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Enzymatic Formation of 5-Fluorouracil from 1-(Tetrahydro-2-furanyl)-5-fluorouracil (Tegafur) in Human Tumor Tissues*

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1-(Tetrahydro-2-furanyl)-5-fluorouracil (Tegafur) has an antitumor activity with a wide spectrum of activity similar to 5-fluorouracil (FU) and is considered to be a chemical depot form of FU. It has been believed that FU is generated *in vivo* from Tegafur by hepatic metabolism involving cytochrome P-450.

We found that a soluble fraction of human lung cancer catalyzed the phosphorolytic cleavage of Tegafur. The catalysis was suppressed in the presence of excess thymidine, but not in the presence of 1-(2′-deoxy-β-D-glucopyranosyl)-thymine, an inhibitor of uridine phosphorylases.

The phosphorolytic activities of Tegafur and thymidine were much higher in extracts of tumor tissues than in those of normal tissues of human lung. The Tegafur phosphorolytic activity was hardly present in extract of mouse tumor (Sarcoma 180), which showed low thymidine phosphorylase activity.

We assume that the cleavage of Tegafur to FU is catalyzed by a thymidine phosphorylase activity and represents a possible activation mechanism of Tegafur in human tumor tissues.

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** 九州がんセンター.