Cancer Research

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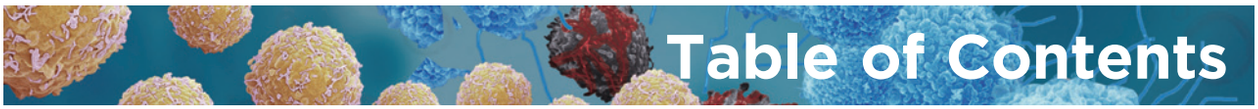

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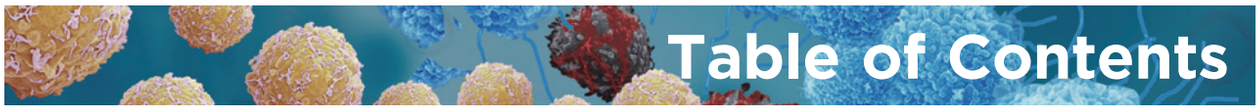

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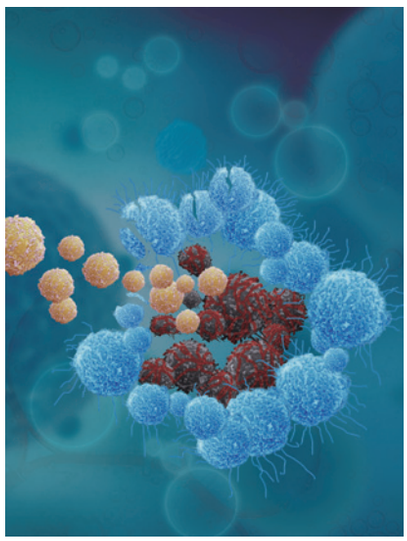

As the most important sensors on cell membrane, G protein-coupled receptors play nonredundant roles in maintaining tumor microenvironment. LGR4, a leucine-rich repeat-containing G-protein coupled receptor, was identified as a novel immune suppressor involved in promoting M2 polarization of tumor-associated macrophages (TAM), which restricts $CD8^+$ T-cell–mediated antitumor immune responses. Blockade of LGR4/R-spondin signaling pathway retrieves TAM-mediated immunosuppressive tumor microenvironment, which overcomes resistance of lung cancer and melanoma to the anti-PD-1 therapy, indicating vital roles of Rspo-Lgr4 in host antitumor immunity and a potential therapeutic target in cancer immunotherapy. For details, see article by Tan and colleagues on page 4929.