

Effect of both PD-1/PD-L1 and ERK inhibitor on triple negative breast cancer cell lines and the non-triple negative cell line MCF-7

Elodie Kabore, Frank Köster, Stephan Polack, Achim Rody, Karen Bräutigam*

University Hospital Schleswig-Holstein, Campus Lübeck (1)

* Corresponding author, email: karen.braeutigam@uksh.de

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Keywords: PD-1/PD-L1 Inhibitor, ERK Inhibitor, triple negative breast cancer cell lines, map kinase pathway

Objectives: Diagnosis of triple negative breast cancer (TNBC) is associated with adverse prognosis. The goal was to identify a novel therapy approach for treatment of TNBC cell lines by combination of a PD-1/PD-L1 and an ERK inhibitor.

Methods: After single and combined inhibitor treatment the concentration of 50 % reduction of cell viability (IC₅₀) was determined in three TNBC cell lines and the non-TNBC cell line MCF-7 by MTS assay. Impact on Jak/Stat and MAP kinase pathway and apoptosis induction by inhibitor was checked by immunoblot. QPCR experiments were performed to prove expression ratios of PD-L1, CDK5, Notch1, IL-8, IL-6, CXCL1 und CXCR2 after treatment.

Results: The PD-L1/PD-1 inhibitor provoked 50 % reduction of cell viability with concentrations of 1.26 to 2.25 μ M in TNBC and 3.20 μ M in MCF-7. For the ERK inhibitor IC₅₀ values were determined of 4.42 to 6.03 μ M in TNBC and of 20.44 μ M in MCF-7. Combined treatment effected a synergistic or additive inhibition of proliferation. The MAP kinase ERK and S6 were dephosphorylated and expression of Stat3 was increased by ERK inhibitor. Gene expression of IL6 and CXCR2 were repressed by combined treatment.

Conclusion: Though the use of the PD-1/PD-L1 inhibitor and the ERK inhibitor showed contrary effect on phosphorylation of various proteins of the Map kinase signaling pathway, the combined treatment provoked a synergistic or at least additive inhibition of proliferation especially in TNBC and a reduced expression of genes involved in inflammatory processes.