Development of an animal model for congenital rubella syndrome using pregnant ferrets: Systemic and persistent infection and various disorders were induced in infected fetuses

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Rubella virus infection at the early stage of pregnancy often induces disorders, such as congenital rubella syndrome (CRS) in the baby. The pathogenesis of the virus has not been studied well because of the lack of an adequate animal model. We developed a sensitive and promising animal model, using pregnant ferrets. Pregnant ferrets were inoculated through a combination of intranasal and subcutaneous routes with the rubella virus TO-336 wild or TO-336 vaccine strain at the third day of pregnancy. They were autopsied at the 38th day of pregnancy, that is, 4 days before delivery. The higher dose of the wild strain inoculated, the higher ratio of abortion, however, on the contrary, the lower ratio of disorders was observed. Dominant disorders induced in the fetuses are cranioschisis, iris hypoplasia, spinal deformity, visceral ectopia and coccygeal hypoplasia. Neither the content of the disorders, nor the variation of the groups, inoculated with the wild nor vaccine strain nor higher or lower dose was observed. Although, the vaccine strain induced disorder with less frequency than the wild strain. Induction of abortion and disorder has dependency on pregnant stage. The successful detection of virus genome from placenta and fetal organs with a wide spectrum indicates a persistent and systemic infection occurred in the fetus even in those without disorder. As these observations in ferret fetuses were quite similar to those observed in human CRS babies except content of major disorders, pregnant ferret is a promising animal model for studying the pathogenesis of rubella virus in the fetus.

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