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3-Bromopyruvate inhibits calcium uptake by sarcoplasmic reticulum vesicles but not SERCA ATP hydrolysis activity.

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Abstract

3-Bromopyruvate (3BrPA) is an antitumor agent that alkylates the thiol groups of enzymes and has been proposed as a treatment for neoplasias because of its specific reactivity with metabolic energy transducing enzymes in tumor cells. In this study, we show that the sarco/endoplasmic reticulum calcium (Ca(2+)) ATPase (SERCA) type 1 is one of the target enzymes of 3BrPA activity. Sarco/endoplasmic reticulum vesicles (SRV) were incubated in the presence of 1mM 3BrPA, which was unable to inhibit the ATPase activity of SERCA. However, Ca(2+)-uptake activity was significantly inhibited by 80% with 150 μM 3BrPA. These results indicate that 3BrPA has the ability to uncouple the ATP hydrolysis from the calcium transport activities. In addition, we observed that the inclusion of 2mM reduced glutathione (GSH) in the reaction medium with different 3BrPA concentrations promoted an increase in 40% in ATPase activity and protects the inhibition promoted by 3BrPA in calcium uptake activity. This derivatization is accompanied by a decrease of reduced cysteine (Cys), suggesting that GSH and 3BrPA increases SERCA activity and transport by pyruvylation and/or S-glutathiolation mediated by GSH at a critical Cys residues of the SERCA.

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