# BPM31510 Engagement of the Warburg Effect in GBM to Therapeutically Modulate Tumor Metabolism Through ROS Mediated Processes Preclinically and Clinically

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## INTRODUCTION

### Background

**Warburg effect**: Tumor metabolism is reprogrammed (↑ glycolysis, ↓ mitochondrial function) to protect the tumor against reactive oxygen species (ROS) mediated apoptosis. This shift promotes tumor growth and survival.

### Therapeutic Concept

**BPM31510** is a nanoparticle formulation of ubiquinone (CoQ10) for enhanced bioavailability. Designed to restore mitochondrial function and enhance oxidative stress in tumors. Currently evaluated in GBM (Phase 2 clinical trial, NCT04752813).

### Objectives

- Identification of cancer types with potential susceptibility to BPM31510 (cancer types with high ROS pathway expression score )
- Investigate BPM31510 efficacy and mechanism in a GBM preclinical model.
- Investigate circulating biomarkers in glioma patients treated with BPM31510 for evidence of mechanistic engagement.

## CANCER TYPES POTENTIALLY RESPONSIVE TO BPM31510 VIA ROS-LINKED APOPTOTIC SUSCEPTIBILITY

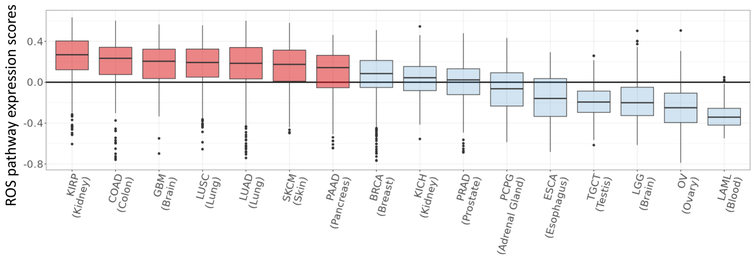


Figure 1: ROS pathway expression score for 16 TCGA cancer types. Cancer types with higher ROS pathway expression score (> 0.1) may be much more susceptible to apoptosis compared to those with lower ROS expression scores, since a lower amount of ubiquinone would be needed to induce apoptosis. Seven cancers (in red) stand to benefit from ubiquinone therapy – KIRP, COAD, GBM, LUSC, LUAD, SKCM, and PAAD.

## BPM31510 EFFICACY IN C6 GLIOMA RAT MODEL

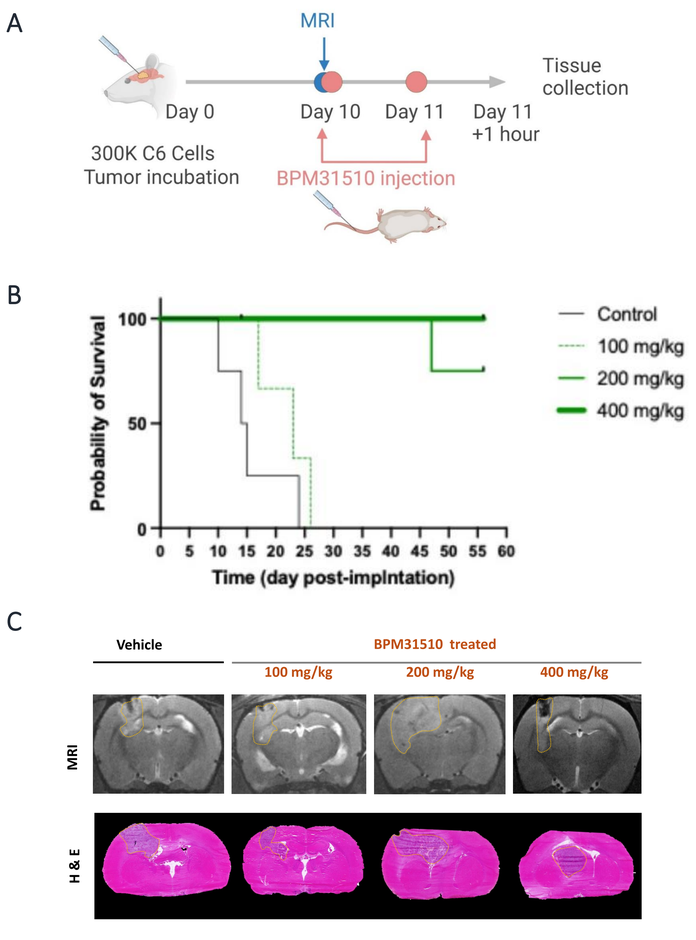


Figure 2: (A) Overview of experimental workflow. (B) Interim survival outcome of study. (C) MRI and histological assessment of GBM tumors treated with increasing doses of BPM31510.

