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Tyrosine Isomers mediate the classical phenomenon of concomitant tumor resistance and exhibit a powerful anti-metastatic effect with undetectable toxic-side effects

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Concomitant resistance (CR) is a phenomenon in which tumor-bearing hosts inhibit the growth of secondary tumor implants. Its relevance to the control of metastases is highlighted by the fact that the removal of tumors is sometimes followed by abrupt metastatic growth, suggesting that a primary tumor may exert a controlling action on its metastases, which can be considered natural secondary tumor implants.

CR induced by both immunogenic and non-immunogenic tumors had been associated with an anti-tumor serum factor that remained elusive for many years. Recently, we identified that factor(s) as a mixture of meta- and ortho-tyrosine, two unnatural isomers of tyrosine, as responsible for 90% and 10% of the total serum anti-tumor activity, respectively.

The antitumor effects of these tyrosine isomers were mediated in part by the early inhibition of the MAP/ERK pathway and inactivation of STAT3, potentially driving tumor cells to dormancy in G0-phase. Additionally, the activation of a putative intra-S-phase checkpoint would accumulate tumor cells in S-phase. Periodic intravenous administration of meta-tyrosine dramatically reduced lung and hepatic spontaneous metastases in mice bearing three different murine tumors, and decreased death rates from 100 up to 25% in tumor-excised mice with established metastases at the time of surgery. These effects were achieved even at very low concentrations and without displaying any detectable toxic side effects. Results suggest that the use of meta-tyrosine may help to develop new and less harmful means of managing malignant diseases, especially those aimed to control metastatic growth, an issue of pivotal clinical importance.

Biography

Raul A. Ruggiero is PhD in Biological Science from the National University of Buenos Aires, Argentina. He is the director of the Laboratory of Experimental Oncology, National Academy of Medicine of Buenos Aires. He has published more than 40 scientific papers in reputed journals and books in the area of Experimental and Theoretical Oncology.

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