Drug therapy for allergy moves forward

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Researchers have identified several target molecules which are suitable for the development of new allergy drugs. The *Journal of Allergy and Clinical Immunology*, the most prestigious journal in the field of allergology, has recently published an extensive review article on the prospects of drug therapy for allergy. Completed in a large-scale EU project, the lead author of the review article is Professor Ilkka Harvima of the University of Eastern Finland and Kuopio University Hospital.

Immediate allergic reactions and allergic diseases such as allergic rhinitis, asthma and urticaria are extremely widespread in the population. Traditionally, drug therapy for allergy is based on the use of non-sedative antihistamines, i.e. blocking of the histamine H1 receptors, but sometimes additional help is obtained from blockers of the cysteinyl leukotriene receptor-1.

Antihistamines seek to prevent allergic symptoms caused by histamine released by mast cells. Mast cells, also known as "allergy cells", are cells of the immune system which become activated by environmental allergens.

"However, even high doses of H1 antihistamine drugs aren't enough to alleviate the symptoms of some patients. This is understandable, as when the mast cell becomes activated, several other strong mediators besides histamine get released, too. Histamine can also affect other receptors of the cell surface than the H1 receptor," Professor Harvima explains.

Over the past years, researchers have identified several mast cell

molecules which can be targets of new drugs. Several of these have already proceeded to clinical trials. These targets include, for example, serine proteinases tryptase, chymase, cathepsin G, which are enzymes that break down proteins, as well as 5-lipoxygenase-activating protein FLAP, 15-lipoxygenase-1, prostaglandin-D2, and proinflammatory cytokines such as TNF-alpha, IL-4, IL-6 and IL-17. New drugs targeting the histamine H4 receptor are also undergoing clinical trials. In the near future, it is possible that drug therapy for allergy is a combination of H1 and H4 receptor blockers.

Several target molecules have also been identified in intracellular signalling pathways and in cell survival proteins. Inhibiting these molecules can lead to the prevention of activation of the cell and to the prevention of mediator release. Various receptors which can either activate or inhibit the cell have been identified on cell surface. Different drug molecules make it possible to affect the function of these receptors and, consequently, to prevent cell activation and mediator release.

The Mast Cells and Basophiles: Targets for Innovative Therapies project, funded by COST funding BM1007 of the EU, brings together European experts focusing on the identification of new target molecules for drug development, including allergy drugs. The University of Eastern Finland and Kuopio University Hospital were represented in the project by Professor Harvima, who is also the lead author of the review article.

More information: The *Journal of Allergy and Clinical Immunology*, May 2014, Vol. 133, No. 5. "Molecular targets on mast cells and basophils for novel therapies," Ilkka Harvima, Francesca Levi-Schaffer, Petr Draber, Sheli Friedman, et al.

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