Molecular characterization and antiviral activity analysis of the interferon-inducible Mx gene in mice

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bryonic lethality and hematopoiesis in Td^{bo} males, and hyperkeratosis in Td^{bo} adult females.

In humans, it is also demonstrated that the mutations of EBP result in X linked dominant chondrodysplasia punctata (CDPX 2). Therefore, Td^{bo} mutant mouse is expected to be one of useful animal model for CDPX2.


The mouse genome contains two related interferon-regulated genes, Mx 1 and Mx 2. Mx 1 codes for the nuclear 72-kDa protein that interferes with influenza virus replication after interferon treatment. On the other hand, the Mx 2 gene is nonfunctional in all laboratory mouse strains examined, since its ORF is interrupted by insertional mutation and a subsequent frame shift. In the present study, the characterization and identification of IFN-inducible Mx 1 and Mx 2 genes in the feral-origin strains have been demonstrated.

On part 1, several mouse strains established from feral-origin mice were tested to determine their Mx 1 + or Mx 1 - allele status with PCR-RFLV, sequence analysis, RT-PCR and immunofluorescence staining. All of the mouse strains originating from feral-origin mice were found to uniformly carry the Mx 1 + allele. Therefore, it is conceivable that the Mx 1 + allele in feral-origin populations serves a function against some pathogens related to orthomyxoviruses. The PCR-RFLV and sequence analysis allowed to classify the Mx 1 + alleles of the laboratory and feral-origin mouse strains into distinct classes.

RT-PCR and immunofluorescence staining demonstrated that the Mx 1 transcripts and proteins were induced by IFN α/β in macrophages from feral-origin mouse species.

On part 2, the author demonstrated that Mx 2 mRNA of cells from the feral-origin mouse strains NJL (Mus m. musculus) and SPR (Mus spretus) differed from the nonfunctional mRNA of the laboratory mouse strains tested. The Mx 2 mRNA of the feral-origin strains contained functionally a single long ORF consisting of 656 amino acids. The author further showed that Mx 2 protein in the feral-origin strains was expressed upon interferon treatment and localized to the cytoplasm much like the rat Mx 2 protein, which inhibited VSV replication. Furthermore, transfected 3T3 cell lines of laboratory mouse origin expressing Mx 2 from the feral-origin strains acquired slight resistance to VSV.

In the study of part 3, the author has demonstrated that the embryonic fibroblastic
Information

A study on the differentiation therapy of canine osteosarcoma
with vitamin D and retinoids

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The possibility of inducing normal differentiation of canine osteosarcoma cells into osteoblasts may reverse the disruption of their differentiation and result to the inhibition of growth and reduction of the malignant behavior. This was initially ascertained in a series of three in vitro experiments. Firstly, Treatment with 10^{-10} - 10^{-8} mole (M) concentrations of calcitriol, 22-oxa-calcitriol (OCT), cholecalciferol, all-trans retinoic acid (ATRA) and 9-cis retinoic acid (9-cis RA) for 48-120 hours culture changed the morphology of POS canine osteosarcoma cells, POS 53B (chondroblast type), POS 53C (undifferentiated type) and POS 53D (osteoblast type) cells to cells that were elongated and spindle shaped; increased number of cytoplasmic organelles and pronounced nuclear activities; and inhibited the growth of POS cells dose dependently (P<0.05).

Secondly, functional differentiation was investigated in vitro via bone differentiation markers: alkaline phosphatase (ALP) staining, intracellular ALP activity, gamma-carboxyglutamic acid-osteocalcin (GLA-OC) production and type I collagen (P1P) production. Treatment with 10^{-8} M concentrations of OCT, calcitriol and ATRA for 72 hours significantly increased (P < 0.05) ALP, GLA-OC and P1P of these tumor cells except POS 14A.

Thirdly, apoptosis was also induced on POS cells in vitro by all drugs at a concentration of 10^{-6} M at 48 hours, 10^{-7} M at 96 hours, 10^{-8} and 10^{-9} M at 120 hours after incubation with the drugs.

A series of two experiments were consequently undertaken to evaluate the inhibitory effects of these drugs in vivo. Firstly, a highly metastasizing model of canine osteosarcoma to the lungs in nude mice was established by