Treatment of Human Melanoma: Overcoming Cell Resistance by Glutathione Depletion (Phase II)

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Melanoma is the most aggressive type of skin cancer. It is estimated that 7703 people will have melanoma and 2463 will die because of it in 2020 in Brazil. One of possible treatments for it is the chemotherapy drug cisplatin, which is cheap and, therefore, accessible. However, it has low efficacy due to cell resistance. Considering that one of the resistance pathways to cisplatin treatment is the overexpression of the antioxidant glutathione, we hypothesize that the inhibition of glutathione could be effective to sensitize these cells to cisplatin treatment. Thus, we selected l-buthionine-sulfoximine (BSO), an inhibitor of glutathione synthesis, to test if it would overcome cisplatin resistance. Cells can develop resistance in response to the drug or to hostile microenvironment conditions such as hypoxia. Hypoxia is a common situation in solid tumors, like melanoma, due to poor vascularization. This project aims to develop cisplatin resistant cells to test if a treatment with BSO could sensitize these melanoma cells to cisplatin. To do so, cells were treated with cisplatin in three different approaches, with a high, low and increasing concentration of the drug. Neither one of these approaches were effective to generate a cisplatin resistant cell line. However, the induction of cell death in melanoma cells exposed to cisplatin for 72 hours followed by BSO treatment and, subsequently, cisplatin, was higher than in the cells treated with cisplatin only. Thus, this preliminary result suggests that BSO can sensitize melanoma cells to cisplatin induced cell death. To confirm this result, the experiment will be repeated and the development of resistance by hypoxia will also be tested to verify if the same promising results will be achieved.

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