Solid-Phase Synthesis of C-Terminal Peptide Libraries for Studying the Specificity of Protein Prenyltransferases

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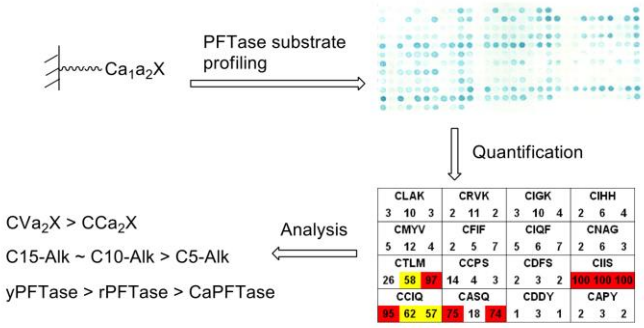
Protein prenylation is a common post-translational modification of specific protein-derived cysteine residues in eukaryotic cells. Considerable interest exists for developing inhibitors of these enzymes for a number of diseases including cancer. To study the substrate specificity of prenyltransferases, the primary strategy employed to date has involved the synthesis, purification and assaying of individual peptides. As an improvement, here we report the synthesis of peptide libraries containing free *C*-termini using SPOT synthesis. Following synthesis, libraries containing 70-600 different peptides were enzymatically prenylated with an alkyne-containing isoprenoid diphosphate substrate and the resulting modified peptides detected via click reaction with biotin azide followed by detection with streptavidin-AP. Prenyltransferases from several species were examined to identify interspecies differences in enzyme specificity.[1] Libraries of this type should be widely applicable for studying the specificity of prenyltransferases as well as other enzymes that use prenylated proteins as substrates.



[1] Wang, Y.-C.; Dozier, J. K.; Beese, L. S.; Distefano, M. D. *ACS Chem. Biol.* **2014**, *9*, 1726-1735.
Note: References and Figures are not required but are optional if you would like to include them.