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Yang Wang
University of Massachusetts Medical School

Et al.

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

Yang Wang, MD PhD[1], Aurélie Kern, PhD[2], Naomi K. Boatright, BS[1], Zachary Schiller, BS[1], Andrew Sadowski, BS[1], Monir Ejemel, BS[1], Colby A. Souders, PhD[1], Keith A. Reimann, DVM[1], Linden Hu, MD[2], William D. Thomas, Jr., PhD[1], Mark S. Klempner, MD[1*]

[1]MassBiologics, University of Massachusetts Medical School, Boston, Massachusetts, USA
[2]Sackler School of Graduate Biomedical Sciences, Tufts University School of Medicine, Boston, Massachusetts, USA
*Corresponding Author: Mark.Klempner@umassmed.edu

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.

Yang Wang, M.D Ph.D
Senior Director, Product Discovery
Assistant Professor of Medicine
T 617-474-4091 MassBiologics
F 617-474-5354 460 Walk Hill Street
Boston, MA 02126
yang.wang@umassmed.edu
www.umassmed.edu/massbiologics