

A substantial body of evidence indicates that reactive oxygen intermediates (ROIs) are implicated in pathogenesis of diverse human diseases, including cancer, diabetes, and neurodegenerative disorders. Recent studies have revealed that moderate amounts of intracellular ROIs can cause cell death via apoptosis while their excessive cellular accumulation leads to necrotic death. Cell death is regulated by plenty of functional genes and their protein products. Bcl-2 which is an integral inner mitochondrial membrane protein blocks cell death induced by a wide variety of toxicants. In the present work, we have investigated the possible protective role of *bcl-2* on oxidative death induced by hydrogen peroxide and beta-amyloid in cultured PC12 cells. Hydrogen peroxide is a typical ROI produced by xenobiotic redox molecules. It is also generated under normal physiological conditions and is recognized as an important messenger mediating the intracellular signaling in response to external stimuli. Beta-Amyloid is a peptide accumulated in the certain brain regions of patients with Alzheimer disease, and is known to exert its toxicity through ROI generation. When PC12 cells were treated with hydrogen peroxide or beta-amyloid, they underwent apoptotic death as determined by morphological features, internucleosomal DNA fragmentation and positive *in situ* terminal end-labeling (TUNEL staining). Transfection of PC12 cells with the anti-apoptotic *bcl-2* gene protected these cells from oxidative damage caused by either hydrogen peroxide or beta-amyloid. PC12 cells overexpressing *bcl-2* exhibited relatively high constitutive DNA binding and transcriptional activities of NF-kappa B, compared with the vector-transfected control cells. In addition, sustained NF-kappa B activation was observed in the *bcl-2*-overexpressing cells after treatment with hydrogen peroxide or beta-amyloid. Western blot analyses revealed that *bcl-2* transfected PC12 cells exhibited the higher level of p65, the functionally active subunit of NF-kappaB, in the nucleus than did the vector-transfected controls. In contrast, the cytoplasmic inhibitor I-kappaB-alpha was present to a lower level in the cells overexpressing *bcl-2*. These results suggest that the ubiquitous eukaryotic transcription factor NF-kappa B plays a role in cell survival against oxidative stress. Supported by the Genetic Engineering Grant from the Ministry of Education, Republic of Korea (1998-019-F00073).

[OD-1] [04/21/2000 (Fri) 11:10 - 11:25 / Rm B113, Bldg 26]

Computer Graphics: Theoretical Study of DNA-Intercalation

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Most DNA-intercalators bind to DNA bases, cytidines and guanidines, which are affected by hydrogen-bonding, electrostatic energy and Van der Waals energy in the DNA. Generally, the study of DNA-intercalation has been carried out with NMR analysis, Gel-electrophoresis and so on. By the computer-aided molecular modeling, we inserted anticancers, 9 types of the Ellipticin derivatives which are already well-known as DNA-intercalators, into the DNA centers of a form (CGCG)₂- DNA and b form (CGCG)₂- DNA and then DNA-drug complexes were formed via docking. After energy minimization for the complexes, we observed whether hydrogen bonding was made up or not. At the results, the existing DNA-intercalators formed hydrogen bonding with a form (CGCG)₂- DNA but didn't with b form (CGCG)₂- DNA.

[OD-2] [04/21/2000 (Fri) 11:25 - 11:40 / Rm B113, Bldg 26]

Facile Construction of Oxaphenalene Skeleton by peri Ring Closure. Total Synthesis of Mansonone F

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