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A Novel Antiviral Protein Generated by Mutation of Pokeweed antiviral Protein(PAP) cDNA

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Pokeweed antiviral protein(PAP) isolated from pokeweed plants showed broad spectrum antiviral activity against plant and animal viruses. PAP is a single chain ribosome inactivating protein(RIP) found in the cell walls of *Phytolacca americana*(a pokeweed). PAP inhibits protein synthesis by removing an adenine residue from a conserved region of the large ribosomal RNA. RIPs have been of considerable interest in recent years due to their use in the development of chimeric toxins, which can be targeted to a particular cell type, such as tumor cells. In addition, PAP has been targeted to CD4+ T cells by conjugating it to monoclonal antibodies and has inhibited HIV replication in these cells. The expression of PAP cDNA in transgenic tobacco plants conferred broad spectrum resistance to viral infection. To determine if ribosome inhibitory activity of PAP is responsible for its antiviral activity, the mutated PAP-cDNA was expressed in yeast using the galactose inducible GAL1 promoter and the protein mutants deficient in RIP activity were selected. A number of mutants that can grow in the presence of galactose were isolated and characterized with respect to their RIP and the protein was enough to remove its RIP activity, but to maintain its antiviral activities.