

## **CMV MODELS**

### **Immunocompromised GPCMV Model**

This guinea pig model mimics CMV infection of the immunocompromised host, a common target population of cytomegalovirus infections. Young Hartley guinea pigs are immunosuppressed with cyclophosphamide administered 1 and 7 days prior to viral inoculation with  $\sim 10^5$  pfu salivary gland passaged guinea pig cytomegalovirus (GPCMV). In a typical experiment, two groups of 12 animals each will receive the experimental compound or placebo beginning 24 hours after infection. Animals are followed daily for evidence of disease and death which usually occurs by day 14 (1). Effects on viral replication are made by sacrificing animals and quantitating virus in specific organs and blood by Real-Time PCR and/or culture

Volume: The amount of compound is based on an average guinea pig weight of 350-500g.

### **Neonatal GPCMV Model**

CMV infection of premature newborns may be life-threatening disease if untreated. The neonatal guinea pig model resembles perinatal CMV infection and allows systematic evaluation of antiviral compounds in a relatively immature host. In this model, newborn Hartley guinea pigs are infected with  $\sim 10^6$  pfu of salivary gland derived GPCMV 24-48 hours after birth. Antiviral or placebo treatments, administered orally or by intraperitoneal injection are begun at 0-24 hours after infection. Infection results in decreased weight gain and mortality as high as 70% due to dissemination to target organs such as the liver, spleen and brain by day 10 post-infection (2). Animals are thus followed daily for signs of disease and death. The effects on viral replication are assessed by sacrificing animals and comparing viral titers in various target organs and blood by Real-Time PCR and/or culture

Volume: Dosing is based on an average newborn guinea pig weight of 100g.

### **Congenital GPCMV Model**

CMV is the most common congenital infection. The guinea pig is the only small mammal in which virus crosses the placenta to cause fetal infection and disease thus allowing the study of new antivirals and unique therapies that may target placental and congenital infection. In this model, Hartley pregnant guinea pigs are infected with  $\sim 10^5$  pfu GPCMV at approximately 45 to 55 days of a 70 day gestation. Animals can be treated by systemic or oral routes. Endpoints include prevention of premature delivery, survival of the offspring and PCR analysis of placenta, and other maternal tissues (blood, liver and spleen) and pup organs (liver and spleen) harvested 3, 5 or 10 days post infection (3), .

Volume: The dose is based on a pregnant guinea pig weight of approx. 1200 g.

### **CMV model of hearing loss**

Hearing loss is the most common manifestation of congenital CMV infection. Using direct inoculation of GPCMV ( $\sim 10^5$  pfu) into the cochlea through the round window we are able to induce hearing loss in guinea pigs as measured by ABR.. Animals can then be treated to prevent the hearing loss. Antivirals can be administered either systemically or orally and we are currently investigating the use of direct intratympanic administration

Volume: The dose is based on the weight of the animals, approximately 350 gms.

### **Murine CMV Model**

The murine CMV model is a well characterized model used to study CMV pathogenesis and to evaluate new anti-CMV drugs. In this model, 5-week old

female mice are infected with  $1 \times 10^6$  pfu of MCMV by intraperitoneal injection. Treatment can be begun before or following infection and lasts 3-5 days. Animals are sacrificed at 3 to 5 days after infection and viral titers of the spleen and liver are determined by plaque assay. Other tissues such as salivary gland and lungs can be analyzed as well. Ganciclovir (50 mg/kg, twice daily) serves as a control drug and inhibits MCMV replication in this model.

Volume: Dosing depends on the weight of the animals ( about 25 gm)

### REFERENCES

- 1- Bourne N, Bravo FJ, Bernstein DI: Cyclic HPMPC is safe and effective against systemic guinea pig cytomegalovirus infection in immune compromised animals. *Antiviral Research* 47:103-09, 2000.
- 2- Bravo FJ, Bourne N, Schleiss MR, Bernstein DI. An animal model of neonatal cytomegalovirus infection. *Antiviral Research* 60:41-49, 2003.
- 3- Bravo FJ, Cardin RC, Bernstein DI: Effect of maternal treatment with cyclic HPMPC in the guinea pig model of congenital infection. *Journal of Infectious Diseases* 193:591-7, 2006.