Antibiotics target MCF-7 breast cancer stem cells in hypoxic environment.

Regina R. Miftakhova, Almaz Akhunzyanov, Julia V Filina, Svetlana F Khaiboullina, Albert A Rizvanov

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Abstract e14068

Background: Deregulated cellular metabolism is characteristic for cancer cells which heavily rely on glycolysis to meet metabolic demands. Studies have shown that increased glucose metabolism promotes tumor cell survival through mechanisms related to mitochondrial activities. Recently, mitochondrial inhibitors have been proposed as a potential anticancer therapeutics. In 2015 Lamb et al. presented anti-cancer activity of several antibiotics targeting mitochondrial function. Interestingly, these drugs have the highest inhibitory effect on cancer stem cells (CSCs), a small population of cancer initiating cells. It is believed that tumor microenvironment plays significant role in maintaining CSC population. The hypoxia is a major feature of the tumor microenvironment contributing into CSC phenotype, tumorigenicity and metastasis. Therefore, we sought to determine the effect of five antibiotics targeting mitochondrial function on CSC survival in hypoxia conditions. **Methods:** MCF-7 cells were cultured in normoxic (20% O_2) and hypoxic (4% O_2) conditions for 14 days in a presence of azithromycin, doxycycline, tetracycline, erythromycin and chloramphenicol. The ability to form mammospheres was used to determine CSC survival. **Results:** Incubation of CSCs with erythromycin, doxycycline, tetracycline and chloramphenicol reduced the number of mammospheres, the decrease in mammosphere number was comparable for MCF-7 cells incubated under normoxic and hypoxic conditions [erythromycin (62.5 % ± 10.8% vs. 58.9% ± 2.2%), doxycycline (75.2% ± 5.9% vs. 68.5% ± 5.4%), tetracycline (56.0% ± 3.2% vs. 65.0% ± 15.0%) and chloramphenicol (71.5% ± 6.7% vs. 73.7% ± 5.5%)]. Interestingly, azithromycin did not show inhibiting activity on sphere formation under hypoxic condition, while number of spheres was reduced in normoxic conditions **Conclusions:** These data indicate that four out of five antibiotics in our study can be potentially applied for targeted eradication of breast CSCs in hypoxic conditions.
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