Editorial

An Update on Biomarkers for Tumor Angiogenesis

Folkman in 1971 proposed that tumor growth is dependent on angiogenesis. Angiogenesis is an essential process in the progression of malignant tumors since solid tumors cannot grow beyond 1 to 2 mm in diameter without angiogenesis.[1,2]

Neoangiogenesis or new blood vessel formation is fundamental to tumor growth and its spread. New blood vessels formed by angiogenesis provide substrates, such as nutrients and oxygen which the tumor requires to grow.[3] Vascular endothelial growth factor (VEGF) is the key mediator of angiogenesis and its expression is regulated by an array of intrinsic and extrinsic factors, the major stimuli being hypoglycemia and hypoxia. Tumor angiogenesis is regulated by a balance of antiangiogenic and angiogenic cytokines.

In the recent past VEGF, CD 31, CD 34, CD 105, angiopoietin 1 and 2 and tumor angiogenesis factor have been demonstrated in malignant tumors.[4] Their role in tumor angiogenesis has been well established. Many studies have correlated their expression with tumor aggressiveness, biologic behavior, tumor differentiation, lymph node metastasis and prognosis. The novel outcome of such studies is eventually to develop drugs that block these receptors thereby preventing growth and progression of the tumor itself. A major drawback is that most of these angiogenic markers are not specific to newly formed tumor vessels within cancer tissues. Therefore, exact quantification of tumor vessels is essential to evaluate prognosis. Selective detection using specific markers increases the possibility of molecular targeted therapy through the inhibition of tumor angiogenesis.

One such novel marker for angiogenesis is Nestin.[5] Nestin expression is observed mainly in the embryonic endothelial cells which develop through angiogenesis of the budding capillaries in the corpus luteum during embryogenesis. Such expressions are not observed in mature endothelial cells, therefore expression is related to only proliferating endothelial and progenitor cells. Nestin expression is also observed in capillaries within glioblastoma, prostate cancer and other malignancies with high expression in proliferating endothelial cells. Thus, nestin positivity is related to neovascularization within the tumor. Nestin expression can thus be used as a marker and prognostic indicator of tumor progression and metastasis. Furthermore, nestin targeted therapy can effectively reduce tumor growth through suppression of angiogenesis. Thus, nestin opens a new direction for further research related to cancer diagnosis and therapy. Targeting of tumor neovasculature specific antigens offers the possibility of future therapeutic approaches.

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