# Effect of theophylline and specific phosphodiesterase IV inhibition on proliferation and apoptosis of progenitor cells in bronchial asthma

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## Abstract

Theophylline possesses anti-inflammatory activities in asthma. We examined whether theophylline and agents that modulate cyclic AMP can determine the survival and proliferation of progenitor cells.

Progenitor cells from the blood of normal and asthmatic subjects were cultured for 14 days in methylcellulose with GM-CSF, stem cell factor, IL-3 and IL-5. Apoptosis was measured by flow cytometry of propidium-iodide-stained cells.

A greater number of colonies with a higher proportion of cells of eosinophil lineage from asthmatics compared to normal subjects were grown. Theophylline (at 5 and 20 μg ml−1) significantly inhibited colony formation and increased apoptotic cells in asthmatics compared to control. Salbutamol (0.1, 1, 10 μM), dibutyryl-cAMP (0.1, 1 mM) and rolipram (0.1, 1 mM), a phosphodiesterase IV inhibitor, also dose-dependently decreased colony numbers and increased apoptosis of progenitor cells from asthmatics.

There was no significant effect of theophylline, db-cAMP, salbutamol or rolipram on colony formation or the survival of progenitor cells from normal subjects. AMP did not affect the colony formation and apoptosis. Expression of Bcl-2 protein on progenitor cells of asthma was downregulated by theophylline, salbutamol, db-cAMP and rolipram.

Theophylline and rolipram decreased colony formation committed to the eosinophil lineage, together with an increase in apoptosis through an inhibition of Bcl-2 expression effects that may occur through cAMP. The anti-inflammatory properties of theophylline include an inhibition of circulating progenitor cells.