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Rapid inhibition of ongoing DNA synthesis in human glioma tissue by genistein.

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Abstract

The effect of **genistein**, a protein tyrosine kinase and topoisomerase II inhibitor, on the DNA synthesis rate was studied in 21 human **glioma** specimens obtained at routine craniotomies for tumor resection. Ongoing DNA synthesis rate was determined by using a method based on the generation of tissue mini-units immediately after tumor resection and short incubation time (0-120 min) with [methyl-3H]-thymidine. A 9-77% inhibition of DNA synthesis rate by 100 microM **genistein** was observed in 18/21 of the **glioma** specimens. In these cases, the average percentage of inhibition was 55+/-20% (mean+/-SD, P<0.0001, Student's t-test) and the inhibitory effect was >50% in 12/18 of the cases. In 3 cases **genistein** increased the DNA synthesis rate. The inhibitory effect of **genistein** had a short-time onset and was concentration-dependent. Additional experiments in 4 cases showed that herbimycin A had no effect on DNA synthesis rate while etoposide inhibited similarly to that of **genistein**. Our results suggest that the effect of **genistein** on DNA synthesis rate in gliomas is independent of protein kinase inhibition and probably mediated by topoisomerase II inhibition. In the RG2 model, 50 microM **genistein** inhibited ongoing DNA synthesis in **glioma** cells with little or no effect in normal tissue. The data also encourage further investigations on the therapeutic potential of **genistein** for gliomas.

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