Title
Imaging of methioninase-induced S/G(2)-phase-trapping for subsequent effective chemotherapy

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Abstract 3412: Imaging of methioninase-induced S/G\textsubscript{2}\text{-phase-trapping for subsequent effective chemotherapy.

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Abstract

Methionine-dependence of cancer cells may be due to excessive methylation reactions in cancer cells. Deprivation of methionine α,γ lyase (methioninase or METase) selectively arrests cancer cells during late S-phase, where they are highly sensitive to DNA-damaging chemotherapy. Fluorescent ubiquitination-based cell cycle indicator (FUCCI), was used to monitor the onset of the S/G2-phase block due to methionine deprivation effected by METase. The S-phase-blocked cancer cells fluoresced yellow or green, in contrast to cancer cells in G\textsubscript{1} which fluoresced red. Cancer cells, synchronously blocked in S-phase by METase and identified by their yellow-green fluorescence, were administered DNA-damaging chemotherapy drugs such as doxorubicin, cisplatin, or 5-fluorouracil. Treatment of cancer cells with drugs only without methioninase-effected S-phase synchrony, led to the majority of the cancer cell population being blocked in G\textsubscript{0}/G\textsubscript{1} phase (red fluorescent) where they were resistant to the drugs. In contrast, METase treatment, followed by chemotherapy when FUCCI indicated the S/G2 block was highly effective for killing cancer cells. Color-coded chemotherapy, whereby the cell cycle of cancer cells is selectively and synchronously blocked in S-phase as identified by fluorescent reporters, may be a general approach to effective cancer treatment.


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