

# Identification of a marker for pancreatic precancerous lesions: diagnostic implication for early detection

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## ***Abstract***

Given the early metastasis of pancreatic cancer to distant organs and the limited efficacy of available treatments, the development of strategies for early detection and intervention is an urgent issue. In mouse models of pancreatic cancer (KC; KrasG12D;Ptf1a-Cre), Kras mutations are induced in all acinar cells. However, only a subset of acinar cells undergoes precancerous acinar-to-ductal metaplasia (ADM) induction, leading to the development of pancreatic intraepithelial neoplasia (PanIN) and the progression to cancer. The absence of a specific marker for ADM has limited our understanding of the precancerous lesions. Through mouse in vivo immunohistochemical screening, we have found that CD44v6 is specifically expressed at the ADM lesions in KC mice. Furthermore, CD44v6 is also expressed in cells with acinar characteristics, which are supposed to be the origin of ADM (pre-ADM). Moreover, we have observed the increased expression of CD44v6 within ADM lesions in human pancreatic tissues. Macrophages frequently accumulate around pre-ADM/ADM. The depletion of macrophages decreases the number and size of CD44v6-positive lesions. Single-cell RNA sequencing analysis of pancreatic macrophages has identified the presence of KC mouse-specific macrophage subtypes. These findings suggest a potential interplay between the emergence of CD44v6-positive cells and the accumulation of macrophages. Thus, CD44v6 emerges as a promising marker for the precancerous ADM lesions, and CD44v6 antibody holds potential as a diagnostic tool for early detection.