

Matrix metalloproteinases in chemoresistance: regulatory roles, molecular interactions, and potential inhibitors

ABSTRACT

Cancer is one of the major causes of death worldwide. Its treatments usually fail when the tumor has become malignant and metastasized. Metastasis is a key source of cancer recurrence, which often leads to resistance towards chemotherapeutic agents. Hence, most cancer-related deaths are linked to the occurrence of chemoresistance. Although chemoresistance can emerge through a multitude of mechanisms, chemoresistance and metastasis share a similar pathway, which is an epithelial-to-mesenchymal transition (EMT). Matrix metalloproteinases (MMPs), a class of zinc and calcium-chelated enzymes, are found to be key players in driving cancer migration and metastasis through EMT induction. The aim of this review is to discuss the regulatory roles and associated molecular mechanisms of specific MMPs in regulating chemoresistance, particularly EMT initiation and resistance to apoptosis. A brief presentation on their potential diagnostic and prognostic values was also deciphered. It also aimed to describe existing MMP inhibitors and the potential of utilizing other strategies to inhibit MMPs to reduce chemoresistance, such as upstream inhibition of MMP expressions and MMP-responsive nanomaterials to deliver drugs as well as epigenetic regulations. Hence, manipulation of MMP expression can be a powerful tool to aid in treating patients with chemo-resistant cancers. However, much still needs to be done to bring the solution from bench to bedside.