Chapter 10
Strategies to Suppress Tumor Angiogenesis and Metastasis, Overcome Multi-Drug Resistance in Cancer, Target Telomerase and Apoptosis Pathways

Mohd Aleem
Institute of Nuclear Medicine and Allied Sciences, India

Deepti Sharma
Institute of Nuclear Medicine and Allied Sciences, India

Deepshikha Sharma
Jamia Millia Islamia, New Delhi, India

Siddhartha Dan
Institute of Nuclear Medicine and Allied Sciences, India

Pooja Gupta
Institute of Nuclear Medicine and Allied Sciences, India

Khalid Umar Fakhri
https://orcid.org/0000-0001-6978-8172
Department of Biosciences, Jamia Millia Islamia, New Delhi, India

M. Moshahid Alam Rizvi
Department of Biosciences, Jamia Millia Islamia, New Delhi, India

ABSTRACT

Cancer has been a worldwide topic in the medical field for a very long time. As angiogenesis is essential for tumor growth and metastasis, controlling tumor-associated angiogenesis is a promising tactic in limiting cancer progression. In cancer patients, multidrug resistance (MDR) is most widely used phenomenon by which cancer acquired resistance to chemotherapy. This resistance to chemotherapy occurs due to the formation of insulated tumor microenvironment which remains a major hurdle in the

DOI: 10.4018/978-1-7998-6530-8.ch010

cure of various types of cancer. The mechanisms that cause malignant growth of cells include cell cycle control, signal transduction pathways, apoptosis, telomere stability, and interaction with the extracellular matrix. This chapter focuses on current strategies to suppress tumor angiogenesis for cancer therapy, various mechanisms involved in the development of MDR in cancer cells, which in turn will help us to identify possible strategies to overcome these MDR mechanisms and a variety of procedures that involves targeting apoptotic and telomerase pathways to suppress tumor progression.

STRATEGIES TO SUPPRESS TUMOUR ANGIOGENESIS AND METASTASIS

Introduction

Angiogenesis speaks to a sign of malignancy. A few proteoglycans associate with cell surface receptors and manage angiogenesis inside the tumour microenvironment (TME) (Chakraborty et al., 2020). Cancer growth metastasis comprises of different, complex, communicating and associated steps (Isaiah J. Fidler, 1990). Inability to finish any one of these steps may keep the tumour cell from developing a metastasis. It has already been established that the process of angiogenesis is basic to the development of different types of tumours (Folkman, 1986). The enlistment of angiogenesis is intervened by positive and negative administrative molecules secreted by both tumour and host cells (I. J. Fidler & Ellis, 1994; Liotta et al., 1991). Key to the science of tumour angiogenesis is the commitment of the host environment scale condition (Takahashi et al., 1996).

Angiogenesis and Metastasis

Angiogenesis is a fundamental natural procedure including the growing and development of fresh blood vessels from the prior vascular primordium (Folkman, 1995) and assumes a key role not just in the guideline of different physiological exercises (e.g., early-stage improvement, wound recuperating, female regenerative cycle, and so forth.) but also in tumour development and metastasis (Folkman, 2001). Tumours that develop past a size of 2 mm^3 are reliant on oxygen and supplements provided by encompassing newly formed blood vessels (Eskens, 2004).

Agrin Repertoire Involved in Angiogenesis

Agrin crosstalk between cancer cells and endothelial cells (ECs) is underlined by the perception that high levels of Agrin associates with poor prognosis (Chakraborty et al., 2017). Like Hepatocellular carcinoma (HCC) cells, Agrin is communicated and secreted in a large scale but at lower levels than in malignant growth cells (Njah et al., 2019). Significantly, the angiogenic job of Agrin depends on its receptor complex comprising of Integrin β1, Lrp4, and MuSK, which are likewise communicated in these ECs. Like HCC cells, focal adhesion kinase (FAK) is likewise basic as a component of downstream effectors for Agrin-interceded angiogenesis in ECs. Agrin and its receptors likewise intercede a solid bond of invading ECs to tumour cells. Fragment of Agrinmay promoted an angiogenic phenotype in several ECs and an ex vivo rodent metatarsal sprouting assay. This fragment of Agrin may also effectively recruited more blood vessels in cell-free subcutaneous Matrigel plugs, suggesting a promising avenue for Agrin as an in vivo mediator of angiogenesis.