

MS-3 DNA adductome and mutation analyses of 1-nitropyrene and 3-nitrobenzanthrone

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We comprehensively measured DNA adducts formation in HepG2 human hepatoma cells exposed to 1-nitropyrene (1-NP) and 3-nitrobenzanthrone (3-NBA) with LC/MS/MS. Both nitroarenes are found in urban air. 1-NP is well-studied nitroarene and a possible human carcinogen (Group 2B, IARC), and 3-NBA is known to form several DNA adducts in mammalian cells and to induce cancer in rat.

In the DNA from 1-NP and 3-NBA treated cells, at least seven and eight m/z signals, respectively, from aberrant nucleosides were found. Using stable isotope-labeled internal standards, one major adduct (*N*-(deoxyguanosin-8-yl)-1-aminopyrene) and three major adducts (*N*-(deoxyguanosin-8-yl)-3-aminobenzanthrone, 2-(deoxyadenosin-*N*6-yl)-3-aminobenzanthrone (dA-*N*6-C2-ABA), and 2-(deoxy-guanosin-*N*2-yl)-3-aminobenzanthrone) were identified and quantified in 1-NP- and 3-NBA-treated cells, respectively. Then we constructed plasmids that contains site-specifically single nitroarene adduct and introduced them into *E. coli* for replication. Although dA-*N*6-C2-ABA was most abundant among 3-NBA-produced adducts, it did not block the DNA replication nor induce mutation. The other adducts may highly contribute to induce mutation.

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1-ニトロピレン並びに3-ニトロベンズアントロンのDNAアダクトーム及び突然変異解析

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