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c-Met overexpression of fibroblasts increases angiogenic signal in breast cancer

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We found that c-Met overexpression was induced in normal breast fibroblast (NBF) by the conditioned medium (CM) of cancer cells regardless of subtypes, which made us to hypothesize that c-Met overexpression is a property of cancer-associated fibroblast (CAF). Therefore, we investigated whether c-Met overexpressing NBFs contribute to tumor progression. To this end, extracellular matrix (ECM) gene expression alteration was analyzed from the NBFs transfected with c-Met overexpression plasmid using cDNA microarray since CAF constructs tumor microenvironment by ECM remodeling. In our microarray data, matrix metalloproteinase 1 (MMP1) was most up-regulated in c-Met overexpressing NBF (approximately 10-fold) compared to the control NBF. According to previous studies, MMP1 induces VEGFR2 (Vascular endothelial growth factor receptor 2) expression in endothelial cells (ECs). So, it was assumed that c-Met overexpressing NBF contributes to breast cancer angiogenesis. In our study, the CM of c-Met overexpressing NBF induced a better tube formation of endothelial cells (Hy926) than that of control. On the other hand, tube formation by c-Met overexpressing NBF CM was reduced in the presence of c-Met inhibitor. Similar results were also observed in the co-culture of NBF and breast cancer cell lines (luminal A, B, Her2, and TNBC). The expression of c-Met and MMP1 was increased by the co-culture, whereas was decreased in the presence of c-Met inhibitor. Tube formation of EC was increased by the CM of the co-culture, whereas decreased by c-Met inhibitor-treated co-culture CM. Based on our results, c-Met inhibitor may be able to suppress angiogenesis in breast cancer by decreasing c-Met-induced MMP1 expression of CAFs.

Biography

Seong Gyeong Mun has completed her Bachelor's degree in Molecular Biology from Dankook University. She is currently pursuing Master's degree in Yonsei University School of Medicine. She had studied about breast tumor microenvironment in her graduate school days.

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