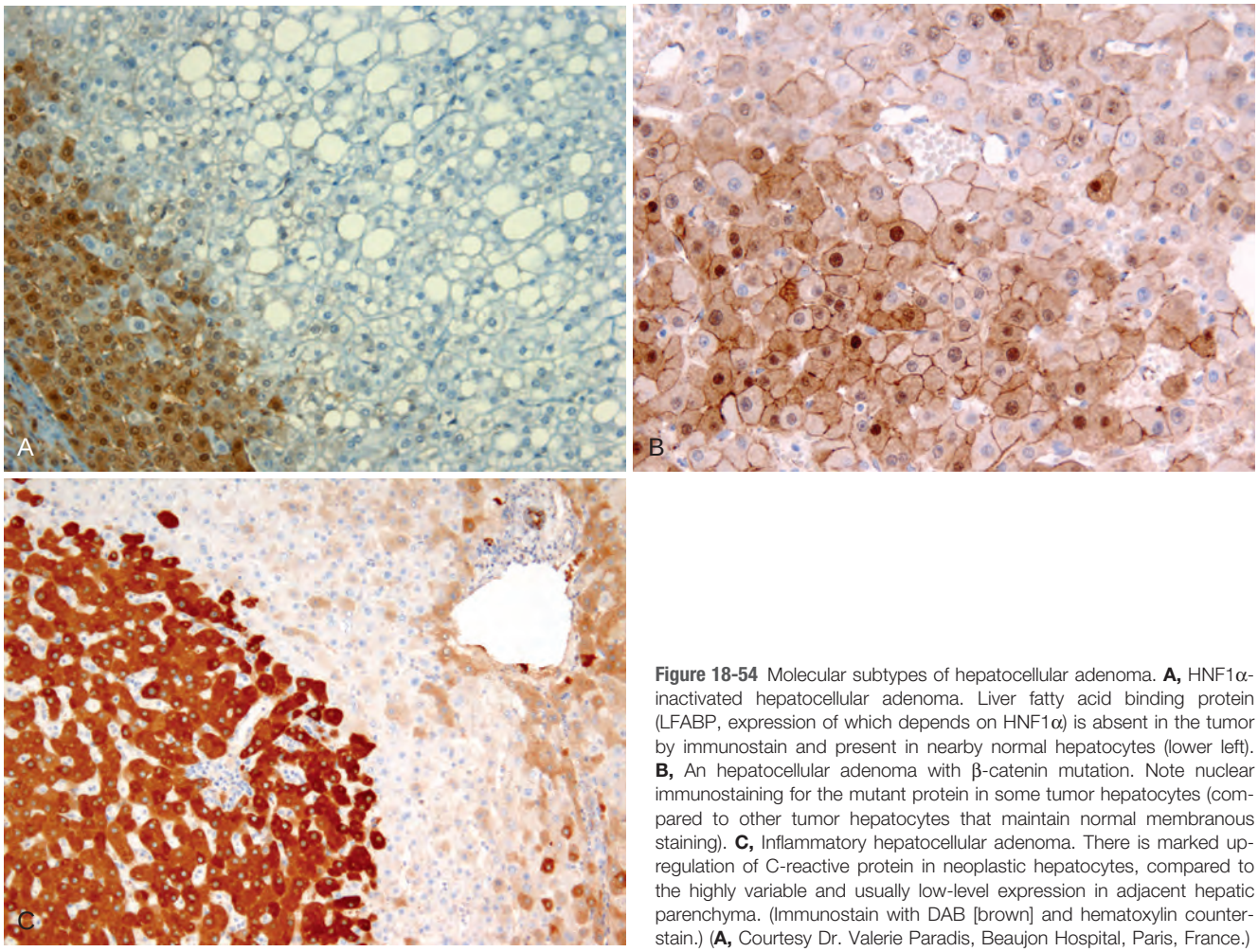

Figure 18-54 Molecular subtypes of hepatocellular adenoma. **A,** HNF1α-inactivated hepatocellular adenoma. Liver fatty acid binding protein (LFABP, expression of which depends on HNF1α) is absent in the tumor by immunostain and present in nearby normal hepatocytes (lower left). **B,** An hepatocellular adenoma with β-catenin mutation. Note nuclear immunostaining for the mutant protein in some tumor hepatocytes (compared to other tumor hepatocytes that maintain normal membranous staining). **C,** Inflammatory hepatocellular adenoma. There is marked up-regulation of C-reactive protein in neoplastic hepatocytes, compared to the highly variable and usually low-level expression in adjacent hepatic parenchyma. (Immunostain with DAB [brown] and hematoxylin counterstain.) (**A,** Courtesy Dr. Valerie Paradis, Beaujon Hospital, Paris, France.)

absent in these tumors due to the inactivating mutation of HNF1-α. Thus, immunostaining for LFABP demonstrating its absence in the tumor is diagnostic of the mutation (Fig. 18-54*A*).

β-Catenin mutated hepatocellular adenomas often have a high degree of cytologic or architectural dysplasia or even overt areas of hepatocellular carcinoma. Immunostain for β-catenin usually shows nuclear translocation indicative of its activated state (Fig. 18-54*B*). This change is diagnostic. Glutamine synthetase, a target of beta-catenin, (normally only positive in perivenular hepatocytes) is also diffusely positive in these tumors, a change that may be seen even when the activating β-catenin mutation doesn't result in nuclear staining. In such tumors, molecular analysis is necessary for definitive confirmation.

Inflammatory hepatocellular adenomas. Unlike the other hepatocellular adenomas, which are comprised of only hepatocytes and vessels with minor amounts of stroma, these lesions characteristically have in addition areas of fibrotic stroma, mononuclear inflammation, ductular reactions, dilated sinusoids, and telangiectatic vessels. Most of these tumors overexpress acute phase reactants such as C-reactive protein and serum amyloid A (Fig. 18-54*C*). These molecules may also be elevated in the serum. 10% of these HCAs that also have β-catenin activating mutations and, as would be anticipated, also show increased nuclear levels of b-catenin by immunohistochemistry.

Malignant Tumors

Malignant tumors occurring in the liver can be primary or metastatic. Most of the discussion in this section deals with primary hepatic tumors. Most primary liver cancers arise from hepatocytes and are termed *hepatocellular carcinoma* (HCC). Much less common are carcinomas of bile duct origin, *cholangiocarcinomas*.

Before embarking on a discussion of the major forms of malignancy affecting the liver, a rare form of primary liver cancer, hepatoblastoma deserves a brief discussion.

Hepatoblastoma

Hepatoblastoma is the most common liver tumor of early childhood. It is rarely occurs over the age of 3 years. Its incidence, which is increasing, is approximately 1 to 2 in 1 million births. Two primary anatomic variants are recognized:

- The *epithelial type*, composed of small polygonal fetal cells or smaller embryonal cells forming acini, tubules, or papillary structures vaguely recapitulating liver development (Fig. 18-55)
- The *mixed epithelial and mesenchymal type*, which contains foci of mesenchymal differentiation that may consist of primitive mesenchyme, osteoid, cartilage, or striated muscle