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New synthetic anti-cancer compounds, LQB-118 and LQB-223, induce apoptosis by distinct mechanisms in glioblastoma cells

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Glioblastoma (GB) is the most common astrocytoma and a lethal human malignancy, with a median survival of 12 months. Therefore, our group is involved in the development of new anti-cancer drugs. This study evaluated the anti-tumoral activity of new synthetic compounds pterocarpans, LQB-118 and LQB-223 in human GB cell lines. Moreover, the relationship between microRNAs and AKT and ERK survival pathways underlying the compounds mechanism of action was investigated. LQB-118 and LQB-223 reduced cell viability to a greater extent than the first line chemotherapy, temozolomide (TMZ). The compounds also inhibited cell proliferation and induced apoptotic cell death demonstrated by caspases activation and annexin V labeling. Furthermore, the compound LQB-223 induced cell cycle arrest at G2/M phase, followed by DNA fragmentation. LQB-118 and LQB-223 reduced ERK1/2 expression and phosphorylation, while TMZ only slightly reduced ERK1/2 phosphorylation and did not significantly induce cell death. LQB-118 promoted an increase in miR-210 expression, while LQB-223 induced miR-7 expression. As miR-7 inhibits RAS in GB models, consequently, inhibiting AKT and ERK phosphorylation, we evaluated RAS expression. LQB-223 reduced RAS protein levels, suggesting an important role of this pathway in the compound mechanism. As LQB-118 showed the higher effect on cell viability, the association of LQB-118 with ionizing radiation was assessed by tripan blue exclusion assay. The association reduced cellular viability synergistically and a similar effect was observed in the combination of TMZ with ionizing radiation. Our results suggest that the compounds LQB-118 and LQB-223 are promising agents with distinct mechanisms of action for GB treatment.

Biography

Paula Sabbo Bernardo is a PhD student from Brazilian National Cancer Institute. She developed her PhD project at the Laboratory of Cellular and Molecular Hemato-Oncology, which is headed by Dr. Raquel Ciuvalschi Maia. She completed her Master´s degree in translational research in the field of anti-cancer drugs development for glioblastoma treatment.

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