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EDITORIAL – TRANSLATIONAL RESEARCH AND BIOMARKERS

Identification, Friend or Foe: Vimentin and α-Smooth Muscle Actin in Cancer-Associated Fibroblasts

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Cancers construct a milieu that helps them grow. One of the compositions of this milieu is cancer-associated fibroblast (CAFs), which are different from mere fibroblasts in terms of their origin, expressing genes, secreting molecules, and effect for cancer cells. The characteristics of fibroblasts have not been well-analyzed. Kalluri described fibroblasts as cockroaches of the human body for their surviving severe stress and resilient adaptation.[1] Activated fibroblasts express α-smooth muscle actin (SMA) and vimentin, together with extracellular matrix production/remodeling, and cytoskeletal rearrangement, and have been identified as being different from resting fibroblasts. CAFs are different from activated fibroblasts as they gain further secretory phenotypes and extracellular matrix production/remodeling, possibly irreversibly.

Whether CAFs are a friend or foe in growing cancers has not yet been identified.[2] There are many reports regarding their supportive effect for cancer growth, however there are also reports of their anti-effect for cancer growth, including immune-activating properties. Presumably, CAFs are a mixed population of different phenotypes and different origin. Pancreatic ductal adenocarcinoma (PDAC) is one of the aggressive cancers, with poor prognosis, and is also known to have desmoplastic histology and an abundance of CAFs.

Maehira et al.[3] analyzed vimentin and α-SMA expression by immunohistochemistry in CAFs of PDAC in 67 patients and found that higher vimentin expression was associated with significantly shorter overall survival. Among these patients, CAFs expressing vimentin alone, without α-SMA expression, were an independent predictor of poor survival. There are few reports analyzing CAFs, separated with markers, in relation to the prognosis of patients. In this context, this report is a milestone for analyzing the precise biology of chaotic CAFs.

It has also been reported that vimentin, a biomarker of epithelial to mesenchymal transition (EMT), is required for lung adenocarcinoma metastasis.[4] The origin of CAFs has not been identified, but is possibly a mixture of tissue-derived fibroblasts, bone marrow-derived mesenchymal stem cells, and EMT from cancer cells. Vimentin may be a biomarker of the origin of CAFs, as well as the growth effect of CAFs for cancer cells.

In the paper by Maehira et al.[3] co-expression of α-SMA cancelled the worse prognostic effect of vimentin-expressing in CAFs. However, a report has been published indicating that α-SMA expression in the stroma of PDAC is correlated to a significantly shorter survival.[5] The reason for this discrepancy should be precisely analyzed. Although analyzing CAFs is still a new beginning for cancer research, separating CAFs with adequate markers would be warranted in this field.

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