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Interleukin-6 secreted by cancer-associated fibroblasts induces endometrial cancer growth

Ivy Chung

University of Malaya, Malaysia

Cancer was once thought to be a 'stand-alone' malignancy where we treat patients with drugs that target only cancer cells. Recently, more evidence is showing that cancer cells do not thrive alone, they rely on their environment to maintain their survival and to progress into an aggressive state. We found that cancer-associated fibroblasts (CAFs) isolated from human endometrial cancer (EC) tissues secreted high levels of interleukin-6 (IL-6), which promotes EC cell proliferation in vitro. Neutralizing IL-6 activity reduced while IL-6 recombinant protein increased EC cell proliferation. IL-6 receptors (IL-6R and gp130) were expressed only in EC epithelial cells but not in CAF, indicating a one-way paracrine signaling. In the presence of CAFs, Janus kinase/signal transducers and activators of transcription (JAK/STAT3) pathway was activated in EC cells, which led to induction of a target gene, c-Myc protein. CAFs-mediated cell proliferation was dependent on c-Myc expression, as RNAi-mediated c-Myc down-regulation led to a significant reduction in cell viability. The effect of CAFs in promoting EC cell proliferation was also evident in a subcutaneous tumor xenograft model. Further investigation showed that IL-6 receptors, phosphorylated-STAT3 and c-Myc were highly expressed in human EC tissues than in benign endometrium. Taken together, our data suggests that IL-6 secreted by CAF induces c-Myc expression to promote EC proliferation in vitro and in vivo. IL-6 pathway can be a potential target to disrupt tumor-stroma interaction in endometrial cancer progression.

Biography

Ivy Chung completed her PhD from State University of New York at Buffalo and Postdoctoral studies from Children's Hospital Boston, Harvard Medical School and Boston. She currently is an Associate Professor in Department of Pharmacology, Faculty of Medicine, University of Malaya, Kuala Lumpur. She is also the Deputy Dean of Wellness Research Cluster for the Institute Management of Research and Innovation in the same university. She is actively looking to expand her collaborative network in various aspect of oncology research in this region.

ivychung@ummc.edu.my

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