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DEVELOPMENT OF A PLANT-DERIVED ANTHRAX VACCINE

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The efficacy, imunogenicity and safety profiles of the only licensed vaccine against anthrax (*Bacillus anthracis*) are currently under review. This vaccine requires six injections over an 18-month period and was developed several decades ago to protect workers who come in contact with infected animal products. Our laboratory has initiated a project to develop plant-derived anthrax vaccines. Plant biotechnology offers practical and economical solutions for the production of new generation biopharmaceuticals; anthrax vaccine research can undoubtedly benefit from this research. Two basic approaches are being applied in our experiments: 1) engineering of stably transformed food plants for administration as "edible" vaccines and 2) transient expression of promising immunogenic protein antigens by a modified plant viral vector. In the first approach, a DNA fragment encoding the *B. anthracis* protective antigen (PA) with a plant consensus sequence surrounding the AUG initiation codon and the KDEL retention signal was incorporated into the binary plant expression vector pGA643 under the control of the universal plant 35S cauliflower mosaic virus promoter. Tomato plants (*Lycopersicon esculentum)* were transformed with this construct utilizing *Agrobacterium tumefaciens*. In the viral vector approach, two constructs were designed: 1) a recombinant gene encoding the receptor-binding domain 4 of PA preceded by the rice α-amylase signal peptide and 2) a fusion gene encoding the cholera toxin B subunit and a short receptor-binding region within domain 4 of PA. The fusion constructs were cloned into the B30 tobacco mosaic virus vector under the control of the viral coat protein promoter. Preliminary results will be presented and discussed.

DEVELOPMENT OF A PLANT-DERIVED SUBUNIT VACCINE CANDIDATE AGAINST HEPATITIS C VIRUS

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Hepatitis C virus (HCV) is a major cause of acute and chronic hepatitis with over 180 million cases worldwide. There is no effective vaccine or therapy against this virus. Our research describes the development of an experimental plant-derived subunit vaccine against HCV. A tobamoviral vector was engineered to encode a hypervairable region (HVR1) consensus sequence genetically fused to the B-subunit of cholera toxin (CTB). This potential neutralizing epitope was designed using the amino acid sequence of the R9 "mimotope" which is capable of inducing cross-neutralizing antibodies against different variants of the virus. Plants infected with recombinant tobacco mosaic virus engineered to express HVR1/CTB chimeric protein, contained intact virus particles and produced the HVR1 consensus peptide fused to the C-terminal of functionally active, pentameric CTB. Plant-derived HVR1/CTB reacted with HVR1-specific monoclonal antibodies and immune sera from HCV-infected individuals representing four major viral genotypes. Intranasal immunization of mice with a crude plant extract containing the recombinant HVR1/CTB protein elicited anti-CTB serum antibody and anti-HVR1 serum antibody which specifically binds to HCV virus-like particles. Using a plant transient expression system to produce this unique chimeric antigen will significantly reduce the cost and facilitate development and production of an experimental HCV vaccine.