Synopsis of Original Research Paper

Peroxisome : biogenesis of phospholipids, oxygen radical scavenger, and peroxisome biogenesis disorders

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We have isolated peroxisome biogenesis mutants from Chinese hamster ovary (CHO) cells by the 9- (1'pyrene) nonanol/ultraviolet (P90H/UV) method, using the wild-type CHO-K1 cells that had been stably transfected with cDNA encoding peroxisome assembly factor-I (PAF-1). Nine P90H/UV-resistant cell clones, ZP104, ZP105, ZP106, ZP107, ZP108, ZP109, ZP110, ZP111, and ZP114, were isolated and examined for intracellular location of catalase, a peroxisomal matrix enzyme, by immunofluorescence microscopy using anti-catalase antibody. These mutant cell clones showed cytosolic localization of catalase, apparently indicating the defect of peroxisome biogenesis. Mutants lacking morphologically recognizable peroxisomes also showed typical peroxisome assembly-defective phenotype such as severe loss of catalase latency and resistance to 12-(1'-pyrene) dodecanoic acid (P12) /UV treatment. By transfection of cDNAs for PAF-1 and PAF-2 and cell fusion analysis between the CHO cell mutants including previously isolated Z24, Z65, and ZP92, six mutants, ZP105, ZP104 and ZP109, ZP110 and ZP111, and ZP114 were found to belong to four novel complementation groups, respectively. Complementation analysis with fibroblasts from patients with peroxisome biogenesis disorders such as Zellweger syndrome revealed that ZP105 and ZP104/ZP109 were found to be in the same complementatin as human groups II and III, respectively. Furthurmore, ZP110/ZP111 and ZP114 were not classified to any of ten human complementation groups, indicating that these two groups of mutants are in the 11th and 12th complementation groups in mammals. Thus, the newly isolated CHO cell mutants defective in peroxisome biogenesis would be very useful for not only isolating peroxisome biogenesis factors but also delineating pathogenic genes responsible for peroxisome biogenesis disorders.