IJAE
Vol. 120, n. 1 (Supplement): 6, 2015
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

Tumor angiogenesis. From bench to bedside

Domenico Ribatti

Dipartimento di Scienze Mediche di Base, Neuroscienze ed Organi di Senso, Università degli Studi di BARI, BARI, Italy

Under physiological conditions, angiogenesis is regulated by the local balance between endogenous stimulators and inhibitors. In recent years, evidence has accumulated that, in addition to the classic factors, many other endogenous peptides play an important regulatory role in angiogenesis, especially under pathological conditions. In chronic inflammation and tumor growth, there is an imbalance between endogenous stimulator and inhibitor levels, leading to an "angiogenic switch". Various regulatory elements control the switch to the vascular phase. Endothelial cell turnover in the healthy adult organism is low, the quiescence being maintained by the dominant influence of endogenous angiogenesis inhibitors over angiogenic stimuli. In pathological situations angiogenesis may be triggered not only by the overproduction of pro-angiogenic factors, but also by the down-regulation of inhibitory factors. The stromal microenvironment is essential for cell proliferation and angiogenesis through its provision of survival signals, secretion of growth and pro-angiogenic factors, and direct adhesion molecule interactions. Tumor cells are surrounded by an infiltrate of inflammatory cells, namely lymphocytes, neutrophils, macrophages, and mast cells, which communicate via a complex network of intercellular signaling pathways mediated by surface adhesion molecules, cytokines, and their receptors. Much research effort has been concentrated on the role of angiogenesis in cancer, and inhibition of angiogenesis is a major area of therapeutic development for the treatment of this disease. New pathophysiological concepts generated in the past few decades have given rise to the development of a large variety of new drugs to interfere with angiogenesis. Angiogenesis inhibitors are now being approved and introduced into medical practice throughout the world and inhibition of angiogenesis is a major area of therapeutic development for the treatment of cancer. However, even if the majority of pre-clinical studies have shown that the growth of all experimental tumors can be effectively inhibited by various anti-angiogenic agents, the clinical benefits of anti-angiogenic treatments are relatively modest, and in the majority of cases, the drugs merely slow down tumor progression and prolong survival by only a few more months.