

Immunoreceptor Complexes of the Innate Immune System

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Abstract

The gnotobiotic miniature swine model has been used for immunological research, such as the ontogeny of the adaptive and innate immune system. The functions of natural killer (NK) cells and myeloid cells are regulated by their immunoreceptor complexes. Our recent studies present molecular cloning and characterization of porcine immunoreceptor complexes MDL-1/DAP12 and NKG2D/DAP10. These receptors are involved in cell activation of the innate immune system. Porcine DAP12 and DAP10 genes were cloned from PBL cDNA library. DAP12 contains an Immunoreceptor Tyrosine-Based Activation Motif (ITAM) and DAP10 contains a PI-3 kinase binding site. Porcine DAP12 and DAP10 genes are located on chromosome 6q21. They are genetically linked in opposite transcriptional orientation. DAP12 and DAP10 are predominantly expressed in lymphohematopoietic cells. Myeloid DAP12-associated lectin-1 (MDL-1) is a type II membrane protein that is associated with DAP12. Two isoforms of porcine MDL-1 cDNA were cloned from pulmonary alveolar macrophages. The long form had 185 amino acids and 71% sequence identity with human MDL-1. MDL-1 transcripts were detected mainly in macrophages and monocytes. MDL-1 is expressed on the cell surface associated with DAP12. NKG2D is a C-type lectin family receptor that associates with DAP10. Porcine NKG2D cDNA has an open reading frame of 642 bp. Its expected polypeptide sequence is 214 amino acids. Porcine NKG2D has 66% sequence identity with human NKG2D. Porcine NKG2D requires DAP10 for cell surface expression. Porcine CD69 was cloned. CD69 mRNA was detected in activated PBL, NK cells, macrophages and granulocytes, but not in resting cells. NKG2D and CD69 genes are located on chromosomes 5q25, indicating that chromosome 5q25 contains pig NK receptor gene complex. Further studies on porcine immunoreceptor complexes of the innate immune system may prove useful for the development of xenotransplantation and xenoinmunotherapy.