## TISSUE METABOLOMIC IMAGING ANALYSIS AFTER BPM31510 TREATMENT

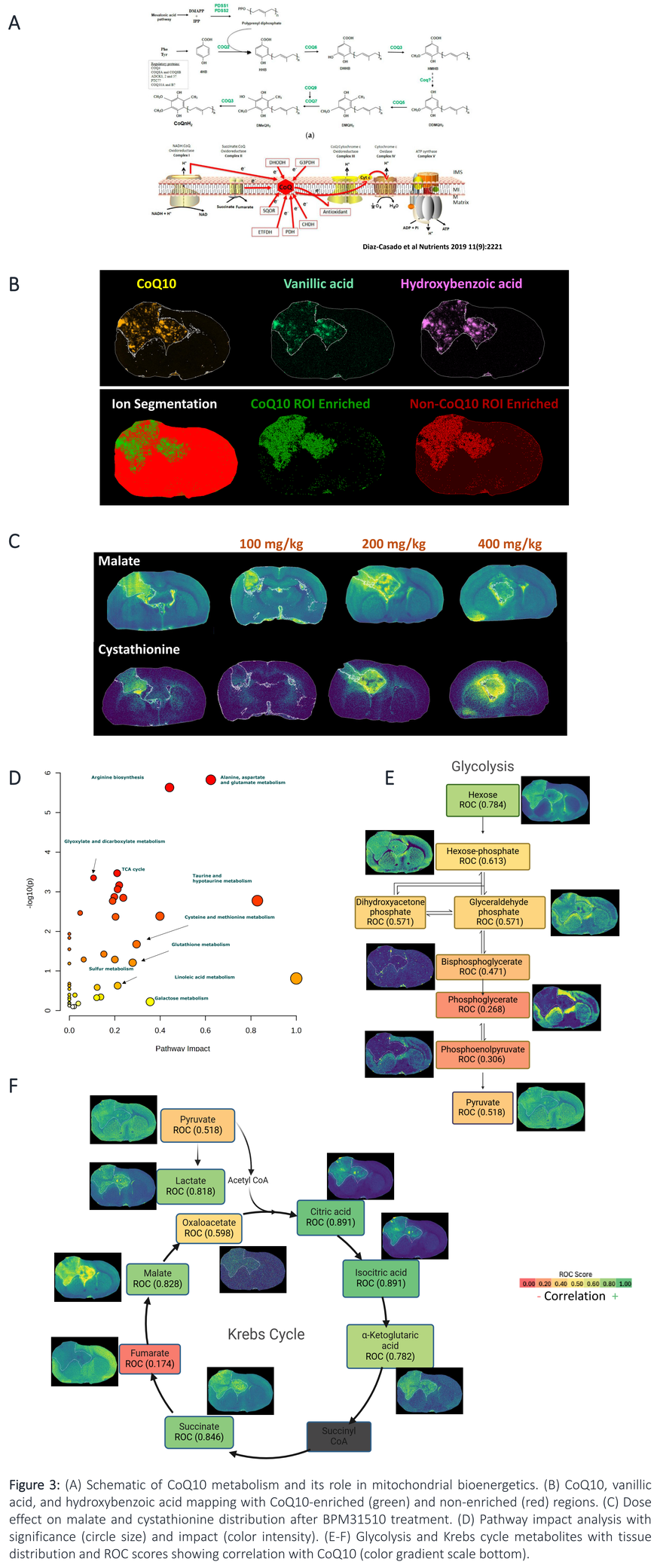


Figure 3: (A) Schematic of CoQ10 metabolism and its role in mitochondrial bioenergetics. (B) CoQ10, vanillic acid, and hydroxybenzoic acid mapping with CoQ10-enriched (green) and non-enriched (red) regions. (C) Dose effect on malate and cystathionine distribution after BPM31510 treatment. (D) Pathway impact analysis with significance (circle size) and impact (color intensity). (E-F) Glycolysis and Krebs cycle metabolites with tissue distribution and ROC scores showing correlation with CoQ10 (color gradient scale bottom).

