

## **Clinical protection of neonatal SCID foals against EIAV by passive transfer of plasma containing broadly neutralizing antibodies**

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Equine infectious anemia virus (EIAV) is a lentivirus that infects equids worldwide. Although neutralizing antibody and T-lymphocyte responses are critical for lentiviral control, the correlates of protective immunity are still not known. Infusion of neutralizing antibodies into rhesus macaques is protective when administered 24 hours prior to intravenous SHIV challenge. However, T lymphocyte responses might contribute to protection in immunocompetent animals. Foals affected with severe combined immunodeficiency (SCID) provide a unique and powerful large animal model in which to dissect the protective effects of lentiviral-specific neutralizing antibodies in the absence of T-lymphocyte responses. In the current study, we hypothesized that plasma containing broadly neutralizing antibodies would prevent infection in EIAV-challenged SCID foals. Plasma was collected from a long-term infected EIAV inapparent carrier horse, and treated with methylene blue and white light to inactivate virus. This plasma contained antibodies capable of neutralizing five EIAV envelope variants, and was administered IV to four experimental SCID foals, 24 hours prior to EIAV challenge. Four age-matched control foals received methylene blue-treated normal horse plasma. Plasma infusions were repeated at 7 and 14 days post-challenge. Although all four experimental SCID foals developed detectable plasma viral RNA by real-time RT-PCR, all were protected from clinical disease out to 60 days post-challenge. Whole blood was collected from each of two experimental SCID foals at 40 DPI and transfused IV to two normal naïve horses. One recipient horse became infected as determined by clinical disease, plasma viremia, and positive serology (AGID and ELISA), and one remained uninfected. This horse did not develop clinical disease, and was confirmed negative by serology at days 30 and 45 post-transfusion, and proviral DNA was not detected in the spleen. Three immunocompetent and one SCID foal served as controls, all of which became viremic. The SCID control developed clinical disease as determined by pyrexia, thrombocytopenia, and anemia, and was euthanized. Immunocompetent controls did not develop clinical disease, most likely because the challenge virus was less virulent in immunocompetent foals. These results provide proof of concept that broadly neutralizing antibodies are sufficient to prevent clinical lentiviral disease in the complete absence of T lymphocyte responses.