PLANTPEPTIDOMICS Report Summary

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Final Report Summary - PLANTPEPTIDOMICS (Identification, isolation and characterization of novel pharmaceutically active cysteine-rich peptides from plants)

Executive Summary:

Natural products represent a pool of privileged structures that are optimized by evolution to interact with proteins and other biomolecules. Thus, they constitute a valuable resource in the search for new therapeutic agents. Around 50% of all small-molecule drugs approved over the last years are either natural products or derived therefrom. Plants are a particularly interesting source of bioactive compounds since they are used to treat diseases and maintain health since prehistoric times.

The idea behind this project was, that - while typical plant secondary metabolites such as flavonoids, alkaloids, and terpenoids are already very well studied - plant defense peptides are a largely underinvestigated compound class. This is partly due to the lack of an established peptidomic workflow for the systematic screening of peptides in plant material. Within this project, we have established exactly such a workflow that comprises a generally applicable protocol for the extraction and purification of peptides from plant material, their detection by the hyphenation of high-performance liquid chromatography (HPLC) and mass spectrometry (MS), and a strategy for the efficient data analysis.

With a suitable methodology at hand, the next focus was on the identification, isolation and characterization of novel plant defense peptides, which often show remarkable pharmacological activities. For this purpose, we have screened a total of 179 mainly ethnomedicinally used plant and lichen species, of which 11 were found to contain significant amounts of peptides. Interestingly, only two of them were previously described to contain peptides, while this fact was completely new for the other nine species.

In the next stage, those five plants that had the highest relevance as herbal drugs and/or food ingredients were selected for in-depth studies. Their major peptides were purified and characterized by chemical, enzymatic, and mass spectrometric methods. Full de-novo sequencing was achieved for a total of 17 peptides, which ranged from relatively small (7-12 amino acids), linear, acidic ones up to 30-39 amino acid-long peptides that are stabilized by 3-4 disulfide bridges.

Finally, we have established external collaborations for testing the bioactivity of one particularly interesting peptide fraction in relevant cell assays, which yielded very promising preliminary data with respect to a potential immunomodulatory and antiviral activity.

The fact that our approach led to the discovery of several new abundant peptides – some of them even without significant homology to any known sequences - even in already very well studied herbal drugs and food plants, proofs our assumption that this compound class was previously often overlooked and underscores the innovative nature of this project. Based on the very promising results with the immunomodulatory and antivirally active peptides, we will continue to investigate their potential as lead compounds.
The postdoc researcher, Dr. Martin Zehl, was very well integrated into the Department of Pharmacognosy of the University of Vienna. The ERG allowed him to establish and lead a new research topic at his host institution and soon after the end of the funding period, his application for a permanent position as senior scientist was accepted.