This Month in AJP

Predisposition to Renal Cell Cancer in Familial Multiple Cutaneous Leiomyomatosis

Kiuru et al (Am J Pathol 2001, 159:825–829) studied a multiple cutaneous leiomyomatosis (MCL) kindred with seven affected members. The study, which involved clinical data and histopathological and molecular analyses, demonstrated features of a cancer predisposition syndrome linking hereditary leiomyomatosis with renal cell cancer (HLRCC syndrome). Multiple cutaneous leiomyomas from the proband in the study had loss of heterozygosity (LOH) in chromosome 1q. The linkage analysis, LOH, and clinical data suggest that MCL and HLRCC are a single disease displaying a variable phenotype regarding renal involvement.

Chromosomal Defects and Presumed Origin of Lipoblastomas

Lipoblastomas are soft tissue tumors containing adipocytes and mesenchymal cells which can evolve into lipoma-like lesions. Gisselsson et al (Am J Pathol 2001, 159:955–962) report that the 8q12 PLAG1 region was rearranged in 11 of 16 lipoblastomas, and three other lipoblastomas had polysomy for chromosome 8 (up to five copies in one case) in the absence of PLAG1 abnormalities. PLAG1 alterations were detected not only in lipoblasts, but also in mature adipocytes, primitive mesenchymal cells, and fibroblast-like cells. These findings suggest that lipoblastomas originate in a primitive mesenchymal cell precursor which may differentiate into mature adipocytes.

Labeling of Lesions in Human Neurodegenerative Brain Diseases

The Congo red fluorescent dye BSB binds to amyloid plaques in postmortem brain specimens from Alzheimer’s disease patients and has been used as an in vivo imaging agent in transgenic mice. Schmidt et al (Am J Pathol 2001, 159:937–943) show that BSB binds not only to extracellular amyloid protein but also to intracellular lesions containing abnormal tau and synuclein in postmortem human brains. Radioiodinated derivatives of BSB may prove to be useful for in vivo imaging of brain lesions containing diverse types of amyloids.

Fluorescence Scanning Method to Detect DNA Mutations

Single-base mutations in DNA are usually detected by gel electrophoresis which can separate double-stranded DNA molecules based on melting temperature and secondary structure of the molecules. Simpler techniques using solution-based methods can detect mutations only in short segments of DNA of approximately 20 bp. Elenitoba-Johnson and Bohling (Am J Pathol 2001, 159:845–853) describe a solution-based fluorescence method which can discriminate between wild-type and mutant DNA sequences in regions longer than 200 nucleotides. Heterozygosity is identified by the lower melting temperature of less stable heteroduplex mismatches. The new method simplifies mutation analysis and can be adapted for automation and use in high-throughput systems.

Merging of Tissue Microarray Databases with Pathology and Clinical Information

The amount of information obtained by large-scale analysis of gene expression and tissue pathology is increasing rapidly with the use of new techniques. A major challenge in this type of work is to integrate the information gathered by different methods into a coherent, useful, and accessible format. Manley et al (Am J Pathol 2001, 159:837–843) describe a system to study prostate cancer in use at the University of Michigan. The system includes tissue microarray and image databases, as well as databases on prostate pathology and clinical information. The system links information on patient, tissue, block, diagnosis, and array location with clinical and pathology data. It facilitates statistical analysis of large-scale tissue array data and is highly suitable for collaborative multi-institutional studies because it can be operated through the Internet.
Ornithine Decarboxylase and UV-Induced Skin Carcinogenesis

Several studies have shown that ornithine decarboxylase (ODC), the rate-limiting enzyme in polyamine biosynthesis, is involved in skin carcinogenesis. Ahmad et al (Am J Pathol 2001, 159:885–892) analyzed the response of transgenic mice that overexpress ODC (K5/ODC transgenics) to limited UVB exposure. The dosage used is considered to be sufficient to initiate but not to promote carcinogenesis. Neither non-transgenic littermates nor SKH-1 hairless mice (widely used in studies of UV carcinogenesis) developed skin tumors or cysts after UV irradiation at this dosage. In contrast, 8 of 20 UVB-exposed K5/ODC transgenics developed tumors and multiple pigmented cysts. The data indicate that ODC overexpression enhances tumor progression in the skin.