

These results suggest that ADL elicit detectable cytokines from PBMC.

[PC1-17] [ 10/20/2000 (Fri) 15:30 – 16:30 / [Hall B] ]

### **Costunolide Induces the Differentiation of Human Leukemia cells HL -60**

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The present work was carried out to examine the effect of costunolide on the growth of several cell lines and the differentiation of human leukemia-derived cell line HL-60. Costunolide produced a potent antitumor activity in vitro against several tumor cells dependent on concentration. However, it showed less cytotoxicity on normal cells such as *Macacoccus rhus* monkey kidney cells (MA-104) up to 200 M concentration. Costunolide was found to be a potent inducer of differentiation in human leukemia derived cell lines HL60 cell by examination of differentiation marker as assessed by the surface antigens of CD14 and CD66b, reducing nitroblue tetrazolium and measuring esterase activity. These events were accompanied by a decline in expression of the c-myc and p-tyr protein by 4 days costunolide treatment. These results suggest that costunolide induces differentiation in human leukemia cells lineage by altering the expression of this protein involved in differentiation.

[PC1-18] [ 10/20/2000 (Fri) 15:30 – 16:30 / [Hall B] ]

### **Suppression mechanism of inducible nitric oxide synthase and cyclooxygenase - 2 expression in RAW 264.7 macrophages by sesquiterpene lactones from *Ainsliaea acerifolia***

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Nitric oxide (NO) and prostaglandin (PG), produced by inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2), respectively, act as a causative regulator in various inflammatory disease states. *Ainsliaea acerifolia* has been used in Korean traditional herbal medicine for its antipyretic, analgesic and anti-inflammatory properties. We investigated the molecular mechanism for the suppression of LPS/IFN- $\gamma$ -induced NO and PGE<sub>2</sub> production in RAW 264.7 macrophages by sesquiterpene lactones, zaluzanin-C and estafiatone, which are isolated from *A. acerifolia*. Zaluzanin-C and estafiatone decreased NO production in LPS/IFN- $\gamma$ -stimulated RAW 264.7 macrophages with an IC<sub>50</sub> of about 6.61  $\mu$ M and 3.80  $\mu$ M, respectively. In addition, these compounds inhibited the synthesis of PGE<sub>2</sub> in LPS/IFN- $\gamma$ -treated RAW 264.7 macrophages. Furthermore, treatment with zaluzanin-C and estafiatone led to a decrease in iNOS protein as well as mRNA expression levels. These effects appear to be due to inhibition of the binding activity of NF- $\kappa$ B, a transcription factor necessary for iNOS and COX-2 expression, because these compounds inhibited NF- $\kappa$ B activation. These results suggest that the ability of zaluzanin-C and estafiatone to inhibit iNOS and COX-2 gene expression through the inhibition of DNA-binding activity of NF- $\kappa$ B might be responsible, in part, for their anti-inflammatory effects.

[PC1-19] [ 10/20/2000 (Fri) 15:30 – 16:30 / [Hall B] ]