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W. Christopher Scruton
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Layout
David Brown

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Ruth Cronje, and Jan Swanson;
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Reactivation of Latent Porcine Cytomegalovirus by Allogeneic Stimulation

Maria Isabel M.C. Guedes*[1], Shidong Ma[1], Jack M. Risdahl[2], Barry Wiseman[2], Carlos Paya[3], Thomas W. Molitor[1]

[1]Department of Clinical and Population Sciences, University of Minnesota, St. Paul, MN 55108; [2]Nextran, Inc. Princeton, NJ; [3]Mayo Clinic, Rochester, MN

Introduction

The importance of porcine cytomegalovirus (PCMV) pathogenesis has been highlighted recently with the increasing interest in xenotransplantation. PCMV is of particular concern due to some characteristics of its infection in pigs, such as high seroprevalency in the normal adult population, diverse clinical manifestations and establishment of latent infection. Similar to other herpesviruses, PCMV establishes lifelong latency in the host after primary infection that is characterized by persistence of the viral genome without the production of infectious virus. Although the site of PCMV latency is unknown, blood cells, particularly the peripheral mononuclear cells (PBMCs), may serve as a viral reservoir. Soderberg-Naucler *et al.* (1997) demonstrated that allogeneic stimulation of naturally infected human PBMCs resulted in reactivation of latent human cytomegalovirus (HCMV). Due to the possibility of reactivation of latent PCMV during xenotransplantation, we proposed a study to demonstrate that latent porcine cytomegalovirus can be reactivated, in vitro, after the co-culture of PBMCs, through allogeneic or xenogeneic stimulation.

Material and Methods

PBMCs from pigs and baboons with different genetic backgrounds were co-culture using 6 pairs (4 pig-pig and 2 pig-baboon). Equal numbers of cells (5 X 10^7 cells/ml) from each component in the pairs were used in the co-cultures. PBMCs from each animal cultured individually were used as controls. Co-cultured cells were harvested for analysis by PCR, for detection of PCMV DNA, and RT-PCR, for detection of PCMV RNA, at 14, 21, 28 and 35 days of co-culture.

Results and conclusion

Three of the four pig-pig PBMCs co-culture pairs were PCR (DNA) positive at days 14, 21, 28 and 35 days of co-culture. The controls PBMCs of only one pig in each pair were PCR (DNA) positive at days 14, 21 and 28 of co-culture. The three co-culture pairs PCR positive were also RT-PCR positive, which is an indication that there was virus replication. All control PBMCs were RT-PCR negative. Based on these results we conclude that PCMV can be reactivated after allogeneic stimulation and that PBMCs appear to be a site of PCMV latency.

Table 1: PCR and RT-PCR results at days 0, 14, 21, 28, and 35

Pig/baboon #	0	14	21	28	35
43	-/-*	+/-	+/-	-/-	-/-
901	-/-	-/-	-/-	-/-	-/-
43/901	-/-	+/+	+/+	-/-	-/-
44	-/-	+/-	+/-	+/-	+/-
927	-/-	-/-	-/-	-/-	-/-
44/927	-/-	+/+	+/+	+/+	+/+
82	-/-	+/-	-/-	-/-	-/-
873	-/-	-/-	-/-	-/-	-/-
82/873	-/-	+/+	+/-	+/-	+/+
88	-/-	-/-	-/-	-/-	-/-
950	-/-	-/-	-/-	-/-	-/-
88/950	-/-	-/-	-/-	-/-	-/-
49	-/-	-/-	-/-	-/-	-/-
OM58	-/-	-/-	-/-	-/-	-/-
49/OM58	-/-	-/-	-/-	-/-	-/-
X	-/-	-/-	-/-	-/-	-/-
OM61	-/-	-/-	-/-	-/-	-/-
X/OM61	-/-	-/-	-/-	-/-	-/-

*PCR/RT-PCR results

References

Soderberg-Naucler, C., Fish, K.N., Nelson, J.A. Reactivation of latent human cytomegalovirus by allogenic stimulation of blood cells from healthy donors. Cell, v. 91, p. 119-126, 1997.