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CANCER IMMUNOLOGY RESEARCH

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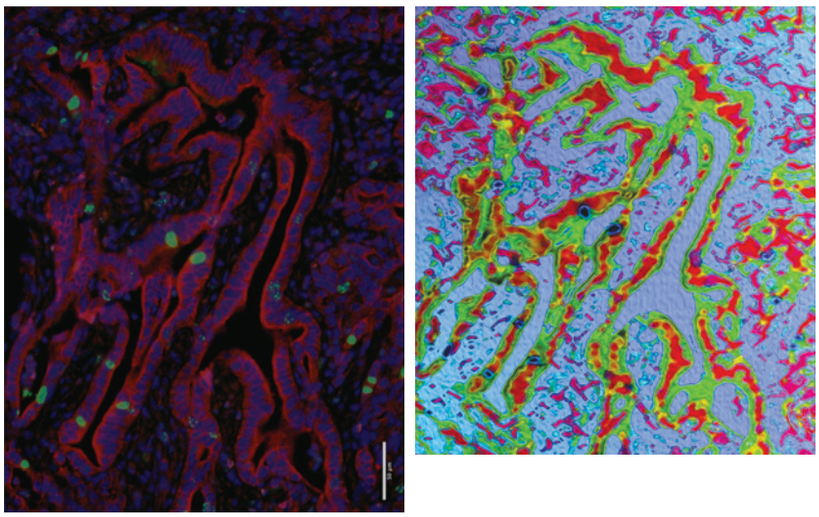
ABOUT THE COVER

B cells can predict response to immunotherapy, particularly when present in specialized tertiary lymphoid structures (TLSs) or immune aggregates (IAs). Pancreatic ductal adenocarcinoma (PDA), an aggressive cancer with low $CD8^+$ T-cell infiltration, is commonly refractory to immunotherapy and contains infiltrating regulatory B cells (Bregs). Mirlekar et al. show that IL35-producing B cells in human PDA primarily localize to IA structures. B cell–derived IL35 in a Kras- and p53-driven mouse model acts to hamper $CD8^+$ T-cell effector function via STAT3 activation, which downregulates key chemotactic and effector molecule expression. Inhibiting STAT3 signaling or deleting B cell–derived IL35 can overcome this suppression, resulting in enhanced antitumor responses and sensitivity to PD-1 blockade. In PDA patients, having high numbers of $IL35^+$ B cells inversely correlates with low cytotoxic T-cell signatures in tumors. These data highlight how Bregs present at IAs can shape antitumor responses that allow progression of disease and identify possible therapeutic targets to boost efficacy of immunotherapy in PDA. Read more in this issue on page 292. Original image from Supplementary Fig. S6. Artwork by Lewis Long.



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