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PRE-EXPOSURE IMMUNOPROPHYLAXIS BY GENETICALLY ENCODED DMAB ANTI-OSPA 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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