An-Najah National University (ANNU)

The multifaceted role of EMILIN2 in cancer

University Students: A

A Thesis presented to

School of Medicine in Partial Fulfilment

of the Requirements for the Degree of Doctor of Medicine

By

Khaled Ishtawi, MD student (ANNU) 11524444

Mohammed Ahmed, MD student (ANNU) 11541522

Sameh Sawalhi, MD Student (ANNU) 11541581

Supervised by

Dr. Yousef Salama

The School of Medicine and Health Sciences, An-Najah National University (ANNU)

Abstract

Malignant melanoma is a cancer originated from melanocytes of the skin and is one of the most aggressive types of skin cancer. Elastin microfibril interface-located proteins (EMILINs) are group of extracellular glycoproteins. One member, EMILIN 2 was suggested to play a role in activating cell death (apoptosis) through its ability to activate DR5 and DR4. In contrast, it also has been shown to bind to EGFR where it promotes tumor growth. We studied the role of EMILIN-2 for malignant melanoma (B16F10) growth. We used gene silencing and over expression to assess EMILIN2 and EGFR functions during melanoma growth. We found that increased levels of EMILIN-2 suppressed tumor proliferation in part through downregulation of EGFR expression and by activating DR5 and caspase-mediated apoptosis. The proteasome inhibitor bortezomib enhanced the expression of both EMILIN-2 and DR5. These data suggest that EMILIN2 overexpression can suppress tumor growth, and that certain anti-tumor drugs by upregulating EMILIN2 might enhance tumor apoptosis and suppression of tumor growth.

Keywords: melanoma, B16F10, gene therapy, bortezomib, EMILIN 2, DR5, EGFR.