Antitumour activity of the ERK dimerization inhibitor DEL-22379 in lung adenocarcinoma /

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Monografía

Lung cancer is the leading cause of cancer-related mortality in both men and women worldwide. The most frequent type is lung adenocarcinoma, which accounts for 40% of all lung cancer cases. The RAS-RAF-MEK-ERK pathway (MAPK pathway) is known for being essential in cellular functions such as cell proliferation, differentiation, and apoptosis. Due to its important roles regulating cell functions, the MAPK pathway is commonly altered in many tumours, including lung adenocarcinomas. In the last years, numerous inhibitors of the cascade have been developed, and some of them have even progressed into the clinics. The most successful ones have been RAF and MEK inhibitors. However, patients treated with these drugs usually present relapses because of acquired resistance. For this reason, ERK has been recently considered as a potential target in cancer therapy, although ERK mutations rarely occur in tumours. In previous results from our laboratory, researchers have demonstrated that the prevention of ERK dimerization is a viable strategy to supress oncogenesis and tumour growth. Using a novel ERK dimerization screening method, Crespo et al. discovered a compound capable of effectively inhibiting ERK dimerization, which they called DEL-22379. This drug presented several antineoplastic properties in melanoma and colorectal cancer cells, such as generation of apoptotic response, a decrease of the tumour mass and lower metastatic spread. To further investigate the inhibitors potential, the purpose of this study is to analyse the antitumour effects of DEL-22379 in lung adenocarcinoma, in both cell culture and chick embryo animal model.

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