POPULAR SCIENCE PROJECT SUMMARY

The aim of the project is to indicate the molecular mechanism of shaping the inflammatory endothelium profile conditioned by the lysine specific demethylase 1 (LSD1) activity. The substrate for LSD1 is histone H3 and its role based on the removal of methyl groups from lysines 4 and 9. These histone posttranslational modifications determine accessibility of transcription factors to specific genes due to changes in chromatin conformation. Moreover scientific reports demonstrate non-histone substrates for histone modifying enzymes, in that LSD1.

The basis of the project are observations that indicate the involvement of LSD1 in stimulating the NFκB-depended inflammatory mediators expression in endothelial cells in response to pro-inflammatory stimuli. Therefore, is required to establish whether the pro-inflammatory properties of LSD1 in endothelial cells are associated with modification of the chromatin conformation, or changes in methylation of lysine residues status of p65 subunit of NFκB. So far, p65 polypeptide chain positions, lysine and arginine residues were designated for methylation by specific histone methyltransferases. However the reverse process - demethylation - is still poorly understood. Therefore, a further aim will be to determine which methyl groups are attached to the specific lysines of the amino acid chain of p65 by LSD-1 and at what level: mono-, di-, or tri- demethylation.

Understanding the role of lysine specific demethylase 1 and the mechanism its action in regulationof the inflammatory response of endothelial cells will complement the knowledge about this protein and will be a next step in understanding the complexity of transcription mechanisms. Furthermore, it is not excluded that in the future LSD-1 may be an attractive therapeutic target in the prevention of the activation of endothelium or cancer because of the mutations or LSD-1 overexpression.