

isolate with the Nancy strain (ATCC-VR 30) as a reference. The nucleotide sequence homologies of 5'-NTR of intra-isolates (14 isolates) were 99.0-99.8% regardless the year of isolation. On the other hand, homologies between 14 isolates and the Nancy strain were 84.0-84.7%. In addition, nucleotide sequence of 5'-NTR of one isolate, which was isolated from the patient with acute myocarditis showed very high homology (96.0%) with the reference strain with cardiovirulence. The 5'-NTR of all the viruses retained identical primary clover-leaf (CL) structure with additional unique stems and loops depending on their cardiovirulence. Taken together, these results indicated that the secondary structure of 5'-NTR of CVB3, which resulted from nucleotide divergences, is responsible for a determination of cardio/non-cardiovirulent phenotype in a murine model for acute myocarditis.

F109 Genomic Determinants of Cardiovirulence in Coxsackievirus B3

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Coxsackievirus B3 (CVB3) infections can cause myocarditis in humans and are implicated in the pathogenesis of dilated cardiomyopathy. The natural genetic determinants of cardiovirulence for CVB3 have not been fully identified, although using strains engineered in the laboratory, cardiovirulence determinants have been identified in the CVB3 5' nontranslated region (5'NTR) and capsid. The 5'NTRs of the non-cardiovirulent CVB3 Korean isolates and cardiovirulent Nancy strain were examined to determine their influence on the cardiovirulence phenotype. In order to exactly identify CVB3 cardiovirulence

determinants, infectious full-length cDNA clones of CVB3K and Nancy strain were constructed using mammalian expression vector pCDNA 3.1 (-). The recombinant constructs consisted of the full-length viral cDNA stably inserted into the pCDNA3.1 (-) vector under control of CMV immediate early transcriptional element. Intratypic chimeric virus was constructed in which 5'NTR sequences of the infectious cDNA copy of the cardiovirulent CVB3 Nancy strain genome were replaced by homologous sequences from the noncardiovirulent CVB3K. This chimeric virus (Chi-CVB3) was transfected into Cos7 and hCAR (Human Coxsackievirus and Adenovirus Receptor expressed cell) cells by the lipofectamine reagent and the infectious progeny virus was harvested. The myocarditic potential of chimeric virus was determined using an established murine model of inflammatory heart disease. Chimeric virus was screened for cardiovirulence by inoculation into Balb/c mice. Sections of hearts removed at 7 days postinoculation were examined for evidence of myocarditis by light microscopy and Enterovirus-specific PCR assayed for the presence of virus. These results indicate that 5'NTR plays an important role in the cardiovirulence determinants of CVB3.

F110 Effects of inhibitors on Apoptosis and Adaptive Response Induced by Ultraviolet Radiation in HeLa S3 Cells

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The present study was performed to elucidate the effects of inhibitors on apoptosis and adaptive response induced by Ultraviolet Radiation (UV) in HeLa S₃ cells. After treatment of the cells with UV, cells were incubated with three kinds of inhibitors for various times. DNA fragmentation induced in cells were not

affected by 3-aminobenzamide(3AB). The percentages of apoptotic cells treated with UV and incubated with 3AB were lower than without 3AB in HeLa S₃ cells. The level of 116 kDa poly(ADP-ribose) polymerase(PARP) in cells treated with UV and then incubated with 3AB for 6 hours was higher than that without 3AB. Apoptosis induced in the cells were not affected by cycloheximide(CHX) and 2'3'-dideoxythymidine 5'-triphosphate (ddTTP). The 3AB and CHX inhibited expression of PARP during early stage of adaptive response, whereas ddTTP did not inhibit.

F111 Isolation and Characterization of UV-Inducible Genes from *Schizosaccharomyces pombe*

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The present study intends to characterize the DNA damage-inducible responses in eukaryotic cells. The fission yeast, *S. pombe*, which displays efficient DNA repair systems, was used in this study as a model system for higher eukaryotes. To study UV-inducible responses in *S. pombe*, five UV-inducible cDNA clones were isolated from *S. pombe* by using subtraction hybridization method. To investigate the expression of isolated genes, the cellular levels of the transcripts of these genes were determined by Northern blot analysis after UV-irradiation. The transcripts of isolated gene (UVI30) increased rapidly and reached maximum accumulation after UV-irradiation. Compared to the message levels of control, the levels of maximal increase were approximately 5 fold to UV-irradiation. In order to investigate whether the increase of UVI30 transcripts was a specific results of UV-irradiation, UVI30 transcript levels were examined after treating the cells to Methylmethane sulfonate (MMS). The transcripts of UVI30 were not induced by treatment of 0.25% MMS. These results implied that the effects

of damaging agents are complex and different regulatory pathways exist for the induction of these genes. To characterize the structure of UVI30 gene, nucleotide sequences were analyzed. The nucleotide sequence of 1,340 nucleotide excluding poly(A) tail contains one open reading frame, which encodes a protein of 270 amino acids. The predicted amino acid sequences of UVI30 do not exhibit any significant similarity to other known sequences in the database.

F112 Glucose-Dependent *rrg1*⁺ Expression Is Regulated at Posttranscriptional Level by Control of mRNA Stability Mediated by Downstream Region of Poly(A) Site in *Schizosaccharomyces pombe*

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rrg1⁺ (rapid response to glucose) was previously reported to show rapid glucose-inducible expression at transcript level in *Schizosaccharomyces pombe*. Here, we investigated its transcript level in various glucose conditions. In addition, the glucose-dependent expression of *rrg1*⁺ was revealed to result from changes of mRNA half-life and its rapid regulation of mRNA stability required new protein synthesis. Serial and internal deletions within 3'-flanking region of *rrg1*⁺ revealed that a 210-nt region downstream of distal poly(A) site was critical for the glucose-regulated expression and 3' end formation of mRNA. Taken together, this is the first report on glucose-inducible expression regulated posttranscriptionally by control of mRNA stability in *S. pombe*.

F113 Characterization of