Anti-proliferative effects and metabolic dynamics of menaquinone (Vitamin K2) supplementation to human "acute T cell leukemia" cells

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Abstract

CoMet, a computational metabolomics tool, was designed to predict changes in metabolite levels between normal cells and cancerous cells based only on transcriptional data and database information such as metabolic pathways and enzyme function annotations. These predictions are further extended with the hypothesis that metabolites predicted to be depleted in cancerous cells may have anti-proliferative effects. Based only on this data, CoMet previously predicted that menaquinone (vitamin K2) would show anti-proliferative activity, which has previously been demonstrated. Here, we will discuss our experimental validation of CoMet's predictions based on flow cytometry and systems-level analysis of hundreds of metabolite concentrations in human acute T cell Leukemia (Jurkat cells) and normal lymphoblast cells.

We performed toxicity assays with C12-resazurin and sytox green dyes, analyzed the number of live and dead cells with flow cytometry to show that menaquinone has selective, concentration- and time-dependent toxicity effects on Jurkat cells. Up to 75% of cancerous cells were killed by menaquinone at 30µM, with only a minimal anti-proliferative effect observed in normal lymphoblasts at the same concentration. This provided finer resolution of the effects of menaquinone on Jurkat cells than the previously known results.

These anti-proliferative effects are likely to have a significant impact on the metabolic state of these cells, based at least in part on the fact that menaquinone's antiproliferative effect was predicted solely based on transcription of metabolic genes. Little is known about the changes in cancer cell metabolism caused by menaquinone supplementation. To this end, intracellular and extracellular metabolic samples were analyzed using 2D gas chromatography coupled to mass spectrometry for both Jurkat cells and lymphoblasts in time series experiments with different concentrations of menaquinone supplementation. Multivariate statistical analysis was used to analyze the metabolomic changes in the cancer cells and normal cells at baseline and due to menaquinone supplementation.

Keywords: metabolomics, cancer, leukemia, menaquinone, vitamin K2,