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Pre-exposure Immunoprophylaxis by Genetically Encoded DMAb anti-OspA Human Monoclonal Antibody to Prevent Lyme Disease

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PRE-EXPOSURE IMMUNOPROPHYLAXIS BY GENETICALLY ENCODED DMAB ANTI-OSP A HUMAN MONOCLONAL ANTIBODY TO PREVENT LYME DISEASE

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Tick transmission of Borrelia spirochetes to humans results in significant morbidity from Lyme disease. Animal studies have demonstrated that transmission of Borrelia from tick vector to the mammalian host can be blocked by antibodies against outer surface protein A (OspA). We have recently developed borreliacidal human IgG1 monoclonal antibodies (HuMabs) directed against OspA. HuMab 319-44 was borreliacidal against B. burgdorferi (IC50 <1nM), the main cause of Lyme disease in North America, and in mice was 100% effective in preventing Borrelia transmission after a single dose of 2 mg/kg administered on the day of tick challenge. Since passively administered IgG1 antibodies do not have a sufficient half-life to provide protection for the 6-7 month peak risk period, we investigated a novel approach of vector-mediated gene transfer of HuMabs that could potentially provide protection against Lyme disease during the seasonal risk period.

A modified HuMab, 319-44 mod, expressed by a synthetic DNA plasmid (DMAb) was optimized and characterized in in vitro OspA binding and bactericidal assays. To assess in vivo protection, mice were administered a single DMAb injection into the quadriceps followed by electroporation. The mice were then challenged by B. burgdorferi-infected nymphs. Tissue samples were monitored by dark-field microscopy for spirochete growth. Serum samples were analyzed by ELISA to determine antibody concentrations.

The modified 319-44 DMAb maintained in vitro biological activity comparable to the un-modified wild type antibody, and formulation-based delivery of DMAb resulted in long-term expression. This led to effective pre-exposure prophylaxis preventing transmission of spirochetes in 80% of mice in the murine model of tick-transmitted Lyme disease. These studies represent the first demonstration of employing DNA transfer as a rapid, novel delivery system for biologically relevant functional full-length HuMabs in an in vivo animal model and provide support for such an approach for pre-exposure immunoprophylaxis to prevent Lyme disease.

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