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Color-coded chemotherapy: S/G2-phase-trapping by methioninase pre-treatment, indicated by FUCCI imaging, enables highly effective cancer chemotherapy (923.11)

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Abstract

Methionine deprivation by methionine α,γ lyase (methioninase or METase) selectively arrests cancer cells during late S/G2-phase of the cell cycle, where the cancer cells are highly sensitive to DNA-damaging chemotherapy. Fluorescent ubiquitination-based cell cycle indicator (FUCCI) (Cell 132, 487-498, 2008), was used to monitor the onset of the S/G2-phase block due to methionine deprivation effected by METase. The S/G2-phase-blocked cancer cells fluoresced yellow or green, in contrast to cancer cells in G1/G0 which fluoresced red due to FUCCI. Cancer cells, synchronously blocked in S/G2-phase by METase fluorescing yellow-green, were treated with doxorubicin, cisplatin, or 5-fluorouracil. As a control, cancer cells treated with drugs only without rMETAse, were resistant to the drugs. rMETase treatment, followed by chemotherapy, when FUCCI indicated the onset of S/G2 block, was highly effective. Color-coded chemotherapy, whereby the cell cycle of cancer cells is blocked in S/G2-phase, as identified by fluorescent reporters, may be a general approach to effective cancer treatment.