Subcellular compartmentation of ascorbate and epigenetics

*Dr. Péter Lőw, Dr. Éva Margittai*

The main goal of our work was to prove the epigenetic effects of ascorbate in model systems characterized by either local or generalized ascorbate deficiency.

Our results are the followings: we successfully set up a transmission electron microscopy method to study intracellular distribution of ascorbate directly. We have shown with the above method, that in mammalian fibroblast cells vitamin C is localized mainly in the nucleus, possibly referring to a crucial role of the vitamin in the compartment. We have further shown, that if ascorbate deficiency is localized to the nucleus (in arterial tortuosity syndrome) alteration of epigenetic markers occur at global DNA level, examining cytosine methylation status: methylcytosine level increased, while hydroxymethylcytosine decreased in patient fibroblasts. We have selected specific genes and gene regions for the region-specific epigenetic examination of proteins, which are involved in ascorbate metabolism or function to examine their methylation status. Measured with two different methods, we found decreased hydroxymethylcytosine level in the gene of PPARgamma, which elevated upon the addition of ascorbate selectively in control fibroblasts. In summary, our results firstly shown the role of vitamin C transport in epigenetic regulation.