Monoclonal Antibody Administration Provides Five Weeks of Pertussis Prophylaxis in Newborn Baboons: PoC for Passive Immunization to Protect Infants in the Developing World

J.A. Maynard1, A. Nguyen1, R.F. Wolf2, J.F. Papin2, S. Connelly3, M. Kaleko3
1University of Texas at Austin, Austin, TX, 2University of Oklahoma Health Science Center, Oklahoma City, OK, 3Synthetic Biologics, Inc., Rockville, MD USA

ABSTRACT

Background: Pertussis remains a significant health problem in the developing world, killing up to 200,000 infants annually. Neonatal vaccination in current strategies to protect newborns, but is unlikely to capture 8-10% of eligible mothers. We previously described the humoral immunity of hu1B7, a monoclonal antibody (mAb) that potently neutralizes pertussis toxin (PTX). PTX prevents disease in mice when administered to weaning baboons after infection as part of a binary mAb cocktail. We hypothesized that hu1B7, given at birth, could protect newborns from disease in infancy, when the mortality rate is highest. Here we present a proof-of-concept study designed to determine if hu1B7 administered to newborn baboons could provide protection from pertussis infection 5 weeks later.

RESULTS

Prophylaxis Study Design

Two day old baboons assigned to the treatment group received hu1B7 (40 mg/kg, IV). Hu1B7 antibody levels were monitored weekly. Five weeks later animals were infected with B. pertussis. Leukocytosis, anti-caf tau antibody and clinical symptoms were followed.

Antibody Prophylaxis Suppressed Leukocytosis in Infected Baboons

Control animals infected at approximately five weeks of age exhibited marked elevations in peak white blood cell (WBC) counts. In contrast, animals treated with hu1B7 at 2 days of age and at 5 weeks, had peak WBCs that either remained normal or were slightly elevated. Nasopharyngeal B. pertussis colonization was unaffected by antibody prophylaxis. Clinical symptoms of pertussis were ameliorated in all antibody-treated animals, while 3/6 control animals displayed symptoms severe enough to require euthanasia, including lethargy and coughing.

CONCLUSIONS

• Hu1B7 antibody prophylaxis suppressed leukocytosis and ameliorated clinical symptoms of pertussis in newborn baboons
• Similar to the acellular pertussis vaccine, hu1B7 prophylaxis did not prevent nasopharyngeal bacterial colonization
• Hu1B7 half-life in baboons is 12 ± 4 days; the half-life in humans is expected to be longer
• Evaluation of an extended half-life version of hu1B7 in baboons is in progress

Pertussis prophylaxis using hu1B7, a humanized anti-pertussis toxin monoclonal antibody, may be a viable option to protect newborns for several months after birth when the risk of pertussis mortality is highest

REFERENCES AND DISCLOSURES

3. SC and MK are employees of Synthetic Biologics, Inc. Synthetic Biologics, Inc. manufactured the hu1B7 used in this study. The neonatal baboon study was funded through a grant from the Bill and Melinda Gates Foundation awarded to JAM.

Synthetic Biologics, Inc.