ORIGINAL ARTICLE

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Cytosolic/microsomal redox pathway: a reductive retention mechanism of a PET-oncology tracer, Cu-pyruvaldehyde-bis(N^4-methylthiosemicarbazone) (Cu-PTSM)

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Objective: To clarify the retention mechanism of a PET imaging agent Cu-pyruvaldehyde-bis(N^4-methylthiosemicarbazone) (Cu-62-PTSM) in tumor cells, reductive metabolism of non-radioactive Cu-PTSM in five cultured tumor cell lines, a tumor specimen and non-tumor tissues *in vitro* was evaluated by electron spin resonance spectrometry (ESR).
Results: In the brain, mitochondrial electron transport enzyme reduced Cu-PTSM specifically. On the other hand, Cu-PTSM was not reduced in tumor mitochondria. The mitochondrial electron transport enzyme in tumor cells was not damaged, but NADH was considered to be depleted. In compensation for that, the tumor cells acquired complementary reduction activity in the microsome/cytosol. The reduction was enzymatic and NADH-dependent, possibly similar to the activation mechanism of bioreductive anticancer drugs.
Conclusion: Cu-PTSM and its derivatives are considered to be used as a marker for microsome/cytosol redox ability in PET oncology, although the physiological role of the redox enzyme system in tumor cells has not been clarified. The change in electron (NADH) flow in tumor cells might be a mechanism supporting aerobic glycolysis in tumor cells.

Key words: tumor, electron transport, Cu-PTSM, NADH, Complex I