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Antitumor activity of nutlin-3 in neuroblastoma with wild-type p53

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The small-molecule inhibitor nutlin-3 may be a viable treatment option for neuroblastoma patients with wild-type p53 activity, according to a new study published online November 10 in the *Journal of the National Cancer Institute*.

In this study in mice, Tom Van Maerken, M.D., Center for Medical Genetics, Ghent University Hospital in Belgium, and colleagues evaluated the antitumor efficacy of nutlin-3, a potent and selective antagonist of the p53-MDM2 interaction.

Researchers found that nutlin-3 activates the p53 pathway and suppresses tumor growth in the mice models of chemoresistant neuroblastoma, provided that wild-type p53 is present. (Neuroblastoma is a childhood tumor that often has a poor outcome). Oral administration of nutlin-3 as a single agent reduced tumor growth and metastasis.

"These findings support the initiation of clinical trials of selective MDM2 antagonists for treatment of advanced-stage and chemoresistant neuroblastoma," the authors write.

In an accompanying editorial, Eugene Kim, M.D., and Jason Shohet, M.D., Ph.D., of the Baylor College of Medicine in Houston, review the role of MDM2 and ARF in suppressing p53 during neuroblastoma pathogenesis and the sensitivity of this tumor to MDM2 inhibition. They suggest that the next step is to test agents that "re-activate" p53 in high-risk neuroblastoma by inhibiting MDM2 in human trials.

Source: Journal of the National Cancer Institute (news : web)