have already existed at the time of surgery. Therefore, understanding how metastasis is regulated at the molecular level is required to devise new modalities of gastric cancer therapy. In present study, we measured the invasive potentials of various Korean-derived gastric cancer cell lines and subsequently performed subtractive suppression hybridization to identify metastasis-related genes by comparing differential gene expression profiles between highly invasive SNU-638 and poorly invasive SNU-484 gastric cancer cell lines. Twenty-two cDNAs were identified as overexpressed genes in SNU-638 cells confirmed by Northern blot analysis. Among them, a splicing variant of aspartyl beta hydroxylase (Humbug) was also identified as a gene overexpressed in metastatic SNU-638 cells. Humbug encodes a protein identical to aspartyl-beta hydroxylase through the NH2-terminal half of the protein, but completely lacks the catalytic domain of aspartyl-beta hydroxylase. Therefore, we further investigated the possible involvement of this gene in metastatic progression of cancer cells. Expression analysis showed that the level of Humbug mRNA was well correlated with invasive and metastatic potential in various gastric cancer cell lines. Moreover, gastric tumor tissue exhibited much higher Humbug mRNA expression than the normal counterparts. Transfection of Humbug cDNA into poorly invasive Az-521 cells resulted in the increase of its migratory and invasive potentials. These results imply that Humbug could be an overexpressed gene during metastatic progression of human gastric cancer cells, and promote tumor cell invasion and metastasis.

[PC1-40] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Modulation of Redox-sensitive Transcription Factor, AP-1 by Aging and Calorie Restriction

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Oxidative stress is claimed to be the major cause of aging and many age-related diseases. Recent data strongly suggested that the life-prolonging calorie restriction (CR) might retard aging by its anti-oxidative action on the regulation of the intracellular redox status. Currently, there is little information concerning the influences of age and CR on the redox-sensitive transcriptions factor, activator protein-1 (AP-1). In this present study, we investigated whether age affects the regulation of AP-1, and how the *age effect is modulated* by CR. The kidney isolated from Fischer 344 rats at 6, 12, 18, and 24 months of age fed ad libitum (AL) and CR rats were used. Results showed that AP-1 binding activity markedly increased with age in parallel with increased ROS generation, and CR suppressed the activation at the level of 6 months old. Recently, accumulating evidence indicate that mitogen-activated protein kinase (MAPK) cascade can contribute to AP-1-dependent transcription. Results showed that the aging *process strongly enhanced* all three MAPKs activities, while CR markedly suppressed the age-related activation of MAPK. It is known that thioredoxin (Trx), which is mainly in the cytoplasm, quickly translocates into the nucleus and activates AP-1 transcriptional activity by direct association with an intranuclear redox factor, Ref-1. We present evidence that the increased AP-1 activity during aging is correlates with increased nuclear protein levels of Trx and Ref-1. Based on these data, we concluded that the age-related increases in redox-sensitive AP-1 binding activity are associated with increased ROS, and CR modulates the AP-1 activation by suppressing oxidative stress. This molecular insight provides a better understanding of the regulation of cellular events leading to age-associated pathogenic process and furthermore reveals pertinent clues on possible therapeutic intervention.

[PC1-41] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Homology modeling of human TCTP using three different computer programs

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The translationally controlled tumor-associated proteins (TCTPs) are a highly conserved and abundantly expressed family of eukaryotic proteins that are implicated in both cell growth and the human acute