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New therapeutic approaches in the treatment of triple-negative breast cancer

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The treatment of triple-negative breast cancer (TNBC) has several limitations, mostly because of treatment resistance, and till nowadays women with TNBC have poor prognoses. In these studies, we examined the different responses of triple-negative breast cancer line MDA-MB-231 and hormone receptor-positive breast cancer (HR+BC) line MCF7. We used a combined treatment including olaparib, a poly-(ADP ribose) polymerase (PARP) inhibitor, oxaliplatin, a third-generation platinum compound, and LY294002, an Akt pathway inhibitor. We applied the drugs in a single, therapeutically relevant concentration individually and in all possible combinations. Additionally, we tested as mono-therapy novel mitochondria-trageted compounds, and MitoCP, a positive control. We assessed cell viability, type of cell death, reactive oxygen species production, cell-cycle phases, colony formation, and invasive growth. In the case of PARP inhibitor treatment, in agreement with the literature, MDA-MB-231 cells were more treatment-resistant than the MCF7 cells. However, and in contrast with the findings of others, we detected no synergistic effect between olaparib and oxaliplatin, and we found that the Akt pathway inhibitor augmented the cytostatic properties of the platinum compound and/or prevented the cytoprotective effects of PARP inhibition. Our results suggest that, at therapeutically relevant concentrations, the cytotoxicity of the platinum compound dominated over that of the PARP inhibitor and the PI3K inhibitor, even though a regression-based model could have indicated an overall synergy at lower and/or higher concentrations. In contrast to the combination therapy, we could not detect increased resistance by the TNBC line over the HR+BC line against the mitochondria-trageted compounds. Additionally, these substances were effective at sub-micromolar concentrations in the aforementioned *in vitro* tests. Taken together, these results indicate their potential of the novel mitochondria-trageted compounds in the treatment of TNBC.

Recent Publications

1. Krisztina Kovacs, et.al (2022): Effects of pituitary adenylate cyclase activating polypeptide (PACAP) in corneal epithelial regeneration and signal transduction in rats. International Journal of Peptide Research and Therapeutics. 28(3).

2. Krisztina Kovacs, et.al (2021): The Protective Effects of Endogenous PACAP in Oxygen-Induced Retinopathy. Journal of Molecular Neuroscience. 71 (12). 1-12

3. Krisztina Kovacs, et.al (2021): Cytostatic Effect of a Novel Mitochondria-Targeted Pyrroline Nitroxide in Human Breast Cancer Lines. International Journal of Molecular Sciences. 22 (16). 9016.

Biography

Krisztina Kovacs is a Professor in the Department of Biochemistry and Medical Chemistry at the University of Pecs Medical School, Hungary. Her major research works are the biological effects of benzofuran derivatives, BGP-15 derivatives, effects of PARP inhibitors, and pulmonary hypertension model system. She has participated in various conferences and published many articles in reputed journalsn.

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