

?A new principle for epigenetic changes discovered

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Credit: NIH

In a new study, researchers at Uppsala University have found evidence of a new principle for how epigenetic changes can occur. The principle is based on an enzyme, tryptase, that has epigenetic effects that cause cells to proliferate in an uncontrolled manner.

"Cells that lack tryptase start to proliferate in an uncontrolled fashion and lose their identity. If tryptase is present, it will cleave the tails of histones, which will protect from certain epigenetic changes," says Gunnar Pejler, Professor at the Department of Medical Biochemistry and Microbiology at Uppsala University.

Many properties are determined by genetic factors, but we are starting to recognize that also epigenetic factors are of great importance. With epigenetics we mean such changes in genes that are not determined by changes in the actual DNA sequence, but effects that are superimposed on this, caused for example by environmental effects.

Epigenetic effects include modification of DNA by incorporation of small chemical groups, methyl groups. Another important epigenetic mechanism is that the proteins that are packed together with DNA in the cell nucleus, called histones, can be chemically modified in their tails. Altogether, the different epigenetic mechanisms will lead to either activation or silencing of the respective genes.

In a new study published in the *Journal of Allergy* and *Clinical Immunology*, researchers have now found a new principle for how epigenetic changes can occur. They have showed that one enzyme, tryptase, can be found in the nucleus of cells and that tryptase can cleave off the tails of histones. In this way, certain epigenetic modifications of the histone tails are removed.

A very interesting finding was that this mechanism is important for maintaining the identity of the cells. Cells that lacked tryptase showed major changes, including a loss of their cellular identity and they also started to proliferate in an uncontrolled way.

These effects were seen in mast cells which are central in allergic reactions. The researchers propose that this type of epigenetic <u>effect</u> could be of importance in dealing with allergic disease. However, it cannot be excluded that similar epigenetic effects are operative also in other cell types.

More information: Fabio R. Melo et al. Tryptase-catalyzed core histone truncation: a novel epigenetic regulatory mechanism in mast cells, *Journal of Allergy and Clinical Immunology* (2017). DOI: 10.1016/j.jaci.2016.11.044

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