[PC1-1] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

DA-125, a new antitumor agent, inhibits topoismerase II as topoisomerase poison and DNA intercalator

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Inhibitory mechanism of DNA replication by a new antitumor agent, DA-125, was studied by evaluating formation of DNA-topoisomerase complex in the simian virus 40 (SV40) replicating system. DA-125 induced a dose-dependent formation of DNA-topoisomerase complex, indicating that DA-125 has topoisomerase poison properties. In the experiments used with two different chemicals simultaneously, adriamycin, a known DNA intercalator, blocked formation of DNA-topoisomerase complex induced by etoposide (VP16), a known topoismerase II poison, in a dose-dependent manner. On the contrary, DA-125 inhibited formation of DNA-topoismerase complex induced by VP16 to a maximum level of the complex caused by DA-125 alone, suggesting that DA-125 has strong DNA intercalator properties. However, DA-125 and adriamycin did not inhibit formation of DNA-topoisomerase complex caused by camptothecin, a known topoisomerase poison. On the basis of these observations, therefore, it is suggested that DA-125 inhibits topoisomerase II as topoisomerase II poison and DNA intercalator.

[PC1-2] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Subunit assembly of laminin variants in bovine aortic endothelial cells

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Bovine aortic endothelial cells(BAEC) produce two variant forms of laminin with a subunit composition of AB1B2 and A'B1B2. Anlyses of the intracellular assembly of these subunits revealed that the B1B2 dimer formed first, and that A or A'joined to form the AB1B2 or A'B1B2 trimer. Angiostatic steroids shifted the relative size of the A and A' monomer pool in BAEC, and competition between the A and A' subunits in joining the B1B2 dimer produced AB1B2 and A'B1B2 in different ratios. This result suggests that subunit replacement is the general mechanism for producing laminin variants by various cells for tissue morphogenesis. When laminin subunits in BAEC were cross-linked with dithio-bis-succinimidylpropionate (DSP) and immunoprecipitated with anti-laminin antiserum, monomeric A,A',B1 and B2 monomers and the B1B2 dimer migrated as extremely large molecules in sodium dodecyl sulfate gel electrophoresis under nonreducing conditions. When the crosslinking disulfide bonds were cleaved under reducing conditions, they migrated as the usual subunits. This result suggests that molecular chaperones were involved in the process of the assembly and replacement of laminin subunits.

[PC1-3] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Effect of NQ304, an Antithrombotic Agent, on the Arachidonic Acid Metabolism in Rabbit Platelet Aggregation

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