S11 Antimicrobial Peptides from Aquatic Reduce Lethality in Mice of *Pseudomonas Aeruginosa* Sepsis. Jyh-Yih Chen. *Marine Res. Station, Inst. of Cellular & Organismic Biology, Taiwan.*

We investigated the efficacy of amino acids 55~76 of the synthetic shrimp anti-lipopolysaccharide factor peptide (SALF55-76 cyclic peptide), the C-terminal part of the shrimp anti-lipopolysaccharide factor. This study was conducted to elucidate the effects of the antiseptic action of this peptide. The SALF55-76 cyclic peptide was tested against bacterial clinical isolates and showed broad-spectrum antimicrobial activity. Transmission electron microscopic (TEM) examination of SALF55-76 cyclic peptide-treated *Pseudomonas aeruginosa* showed that severe swelling preceded cell death and breakage of the outer membrane; the intracellular inclusion was found to have effluxed extracellularly. When mice were treated with the SALF55-76 cyclic peptide before bacterial challenge with *P. aeruginosa*, the peptide highly protected mice against death by sepsis. The *P. aeruginosa* recovered from SALF55 -76 cyclic peptide-treated mice after 4 h exhibited reduced bacterial growth similar to that recovered from vancomycin-treated mice. In addition, the syntheses of inflammatory cytokines, such as interleukin (IL)-2, IL-4, IL-10, IL-12, IL-13, interferon-γ, and tumor necrosis factor [TNF]-α, were significantly upregulated 4 h after SALF55-76 cyclic peptide treatment except for IL-4 in the liver. The expressions of Toll-like receptor 4 (Tlr4), Irf3, myd88, and Tram, were considerably elevated, but only Tlr4 existed in the spleen 4 h after SALF55-76 cyclic peptide treatment. The prophylactic administration of SALF55-76 cyclic peptide was begun the TNF-α response in comparison to untreated mice by an ELISA analysis. Due to its multifunctional properties, the SALF55-76 cyclic peptide may become an important prophylaxis against and therapy for bacterial infectious diseases, as well as for septic shock.

S12 Rad2p-PCNA Interaction Regulates Mutagenesis by DNA Replication Blockage as the Response to DNA Damage: Implications for Elevated Skin Cancer Rate in Xeroderma Pigmentosum. Sung-Keun Lee. *Department of Pharmacology, Inha Research Institute for Medical Sciences, College of Medicine and Center for Advanced Medical Education, Inha University College of Medicine by BK21 project, Inha University, Incheon 400-712, South Korea.*

Impairment of nucleotide excision repair (NER) drastically increases skin cancer incidence after exposure to the DNA-damaging agents which might result from the accumulation of mutation in damaged DNA. *XPG* gene that is essential in the incision step of NER, has a PCNA-binding motif at the C-terminal region. However, the role of PCNA binding motif of *XPG* is controversial because its presence does not affect on the NER process. Using yeast *RAD2*, a counterpart of human *XPG*, here we show that Rad2p interacts with Pol30p, a homolog of human PCNA, through its PCNA-binding motif and the binding causes cell-cycle arrest resulting in cell growth retardation. The results indicate that Rad2p functions in the replication process in addition to incision of damaged DNA and transcription elongation. Interestingly, replication stall induced by Rad2p –Pol30p interaction increased the mutation rate. Moreover, the impairment of PCNA-binding motif in Rad2p decreased the mutation rates after UV irradiation in the presence of other NER related gene defects. These findings suggest that the causes of drastically increased skin cancer incidence in XP should be the synergistic effect of replication stall by the interaction between XPG and PCNA and the accumulation of damaged DNA.

S13 Proteomics in Occupational and Environmental Medicine. Roel Vermeulen. *Utrecht University, Netherland.*

In general the function of a cell can be described by the proteins that are present in the cell and the abundance of these proteins. Although all proteins are based on mRNA precursors, post translational modifications (PTM) and environmental interactions make it difficult to predict abundance of specific proteins based on gene expression analysis. In contrast to the genome, the proteome is highly variable over time, between cell types and will change in response to changes in its environment. An important focus of proteomic technologies is the identification of proteins including the presence of PTM of proteins and identification of proteins interacting in protein-complexes. Another focus is quantification of protein abundance. Protein expression levels represent the balance between translation and degradation of proteins in cells. It is therefore assumed that the abundance of a specific protein is related to its role in cell function. However, the high dynamic range of proteins complicates this type of proteomic analysis. Potential applications of proteomics in occupational environmental medicine are a better understanding of disease etiology and the development of biomarkers of exposure and effect based on alterations in expression or modification of proteins. We will discuss our experiences in applying proteomic techniques to detected altered protein expression due to environmental exposures (i.e benzene exposure), and in early detection of breast cancer. In both studies specific protein patterns were identified but what do they mean and how can they be used in practice?

S14 Combination of aCGH and gene expression reveals survival critical Signatures in breast cancer. Tae-Hoon Chung. *Computational Biology Division, Translational Genomics Research Institute.*

With the completion of Human Genome Project and tremendous success of microarrays, a variety of microarray-based high-throughput molecular assay tools become quite popular for cancer research these days. However, the utility of individual platforms is limited due to respective shortcomings and the need for integrating results from heterogeneous platforms is increasing. We introduced a novel approach to uncover survival critical signatures through the integrated analysis of array-based comparative genomic hybridization (aCGH) and gene expression profiling, and applied it to a publicly available breast cancer experiment. Using aCGH data annotated with survival information, we could locate genomic hotspots in which genomic aberrations correlated with poor survival. No hotspot aberrations from different chromosomes were found to occur simultaneously but the accumulation of hotspot aberrations led to poor survival. To uncover survival-associated signatures, we looked for genes whose expressions were closely associated with hotspot aberrations and found 159/57 genes in gained/lost hotspots. We then overlaid survival association results from the expression profiles, and further refined the putative survival markers. Survival prediction analysis in 7 independent breast tumour datasets using our refined genetic markers showed substantially better performance in 3 datasets than those from expression profile alone. Through the analysis of aCGH, genomic regions critical to survival can be successfully identified. Furthermore, the integration of survival signatures from aCGH and expression data uncovers signatures that outperform signatures from either platform alone when applied to independent datasets for patient survival prediction.