

Curcumin: a novel Stat3 pathway inhibitor for chemoprevention of lung cancer.

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In the USA alone 29% of cancer-related deaths are due to lung cancer, which is the leading cause of cancer deaths worldwide as well. Apart from age and obstructive pulmonary disease, cigarette smoking is the major cause of lung cancer in the US.

Hence, apart from smoking cessation, currently there is an urgent need for safe, effective and novel nutrient-derived substances as chemoprevention agents to modulate lung carcinogenesis. Several researchers have showed that members of the signal transducer and activator of transcription (Stat) family of transcription factors are potential targets in lung cancer and other cancers; particularly targeting Stat3 activation could be an important approach toward the prevention of lung cancers.

Research during the past couple of decades has suggested that Curcumin influences several biochemical and molecular cascades involved in cell cycle regulation, apoptosis, proliferation, survival, invasion, angiogenesis, metastasis and inflammation via multiple molecular targets, and thus substantiating its chemoprevention role.

Objective:

To study the effect of bioavailable curcuminoid complex on lung carcinogenesis, primarily by inhibiting Stat3 activation and to inform the design of a phase II chemoprevention trial of curcumin in former smokers.

Study Design:

Stat3 activation and proliferation was done in non-tumor-derived, normal (but immortalized) human bronchial epithelial cells (A461 cells) and human lung adenocarcinoma-derived cells (H460 cells)

CD-1 female nude mice (6-7 weeks) were divided into 3 groups (n=4): Two groups received 50 mg/kg Curcumin for 3 days or 9 days and third group received DMSO for 9 days (control group)

At the end of the study, the mice were sacrificed and whole lung tissue was removed for generating the protein extracts used for immunoblotting assay

Results and Discussion:

Curcumin showed a dose-dependent reduction in the levels of activated Stat3, as measured by the levels of Stat3 phosphorylated on tyrosine-705 (Stat3-P) in both cell lines

Additionally, Curcumin treatment also resulted in reduced cell proliferation in a dose-dependent manner for both the cell lines, indicating suppression of Stat3 pathway

In vivo results indicated that treatment with Curcumin for 3 or 9 days significantly suppressed Stat3-P (but not Stat3 total levels) and further suppressed Cyclin D1 and Mcm2 markers, the latter two indicative of a reduced proliferative capacity of the lung tissues

Conclusion:

Curcumin effectively inhibited the Stat3 pathway, along with a reduction in cell proliferation, thus can be an effective chemopreventive agent in high risk populations, such as former smokers.