

Characterization of Interleukin-1 Beta 2, a Novel Interleukin-1 Expressed by the Early Pig Conceptus During Establishment of Pregnancy

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Abstract

Embryonic mortality is greatest in mammals during the peri-implantation period, a time when the conceptus attaches to the uterine surface epithelium while releasing proinflammatory molecules. Interleukin-1 beta (*IL-1 β*) is a proinflammatory cytokine released by the primate, rodent and pig conceptus during the peri-implantation period and is believed to be essential for establishment of pregnancy. The gene encoding *IL-1 β* has duplicated in the pig resulting in two distinct genes; *IL-1 β 1* and a novel gene referred to as interleukin-1 beta 2 (*IL-1 β 2*). Based on experiments presented in this dissertation we conclude that pig conceptuses express interleukin-1 beta 2 (*IL-1 β 2*) by d 6 of development, recombinant IL-1 β 2 can activate the transcription factor nuclear factor-kappa B (NF- κ B) in the uterine surface epithelium and IL-1 β 2 can increase expression of NF- κ B responsive genes within the endometrium that are considered to be essential during early pregnancy in mammals. Furthermore, recombinant IL-1 β 2 had lesser activity within the endometrium when compared with recombinant IL-1 β 1. Based on protein structure predictions, this may be the result of a lesser number of IL-1 receptor binding sites and non-conserved amino acid substitutions found within IL-1 β 2 when compared with IL-1 β 1. In conclusion, the peri-implantation pig conceptus expresses a novel IL-1 likely creating a balanced proinflammatory microenvironment within the endometrium that may be essential for establishment of pregnancy.