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Activation of 5′-Deoxy-5-fluorouridine by Thymidine Phosphorylase in Human Tumors*

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Activities of pyrimidine nucleoside phosphorylases were assayed in extracts of human tumors, normal tissues of the same organs and tumors of mice (Sarcoma-180) and guinea pigs (Line-10), with thymidine (dThd), uridine (Urd), and 5′-deoxy-5-fluorouridine (5′-DFUR) as substrates. The nucleoside cleaving activities were higher in extracts of human tumor tissues than in those of normal tissues of the same organs. In human tissues, phosphorolytic activity towards dThd was high, while that towards Urd was low. In animal tumors, Urd was the best substrate. 1-(2-Deoxy-β-D-glucopyranosyl)-thymine (GPT), a specific inhibitor of uridine phosphorylase, inhibited the phosphorolysis of Urd and 5′-DFUR in extracts of animal tumors, but not that of dThd and 5′-DFUR in extracts of human tumors. A thymidine phosphorylase preparation was partially purified from human lung cancer. K_m values of the preparation were 2.43×10^{-4}M and 1.69×10^{-3}M for dThd and 5′-DFUR, respectively. We conclude that in human tumors a thymidine phosphorylase activity converts 5′-DFUR to 5-fluorouracil, an activated form.

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