The discovery of montelukast (Singulair): a leukotriene receptor antagonist for the treatment of asthma

Professor Robert N. Young

Merck Frosst // Pharmaceutical Genomics and Drug Discovery, Chemistry Department, Simon Fraser University, Vancouver, Canada

The structure of leukotrienes was elucidated in 1979 and their proposed implication in the etiology of respiratory diseases caused many laboratories to initiate programs to discover blockers of leukotrienes as new treatments for asthma. Merck Frosst started two parallel programs, one to find an inhibitor of the key biosynthesizing enzyme, 5-lipoxygenase and the other to find a selective blocker of the Leukotriene D4 receptor. These projects proceeded for more than 10 years with many failures and 6 compounds, which were brought into human clinical trials before montelukast (Singulair) was identified. The discovery process and the unique chemistry, which made the preparation of many analogs and eventually Singulair itself, will be described. Today Singulair treats millions of patients around the world and has market sales in excess of $5 billion US.