[Atherosclerosis, 146, 133-140 (1999)]

[Lab. of Clinical Pharmaceutics]

## Relationship between Total Plasma Homocysteine, Polymorphisms of Homocysteine Metabolism Related Enzymes, Risk Factors and Coronary Artery Disease in the Australian Hospital-based Population.

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Modest elevations of circulating homocysteine are common in patients with vascular disease. We explored interrelations between total homocysteine levels and mutations in genes for three key enzymes in methionine-homocysteine metabolism, such as methyltetrahydrofolate reductase, cystathionine beta synthase and methionine synthase. We also assessed associations between homocysteine levels and extracellular-superoxide dismutase (EC-SOD). There were significant correlations between plasma total homocysteine, and EC-SOD and LDL. From these results, it is suggested that elevated homocysteine may exert oxidative stress and that levels are associated with unstable angina, but not the occurrence or extent of coronary stenosis.

[J. Med. Chem., 42, 2621-2632 (1999)]

[Lab. of Clinical Pharmaceutics]

## 1,3-Disubstituted Benzazepines as Novel, Potent, Selective Neuropeptide Y Y1 Receptor Antagonists.

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A novel series of potent and selective non-peptide neuropeptide Y (NPY) Y1 receptor antagonists, having benzazepine nuclei, have been designed, synthesized, and evaluated for activity. 3-(3-(Benzothiazol-6-yl)ureido)-1-N-(3-(N'-(3-isopropylureido))benzyl)-2,3,4,5-tetrahydro-1H-1-benzazepin-2-one (21), which was one of the most potent derivatives, competitively inhibited specific [ $^{125}$ I]peptide YY (PYY) binding to Y1 receptors in human neuroblastoma SK-N-MC cells ( $K_i = 5.1$  nM). Compound 21 not only inhibited the Y1 receptor-mediated increase in cytosolic free Ca<sup>2+</sup> concentration in SK-N-MC cells but also antagonized the Y1 receptor-mediated inhibitory effect of peptide YY on gastrin-induced histamine release in rat enterochromaffin-like cells.

[Biol. Chem., **380**, 1333-1336 (1999)]

[Lab. of Clinical Pharmaceutics]

## Isolation of Two Novel Alternative Splicing Variants of Allograft Inflammatory Factor-1.

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Allograft inflammatory factor-1 (AIF-1) was initially cloned from rat cardiac allografts undergoing chronic rejection. AIF-1 with an EF-hand-like motif is thought to be a Ca<sup>2+</sup> binding protein. In this study, we identified two novel alternatively spliced variants of AIF-1 by reverse-transcription polymerase chain reaction. One variant encodes an AIF-1 protein that lacks 14 amino acids corresponding to one exon region. The other variant encodes a truncated AIF-1 protein due to a frameshift introduced by an 85-bp insertion, and its C-terminal region differs from that of AIF-1. Interestingly, these variants have incomplete and no EF-hand-like motifs, respectively. The expression level of the latter is high in peripheral blood leukocytes, and it is selectively expressed in macrophage-like cell lines.

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[Lab. of Health and Physical Education]

## Relationship of Bone Density for Females with Life Style for Two Years after Entering a Nursing College.

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Bone density of females was followed up for two years after the entering a nursing college and the influence of life style, such as nutrition and physical exercise on the bone density was examined.

The bone density decreased by 2.1% after one years of their entering a college, then it increased by 1.1% next one years. The bone density decreased during two years for the students who had relative high bone density at their entrance, on the contrary, the bone density slightly increased for the ones who had low bone density at their entrance. Important factors related to increase the bone density were awareness for strengthening bone, physical activity and frequent intake of eggs, milk, and dairy products. These results indicated that the bone density of nursing college students is influenced by the differences of their life style, therefore, the basic education for life style concerning nutrition and physical exercise is desired to maintain the bone density during their college life.