WHAT WE'RE READING

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CANCER IMMUNOLOGY AT THE CROSSROADS

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CD28 mutations enhance CAR T-cell function by reducing expression of exhaustion-related genes. These data highlight considerations for CAR design that could improve antitumor responses.
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**ABOUT THE COVER**

The prognostic value of tumor-associated macrophages (TAM) remains to be fully elucidated. By combining multiplex immunofluorescence with digital analysis and machine learning, Vasaranen et al. show that TAM subsets have distinct prognostic roles in patients with colorectal cancer. Total intraprismatical and stromal TAM densities are not of predictive. Rather, TAM polarization is key, with M2-like TAMs correlating with worse cancer-specific survival. Interestingly, a survival benefit is not seen when assessing M1-like TAMs in the tumor stromal region, although high M1:M2 density ratio is associated with better survival. The study highlights the importance of utilizing multiplex analysis to more accurately determine the prognostic value of immune-cell subsets, as total population assessment or single-marker analysis may mask underlying associations. Read more in this issue on page 8. Original image from Supplementary Fig. S3B. Artwork by Lewis Long.