

Preface

Caveolae, a subset of lipid rafts, are flask-shaped invaginations of the plasma membrane that play an important role in cellular signal transduction by concentrating several molecules in a confined microenvironment. This clathrin-independent pathway of endocytosis is also involved in other crucial cellular processes, ranging from cholesterol transport to pathogen uptake. Caveolin (Cav) proteins, the main structural components of caveolae, are essential for maintaining caveolar integrity, as well as regulating cell signaling through protein–protein interactions. Cav proteins are composed of three distinct members, namely Cav-1, -2 and -3. However, Cav-1 still remains the best-studied and well-characterized member. More specifically, Cav-1 has been implicated in the pathogenesis of several human diseases such as atherosclerosis, heart disease, stroke, diabetes, and cancer, the latter being the focus of this book.

Most of the functional effects of Cav-1 are mediated through its scaffolding domain, which is located at amino acids 82–101. This domain recognizes a Cav binding motif found within signaling molecules, which can directly regulate their activities and downstream effects on cellular proliferation. Cav-1 primarily acts as a tumor suppressor in several types of human cancer and its downregulation correlates with cancer development and progression. In addition, mutations of the Cav-1 gene have been detected in tumor samples from cancer patients. One specific mutation of the Cav-1 gene results in the replacement of a proline for a leucine at amino acid position 132 (P132L). The Cav-1 (P132L) mutation can be detected in up to 16% of breast cancer specimens and acts as a dominant-negative mutant, which prevents the proper folding and expression of wild-type Cav-1. Recent studies have also reported a role for Cav-1 in tumor-associated stromal cells. Indeed, Cav-1 has been shown to directly regulate the behavior of cancer-associated fibroblasts (CAFs) isolated from invasive breast tumors.

Interestingly, the role of Cav-1 is not restricted to that of a tumor suppressor. Indeed, Cav-1 can also behave as a tumor promoter in certain types of tissues. For example, its over-expression has been associated with the development of aggressive tumors in some cancer patients. In these cases, Cav-1 can be secreted to mediate paracrine effects on neighboring epithelial cells, fibroblasts, and/or endothelial cells. In fact, a secreted form of Cav-1 has been detected in the serum of prostate

cancer and melanoma patients and was recently proposed as a new predictive biomarker of tumor stage associated with poor clinical prognosis.

Due to the complex nature and tissue-specific functions of Cav proteins, there was a need for a reference book that summarized the literature and describes the future of these important proteins in the field of cancer research. As such, we brought together several experts in the field of Cavs and cancer to summarize the role of Cav-1 in six different epithelial cancers and the tumor-associated stroma, as well as its regulation of angiogenesis. We would like to thank all the authors who shared their scientific knowledge and opinions about the important roles of Cavs in cancer.

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