## BPM31510 INDUCES TUMOR METABOLIC REPROGRAMING IN PATIENTS WITH HIGH-GRADE GLIOBLASTOMAS

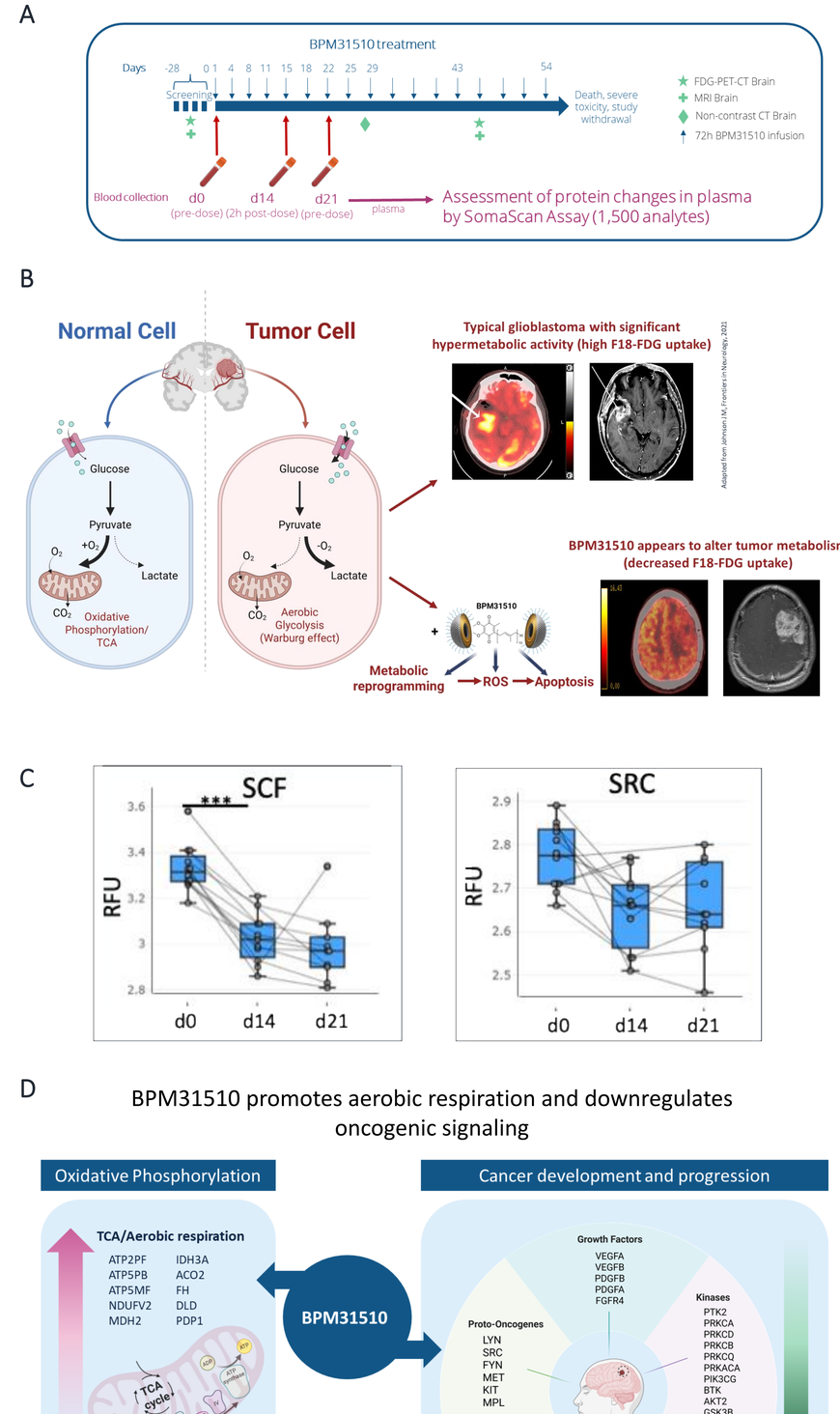


Figure 4: (A) Phase 1 study overview: BPM31510 plus vitamin K in subjects with glioblastoma (GB) that has recurred on a bevacizumab (BEV) -containing regimen were treated with BPM31510. Plasma from 12 patients in BPM31510IV-06 (NCT03020602) was collected on days 0, 14 (2h post-dose), and 21 (pre-dose) and analyzed via SomaScan for 1,500 analytes. (B) Metabolic reprogramming in high-grade glioblastomas patients treated with BPM31510 as evidenced by 18F-FDG PET scans. (C) Reduced plasma levels of SCF (Stem Cell Factor) and SRC (SRC Proto-Oncogene, Non-Receptor Tyrosine Kinase) in patients treated with BPM31510. (C) Summary of BPM31510 impact on plasma biomarkers.

## CONCLUSIONS

- Analysis of TCGA pathways highlighted GBM as a tumor type likely to benefit from BPM31510 treatment.
- BPM31510 efficacy in a preclinical GBM model and in patients with high-grade glioblastomas is associated with reengagement of mitochondrial function and increased redox state.