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Pre-exposure prophylaxis with OspA-specific human monoclonal antibodies protects mice against tick transmission of Lyme disease spirochetes

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Background. Tick transmission of Borrelia spirochetes to humans results in significant morbidity from Lyme disease worldwide. Serum concentrations of antibodies against outer surface protein A (OspA) were shown to correlate with protection from infection with Borrelia burgdorferi, the primary cause of Lyme disease in the United States.

Methods. Mice transgenic for human immunoglobulin genes were immunized with OspA protein of B. burgdorferi to generate human monoclonal antibodies (HuMabs) against OspA. HuMabs were generated and tested in in vitro borreliacidal assays and animal protection assays.

Results. Nearly 100 unique OspA specific HuMabs were generated and four HuMabs (221-7, 857-2, 319-44, and 212-55) were selected as lead candidates based on borreliacidal activity. HuMab 319-44, 857-2 and 212-55 were borreliacidal against one or two Borrelia genospecies, whereas 221-7 was borreliacidal (IC50 <1nM) against B. burgdorferi, B. afzelii and B. garinii, the three main genospecies endemic in the US, Europe and Asia. All four HuMabs completely protected mice from infection at 10 mg/kg in a murine model of tick-mediated transmission of B. burgdorferi.

Conclusions. Our study indicates that OspA-specific HuMabs can prevent the transmission of Borrelia and administration of these antibodies could be employed as pre-exposure prophylaxis for Lyme disease.

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