VEGF Inhibitors for treating inflammatory disorders

OCR Number: OCR 1581

Description:

Exaggerated levels of VEGF are present in asthma. Transgenic mice that over-express VEGF exhibit an asthma-like phenotype with inflammation, parenchymal and vascular remodeling, edema, mucus metaplasia, myocyte hyperplasia, and airways hyper-responsiveness. VEGF also enhanced respiratory antigen sensitization and Th2 inflammation and increased the number of activated DC2 dendritic cells. Thus, VEGF is a mediator of inflammation that enhances antigen sensitization and plays a critical role in adaptive Th2 inflammation. A small molecule inhibitor of VEGF markedly decreased tissue inflammation and airway hyper-responsiveness. Similar results were seen with a soluble VEGF receptor trap. These inhibitors also markedly decreased antigen-stimulated IL-13 and IL-4 production. Therefore, VEGF inhibition may be therapeutic in asthma and other Th2 disorders.

Field of Application: Treatment of Th2-mediated inflammatory disorders (including asthma).

Advantages: A novel mechanism for the therapeutic intervention of asthma and other Th2 mediated inflammatory diseases. Current NSAID therapies for these diseases may have issues in efficacy or safety (e.g. Vioxx). A number of VEGF-directed molecules are entering the market (e.g. Lucentis, Avastin, Nexavar), and anti-inflammatory use may expand the number of approved indications for these drugs.

Stage of Development: Discovery

Publications:

Nat Med. 2004 Oct. 10(10):1095-103

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