

ヒト原発性肺腫瘍の悪性度に関連したチミジンキナーゼのシトソール型アイソザイムの活性

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Activity of the Cytosolic Isozyme of Thymidine Kinase in Human Primary Lung Tumors with Reference to Malignancy

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ABSTRACT Activity increase of the cytosolic isozyme of thymidine kinase (TK) in resected specimens of lung tumor patients would be a useful marker for tumor malignancy and prognosis. In 24 resected cases of malignant lung tumors, the whole enzyme extracts of the tumorous part of the specimens showed that the activities of TK, thymidylate synthetase, and ribonucleotide reductase increased at an average of 469 ($P < 0.001$), 208 (not significant), and 193% ($P < 0.02$) of the corresponding enzymes in the tumor-uninvolved lung parts, respectively. Two TK isozymes, cytosolic and mitochondrial TKs, were separated better by means of *p*-aminophenyl 3'-TMP:CH-Sepharose gel affinity column chromatography for precise quantitation of the activity than by polyacrylamide disc gel electrophoresis. These separated isozymes from the tumorous part of the specimens were characteristically very similar to the isozymes of cytosolic and mitochondrial fractions of the xenograft (CPX-101) of human lung tumor transplanted in athymic nude mice, respectively. The cytosolic isozyme activity isolated by this method from the tumorous part was remarkably higher and more varied than that of the tumor-uninvolved part, while that of the mitochondrial isozyme was lower and less agitated. The tumor doubling time showed a good inverse correlation to the activity of the cytosolic isozyme of TK when compared logarithmically ($r = -0.798$, $P < 0.01$). Poorly differentiated tumors exhibited significantly higher activities of

the TK cytosolic isozyme than did well-to-moderately differentiated tumors (766.0 ± 379.1 and 308.1 ± 119.5 pmol/mg of protein/h, mean \pm SE, respectively), a phenomenon also seen in the activities of the tumors with *versus* without recurrences within 12 mo after resection (803.6 ± 278.7 and 124.1 ± 42.1 pmol/mg of protein/h, respectively). The levels of these relationships using the cytosolic TK activity provided a clearer indication of prognosis and the state of the malignancy than those using the whole extract TK activity.

抄録 肺腫瘍患者の切除標本のチミジンキナーゼのシトソール型アイソザイムの活性増加が、腫瘍の悪性度や予後に対する有用な指標になることを示した。すなわち、悪性肺腫瘍患者の切除標本中の本酵素他、数種の核酸代謝関連酵素活性を検索したところ、健常部に対して有意に増加していた。さらに本酵素について生化学的解析により、シトソール型アイソザイム準位がその増加に寄与していることが明らかになった。

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