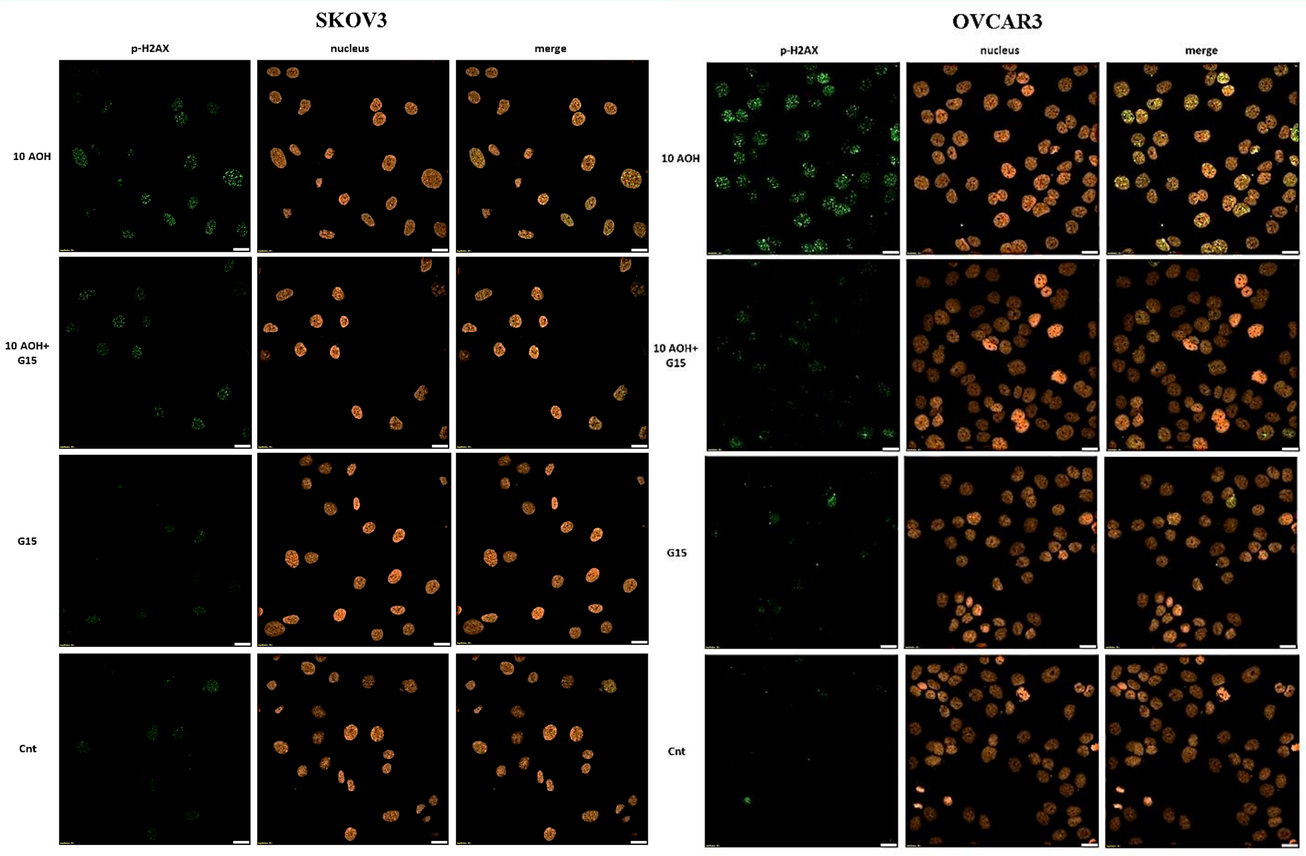


Figure 2. Alternariol induces phosphorylation of H2AX in ovarian cancer cells. A- phosphorylation of H2AX in SKOV3 cells. B- phosphorylation of H2AX in OVCAR3 cells. Representative confocal microscopy images. AOH- alternariol, Cnt- control, p-H2AX- phoshorylated H2A histone family member X, G15- GPER1 inhibitor.

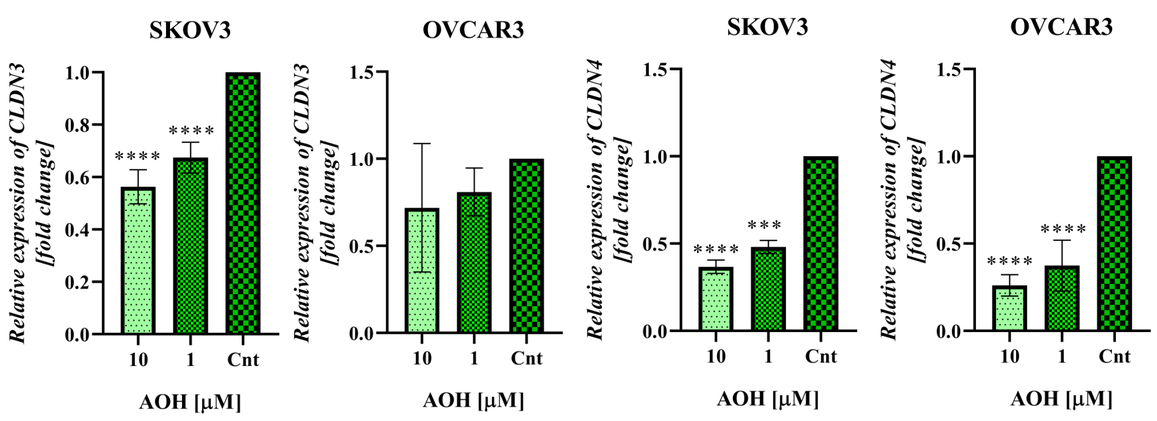


Figure 3. Alternariol induces changes in claudin-3 and claudin-4 expression in ovarian cancer cells. Results are expressed as mean±SE, ****p<0.001*, *****p<0.0001* as compared to control. AOH- alternariol, Cnt- control, CLDN3- claudin-3, CLDN4- claudin-4.

The results showed that AOH significantly increased DNA damage in ovarian cancer cells in a dose-dependent manner. Furthermore, we also observed that GPER1 inhibition partially reduced the induction of DNA damage, suggesting a potential role for GPER1 in AOH-induced DNA damage in ovarian cancer cells. The results also showed that AOH modulates the expression of claudin-3 and claudin-4, which may be a promising future result.

Main scientific achievements

Receiving funding from the National Science Center (NCN) in the PRELUDIUM program- "Are bisphenol S and F safe substitutes for bisphenol A in the face of environmental contamination with estrogenic mycotoxins?"- **PI of the project**, funds: PLN 210,000.

Two publications as first author (IF:9.1) and **two as co-author (IF: 7.3)**. Total contribution to four articles (**IF:16.4**) in 2023/2024 academic year

Participation in international conferences as presenter and co-author
- 45th Mycotoxin Workshop
- 14th International Conference „Mycotoxins and moulds"

PI in "BRaIn Internal Grants Program", funds: PLN 20,000