Liver Stem-Like Cells Express Markers of Bone Marrow Side-Population (SP) Cells

The liver contains a stem cell-like compartment ("oval cells") that is capable of generating both hepatocytes and bile duct cells. Oval cells constitute a reserve cellular compartment that proliferates in liver injury in which there is inhibition of hepatocyte replication. Oval cells express phenotypic markers of both fetal and adult hepatocytes as well as proteins such as Thy-1, which is present in bone marrow stem cells. Side population (SP) is a population of bone marrow cells that is enriched in hematopoietic stem cells. SP cells constitute approximately 0.05% of bone marrow cells in adult humans and mice. They can differentiate into all hematopoietic lineages, and into endothelial and muscle cells. SP cells express an ATP-binding cassette transporter gene known as ABCG2/BCRP1. Transduction of bone marrow cells with a vector expressing this gene markedly increases the SP population. Shimano et al (Am J Pathol 2003, 163:3–9) reasoned that liver oval cells might express some of the same markers as SP cells of the bone marrow. The experimental system used for generating oval cells consisted of a protocol that combined toxic liver damage and partial hepatectomy. Shimano et al report that oval cells that proliferate in the liver under these conditions express the ATP-binding transporter gene presented in SP bone marrow cells. These results show that oval cells have many of the phenotypic markers of bone marrow cells and reinforce the notion that oval cells are intrahepatic stem cells.

Clonality of Human Endometrial Glands

The endometrium continually renews itself during the menstrual cycle. The human endometrium is reconstituted within 2 weeks after shedding. This regenerative capacity is not exhausted during the reproductive years, suggesting that endometrial glands, similar to colonic crypts, contain stem cells, which are the source for its cellular components. The crypts of the colon are monoclonal, that is, each crypt is the product of a single stem cell. Tanaka et al (Am J Pathol 2003, 163:295–301) examined the clonality of human endometrium glands. They isolated intact, individual endometrial glands from surgical specimens and assessed their clonality by analyzing X-chromosome inactivation in each gland. The results show that individual endometrial glands contain single or multiple stem cells and suggest that alterations of the regulation of cell replication in these stem cells play a critical role in endometrial tumorigenesis.

Polypoid and Non-Polypoid Colorectal Adenomas Have a Different Spectrum of Genetic Abnormalities

Two main molecular pathways for colorectal tumorigenesis have been described: a major group of tumors in which there is loss of heterozygosity (LOH) and frequent mutations in the tumor suppressor genes, APC and p53; and a second group which have a high frequency of replication errors at microsatellite loci (genomic instability). Polypoid adenomas show frequent LOH in at least five chromosomes but there is no information on whether non-polypoid adenomas have the same types of genetic abnormalities. Moreover, non-polypoid adenomas, which are difficult to detect, flat lesions without mucosal elevation, may have a different clinical course than that of polypoid lesions. Richter et al (Am J Pathol 2003, 163:287–294) examined chromosomal abnormalities in polypoid and non-polypoid colorectal adenomas, using comparative genomic hybridization (CGH). These two types of tumors had very distinct chromosomal imbalances (no chromosomal abnormalities were present in normal colonic mucosa) and carcinomas evolving from non-polypoid adenomas had a very complex pattern of chromosomal aberrations. The results suggest that polypoid and non-polypoid colorectal adenomas have different pathways of molecular pathogenesis.

Identification of Molecular Markers for Human Endothelial Venules

The endothelium of the vascular beds of different tissues shows considerable heterogeneity. Post-capillary high endothelial venules (HEVs) are an interesting example of endothelial specialization. These vessels are found in lymphoid tissues, in T-cell zones that surround B-cell follicles. It is thought that HEVs play a role in immune diseases, such as rheumatoid arthritis, Crohn’s disease, allergies, and transplant rejection. In these conditions, HEV abnormalities may allow increased migration of lymphocytes into tissues, contributing to the enhancement and persistence of inflammation. Baekkevold et al (Am J Pathol 2003, 163:69–79) used PCR-based subtractive hybridization to clone a gene coding for a nuclear factor, which is preferentially expressed by HEVs. HEV (both the mRNA and the protein) was highly expressed in human tonsils, Peyers’ patches, and lymph nodes. HEV is a novel gene that may play an important role in controlling the differentiation of endothelial cells into HEVs.
C-Reactive Protein and Complement Activation in Myocardial Infarction

Blood levels of C-reactive protein (CRP) correlate with the risk of cardiovascular disease. Moreover, the pattern of changes in the levels of circulating CRP after myocardial infarction may correlate with complications and recovery. It is assumed that CRP is an indirect marker for the degree of inflammation in atherosclerotic plaques and infarcted areas. Nijmeier et al (Am J Pathol 2003, 163:269–275) examined whether CRP may activate complement in the area of injury, thus contributing to the inflammatory process. They obtained myocardial samples from patients who died 5 to 12 days after an acute myocardial infarction. Complement, CRP, and CRP-complement complexes were increased in patients who died 12 hours or later after the infarction. The results suggest that CRP enhances local inflammation in myocardial infarction, through the activation of the complement system.