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

Yan Wang
University of Massachusetts Medical School

Seleeke Flingai
The Wistar Institute

Aurelie Kern
Tufts University

See next page for additional authors

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Presenter Information
Yan Wang, Seleeke Flingai, Aurelie Kern, Sangya Agarwal, Zachary Schiller, Kaori Graybeal, Rianne Esquivel, Ami Patel, Linden Hu, David Weiner, and Mark S. Klempner

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

Yang Wang, MD, PhD1, Seleeke Flingai, PhD2, Aurélie Kern, PhD2, Sangya Agarwal, MS2,
Zachary Schiller, MS1, Kaori Graybeal, MS1, Rianne Esquivel, PhD2, Ami Patel, PhD2, Linden
Hu, MD3, David Weiner, PhD2, Mark Klempner, MD1
1MassBiologics at UMMS, Boston, MA; 2The Wistar Institute, Philadelphia, PA; 3Sackler School
of Graduate Biomedical Sciences, Tufts University School of Medicine, Boston, MA

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.

Contact:
Yang Wang
University of Massachusetts Medical School
Yang.Wang@umassmed.edu