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Post-exposure Immunotherapeutics for Biothreat Agents & Emerging Diseases

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Passive immunotherapies have been traditionally used for the treatment of biological and toxic agents although their use as a post-exposure treatment option has not been widespread for some time. Recently we developed caprine-based immunotherapeutics for the treatment of emerging diseases including SARS CoV, HIV and West Nile virus.

Here we present data on a non-antibiotic based therapy which neutralizes the anthrax lethal toxin (LeTx) both in vitro and in vivo. Goats hyperimmunized with recombinant protective antigen (rPA83) produce high titers of LeTx neutralizing antibodies which are protective following passive antibody transfer. Mice exposed to 5 LD₅₀ of *Bacillus anthracis* Ames spores by intranasal inoculation demonstrated 60% survival up to 14 days when administered 32 mg/kg anti-PA83 IgG 24 hours post spore challenge. When co-administered with ciprofloxacin, 100% survival was seen up to day 6 p.i. and a survival rate of 60% was observed out to the end of the study at day 14 p.i.

In order to circumvent the possibility of adverse reactions in patients receiving caprine passive immunotherapy, we have generated F(ab')₂ fragments of the PA83 antibodies. Removal of the Fc portion of the goat IgG molecules renders the antibodies safer for repeated use in humans by reducing the likelihood of Fc mediated hypersensitivity reactions. The anti-PA83 F(ab')₂ fragments have demonstrated equivalent protection in vitro with respect to the full IgG molecule. Animal data will also be presented supporting our claim that Fab'2 antibodies retain high levels of protection against anthrax infection.

This passive immunotherapeutic provides an efficacious treatment option for patients presenting with symptoms of anthrax who are not expected to recover with antibiotic treatment alone.