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Abstract

Title: Testing of cation carriers as prospective therapeutic agents for the treatment of B-cell-derived malignancies

The first-line treatment for many types of B-cell-derived hematological malignancies includes anti-CD20 immunotherapy, frequently administered in combination with chemotherapy. However, some patients develop resistance to this therapeutic approach. A well-recognized cause of such resistance is the variable expression of CD20 on the surface of malignant B cells, with many cases showing low CD20 levels. This variability significantly limits the effectiveness of anti-CD20 therapies. Therefore, there is an urgent need to develop new strategies to overcome resistance and improve treatment outcomes for these patients.

This PhD dissertation investigated the potential of cation carriers, such as salinomycin (SAL), to increase CD20 expression on the surface of malignant B cells and thereby enhance the efficacy of anti-CD20 immunotherapy in both *in vitro* and *in vivo* models. A secondary focus of the dissertation was to elucidate the molecular mechanisms of SAL-induced CD20 upregulation, using molecular biology techniques such as qRT-PCR and Western blotting. Additionally, the effects of SAL on mitochondrial function and the metabolic profile of treated cells were comprehensively assessed.

The results of this PhD dissertation were published in three scientific articles. The original article, published in the journal *Haematologica*, demonstrated the ability of cation carriers to upregulate CD20 expression, explained the molecular mechanism behind this phenomenon, and confirmed the improved efficacy of therapy using anti-CD20 monoclonal antibodies. A review article and a subsequent original research paper (published in *International Journal of Molecular Sciences*) highlighted the key role of mitochondria in the molecular mechanism of SAL action. These studies revealed SAL's impact on mitochondrial respiration, induction of a metabolic shift toward glycolysis, and its role in depleting L-arginine levels in malignant B cells. The obtained results may have significant implications for future therapeutic strategies.

Keywords: B-cell malignancies, CD20, cation carriers, salinomycin, immunotherapy, mitochondria