ABSTRACT

Lyme disease is the most common tick-borne infection in North American and Eurasian countries with temperate climates. Worldwide, three main genospecies of Borrelia are associated with Lyme disease in humans. B. burgdorferi is the main cause of Lyme disease in North America, while B. garinii and B. afzelii are the prevalent strains that cause the disease in Europe and Asia. The murine antibody LA-2 against outer surface protein A (OspA) of Borrelia prevents tick-transmitted infection with Lyme disease in animal models and is the best serologic correlate of vaccine-mediated protective immunity in humans.

To develop a human monoclonal antibody for pre-exposure prophylaxis (PrEP) of Lyme disease, we created a panel of borreliaclonal human monoclonal antibodies (HuMabs) by immunizing with OspA protein of B. burgdorferi, mice that were transgenic for human immunoglobulin genes and inactivated mouse immunoglobulin genes. Over 93 unique HuMabs bound to OspA and were tested in borreliacidal assays against B. burgdorferi, B. afzelii and B. garinii. Four HuMabs (221-7, 857-2, 319-44, and 212-55) were selected as lead candidates based on high borreliacidal activities (<10 nM of EC50). HuMab 319-44, 857-2 and 212-55 were borreliacidal against one or two species, whereas 221-7 was cidal (EC50 <1mM) against all three genospecies. HuMab 221-7 and 857-2 recognized a conserved conformational epitope comprising amino acids 71-141, a relatively conserved region of OspA. HuMab 212-55 bound to an epitope within a.a. 178-273 and blocked LA-2 binding. Two HuMabs, 319-44 and 221-7, were selected for further study.

RESULTS

Four lead HuMabs recognize distinct epitopes of OspA.

CONCLUSIONS AND FUTURE DIRECTIONS

- Identified and characterized four HuMabs that react with the OspA protein of B. burgdorferi and demonstrated borreliacidal activity in vitro assays.
- These antibodies recognize unique OspA epitopes and some exhibit in vitro activity against all three Borrelia genospecies that are endemic in the US, Europe and Asia.
- Lead HuMabs were further tested in a mouse challenge model to determine potency, PK and cross-strain protection (Poster board # 764).