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Cross-talking between EMT and inflammatory responses

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Epithelial-to-mesenchymal transition (EMT) is a process that converts adherent epithelial cells into motile mesenchymal-like cells and is known to be involved in metastasis/invasion and chemoresistance in cancer cells. Therefore, understanding of molecular mechanisms underlying EMT is beneficial for development of cancer therapies. Recently, we identified Vestigial-like family member 3 (VGLL3) as a novel EMT inducing protein by analyzing gene expression databases of the cells undergoing EMT with the stimulation of the cytokine TGF-b. VGLL3 is a transcriptional co-factor and binds to the transcription factor family TEAD. VGLL3 was shown to be induced by TGF-b stimulation and promote EMT through expression of the stem-cell factor HMGA2.

To understand molecular roles of VGLL3, we performed gene set enrichment analysis in VGLL3-expressing cells and found that VGLL3 activates inflammatory responses together with EMT signaling. Interleukin-1a expression was increased and NF-kB, a well-known pro-inflammatory signaling, was activated in VGLL3-expressing cells. We found that Interleukin-1a-NF-kB signaling promotes starvation-independent autophagy and that this autophagy is involved in cellular metabolic rewiring. These results suggest that the EMT-inducing factor VGLL3 activates starvation-independent autophagy and metabolic rewiring via inflammatory responses. We are currently analyzing involvement of these roles of VGLL3 in cancer progression.