came from the induction of apoptosis. Nowadays, there is a increasing interest in their potential for antitumor agent. But, the weak water solubility is one of their difficulties for in vivo application.
To increase the water solubility, sixteen derivatives of lupane which bearing aminoacetyl moiety at C3 were synthesized. Their cytotoxic activities against three cancer cell lines, SK-MEL-2, A-549, and B16-F10, were tested.
Of synthesized derivatives, only six derivatives were cytotoxic against certain cell lines. On the whole, the activities were weaker than their lead compound, betulinic acid. The cause of reduction of cytotoxic activity might come from the steric effects.

[PD1-24] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Evaluation of Morphogenic Regulatory Activity of Farnesoic acid and Its Derivatives against Candida albicans Dimorphism

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The yeast Candida albicans has a distinguishing feature, dimorphism, which is the ability to switch between two morphological forms: a budding yeast form and a multicellular invasive filamentous form. This ability has been postulated to contribute to the virulence of this organism. Studies on the morphological transition from a filamentous to a budding yeast form in C. albicans have shown that this organism excretes an autoregulatory
substance into the culture medium. This substance was extracted and purified by normal-phase and reversed-phase HPLC. The autoregulatory substance was structurally identified as 3,7,11-trimethyl-2,6,10-dodecatrienoate(farnesoic acid) by NMR and mass spectrometry. Growth experiments suggest that this substance does not inhibit filamentous growth. A series of farnesoic acid derivatives was prepared and their morphogenic regulatory activities were evaluated. Their inhibitory activities against yeast cell growth and yeast-to-hypha transition using C. albicans cells are sensitive to the chain length as well as the substitution patterns on the isoprenoid template. The preliminary structure-activity relationship of theses compounds is described to elucidate the essential structural requirements. These findings have implications for developmental signaling by the fungus and might have medical value in the development of antifungal therapies.

[PD1-25] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Practical Synthesis of (S)-7-(2-Isopropylamino)ethylcamptothecin Hydrochloride, Potent Topoisomerase I Inhibitor

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In our efforts to find a practical large-scale synthetic method for CKD-602, (S)-7-(2-Isopropylamino) ethylcamptothecin hydrochloride, under phase II clinical trials as a anti-cancer drug candidate, we have developed a semi-synthetic method employing the Mannich reaction. Unusually, dimethyl sulfoxide which was used as a solvent, worked as a formaldehyde source in the Mannich reaction of (S)-7-methylcamptothecin with isopropylamine hydrochloride.

[PD1-26] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]