# 7 Summary

**Analysis of differential gene regulation in porcine cell cultures after infection with porcine Circovirus type 1 and type 2**

Porcine Circovirus type 1 and type 2 are closely related and share homologies on nucleotide and protein level between 60% and 80%. In spite of these high consistencies circoviruses differ in their pathogenicity. While PCV1 is a non-pathogenic virus, PCV2 is the etiological agent for the postweaning multisystemic wasting syndrome (PMWS) in young piglets.

The aim of this study was to characterise viral and cellular genes that are involved in the initiation of the PMWS after infection. Cells infected either with PCV1 or PCV2 should differ in their transcription profile of genes that respond to the infection. The formation of viral transcripts or proteins might therefore correlate with the regulation of cellular genes. Using Differential Display analysis differentially regulated cellular transcripts were identified through sequencing and comparison with the public database using the BLAST-algorithm. The transcripts were further characterised in northern blot analysis and absolute transcript concentrations were measured with SYBR Green and TaqMan® real-time PCR in infected and non-infected samples. Flowcytometry analysis compared the transcription level with protein expression.

Different tested cell lines (L23, L35, L52, PS, PK15, WSH, 293) displayed a distinct regulation of several genes after infection with porcine Circoviruses. These genes were divided into functional groups e.g. genes that are immune activated after viral infection like the cytokine Interleukin 18 (IL18) and the major histocompatibility complex class I (MHC I). A virus induced modulation of vesicle- and membrane-associated proteins like EHD3 and Lyncein was observed as well as a viral effect on transcription and translation factors like caspase3, DAP5/eIF4γ2 (Death associated protein5/elongation initiation factor 4gamma2), NSAP1 (NS1 associated protein) and StIP1 (STAT3 interacting protein1).

One PMWS relevant factor could be the new identified fragment 40J, a gene that was transcribed only in lymphocytes and showed up-regulation mainly after PCV2 infection. Concerning the different pathogenicity between PCV1 and PCV2, all investigated genes showed either up- or down-regulation after infection dependent from the cell line. No single gene could be characterised as causative factor of PMWS, but some proteins of the viral influenced transcripts are related to each other and induce mediators that cause PMWS-like symptoms. The PMW Syndrome could therefore be initiated by a shifted regulation of many

factors. The fact that these genes are highly conserved among mammals could be relevant for the xenotransplantation in case of a PCV infection in humans.