Determining the antiproliferative effects of quinolinic acid and kynurenic acid on melanoma, macrophage, and keratinocyte cells using the parametric cell viability function

BIOMATH 2024

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Keywords: Mathematical modelling, cell viability, melanoma, quinolinic acid, kynurenic acid

Melanoma, an aggressive malignancy derived from melanocytes, ranks among the most highly metastatic forms of human cancer [1]. Although major advances have been made in terms of developing treatments against metastatic melanoma, the majority of patients fail to exhibit a sustained response to these treatments [2]. Consequently, effective targeted treatments for metastatic melanoma remain a formidable challenge. In recent years, there has been a significant research emphasis on the potential use of kynurenine metabolites as biologically active substances for the treatment of melanoma [3, 4, 5, 6]. In a recent in vitro investigation, the antiproliferative properties of metabolites within the kynurenine pathway, specifically l-kynurenine (L-kyn), quinolinic acid (quin), and kynurenic acid (ka), were reported [4]. The study found that L-kyn is the most potent metabolite in inhibiting cell proliferation at concentrations ranging from 0 to 4 mM. However, understanding the complex dynamics of cell proliferation is crucial to comprehending the cytotoxic effects of these metabolites. To address this knowledge gap, we use a mathematical model to investigate tumour growth dynamics in response to treatment [7]. In a previous study, a parametric cell viability was constructed and was used in an in vitro setting to explore

the concentration-dependent dynamics of cell proliferation after exposure to L-kyn [8]. However, further exploration into the dynamics of Quin and KA is necessary. Thus, in this study, we apply the same approach to determine the impact of these metabolites on cell proliferation in melanoma, macrophage, and keratinocyte cell lines, leading to a better understanding of their potential to modulate cellular proliferation. Additionally, the model will help identify possible targeted cytotoxic compounds against melanoma at various concentrations from 0 to 5 mM by predicting the cell viability of the metabolites in various cell lines.

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