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In silico prenylation predictions for human proteins as a novel class of naturally occurring post-translational peptides

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Prenylation is a form of post-translational modification in which isoprenoid lipids are covalently bonded to the C-terminus of newly synthesized proteins [1, 2]. This process enhances intracellular protein localization and alters activity of numerous proteins. It is believed that prenylation of proteins assists in their incorporation into human cell membranes [2, 3]. However, even though prenylation has been experimentally identified in bacteria [3], no experimental evidence supports prenylation of human proteins.

The research objective was to collect data of modified human proteins that supports the existence of prenylation in human proteins. Modified human proteins (775) were gathered, based on laboratory evidence, from the EROP-Moscow Database (http://erop.inbi.ras.ru/query-erop.php?submit=%C2%A0%C2%A0Query+EROP), and all of the available unmodified human proteins were collected from the NCBI Homo sapiens mRNA Protein Database (https://www.ncbi.nlm.nih.gov/refseq/). Homo sapiens proteases (6,425) from the CutDB Proteolytic Event Database (http://cutdb.burnham.org/) were applied to the NCBI data in order to generate in silico cut protein segments. Unique Python scripts were created and used to perform in silico bioinformatic experimentation and analysis, resulting in the synthesis of 69,706 protein segments from the NCBI data, in addition to the 775 already collected proteins from the EROP data.

These results were then submitted to PrePS (http://mendel.imp.ac.at/PrePS/) as a batch job to computationally identify human protein prenylation targets. Consequently, 35 peptides were positively predicted as human protein prenylation targets. The proteases, which are involved in peptide modificaton for prenylation, include cathepsin, bacterial collegenase, retropepsin (human T-cell leukemia virus), and eupitrilysin. Of these 4 proteases, bacterial collegenase, retropepsin (human T-cell leukemia virus), and eupitrilysin were identified as physiological proteases due to repetitive occurrence in the formation of prenylated peptides.

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