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Time-dependent 3D-cDNA microarray analyses of candidate genes for target therapy during experimental rat colon carcinogenesis

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To assess possible target genes for colon cancer therapy, a high-density 3D-microarry analysis was used to screen expression of a subset of genes in different colonic regions during multistep stages of colon carcinogenesis in rats. Male F344 rats were divided into two groups. Group 1, were initiated by Amino-1-methyl-6-phenylimidazo [4,5-b]pyridine (PhIP) 200 mg/kg b.wt, 3 times, every day. Group 2 received vehicle only. Groups of rats were sacrificed at 3h, 24h, 1w, 12w, and 52 weeks after last i.g. administration. Clustering analysis showed differential gene behavior under function of time and colonic area in significant relation to PhIP-induced carcinogenesis. For instance, at early post-initiation phase (3h), a high number of genes involved in the three colonic regions were down-regulated, particularly those involved in the cell cycle, xenobiotic metabolism, protooncogenes and DNA repair. However, after 24 hours, most genes were up-regulated in distal-and colorectal areas, but not in the proximal areas. After 1 and 12 weeks, many genes in proximal colons remained down-regulated; however genes in distal and colorectal areas were highly up regulated. After 52 weeks, the case remained as fewer genes to be changed in the proximal colons, and higher numbers of genes were markedly up-regulated in distal colons and colorectum particularly those involved in cellular proliferation, oncogenes, growth factors and DNA repair. In summary, up-regulation of certain genes was concomitant to progression of carcinogenesis process of PhIP as early as 24 hours particularly in distal and colorectal areas, and explains increased induction of tumors specifically in these areas as compared to the proximal colons that showed fewer genes to be changed during cancer progression. An outline of this data could point to certain genes as candidates for future colon cancer targeted therapy.

Biography

Elsayed I. Salim was originally graduated from Tanta University, Faculty of Science-Egypt. He has completed his Ph.D. from Osaka City University Medical School and postdoctoral studies from the same university at Japan. He is the Director of Tanta University Central Laboratories for scientific research. He has published more than 60 papers in cancer research in reputed journals and serving as an editorial board member of some national and international magazines. His research interest is mainly in Cancer research, Toxicological Pathology, Molecular Pathology and Epidemiology. Professor Salim is the coordinator of the Asian Pacific Organization of Cancer Prevention (APOCP) in the Arab World and North Africa and is a subject editor of Toxicological Pathology in the APOCP's scientific magazine (APJCP).

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