DIFFERENTIAL ANGIOGENIC ROLES OF SERUM AMYLOID A 1 (SAA1) ISOFORMS IN ESOPHAGEAL SQUAMOUS CELL CARCINOMA (ESCC)

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Esophageal Caner (EC), a highly metastatic and fatal cancer, is ranked the eighth in mortality rate in Hong Kong cancer patients (Hong Kong Cancer Registry, Hospital Authority, 2010). Esophageal Squamous Cell Carcinoma (ESCC) is the predominant type comprising more than 90% of EC. Using a functional complementation approach, SAA1 was identified as one of the tumor suppressor gene candidates. SAA1 is located at chromosome 11p15.1 and is expressed as a secretary protein in liver, human cultured smooth muscle cells, monocyte-macrophage cell lines, and in histologically-normal human epithelial tissues. Genetic polymorphisms of SAA1 have been identified as a risk factor of diseases such as amyloidosis. Three SAA1 isoforms with two single nucleotide polymorphisms at exon three (SAA1.1, 1.3, and 1.5) were observed in the ESCC patients and healthy individuals.

The SAA proteins contain the functional YIGSR-like and RGD-like motifs, proteins with these motifs can inhibit angiogenesis, cell adhesion to ECM, growth and metastasis. To understand the anti-tumorigenic and anti-angiogenic roles of the three SAA1 isoforms in ESCC progression, both recombinant proteins and secreted proteins from the conditioned media of lentiviral-infected ESCC cell lines were used for functional assays. For the vascular endothelial cell tube formation assay, the treatments with SAA1.1 and 1.3 proteins showed suppression of tube formation, whereas no significant effects could be observed in the treatment with the SAA1.5. Suppression of cell proliferation and induction of cell death were observed when the endothelial cells were cultured with SAA1.1 and 1.3 proteins. To further elucidate the differential effects among the three SAA1 isoforms in anti-angiogenesis, the cytoskeleton arrangement of the vascular endothelial cells was studied. The SAA1.1 and SAA1.3 proteins could abolish the endothelial cell adhesion by disturbing the formation of stress fibers and focal adhesions. As a conclusion, the present data has shown the variation in anti-angiogenic potential of the three SAA1 isoforms.