CRISPR screens uncover factors controlling response to immunotherapy

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Recently developed immunotherapies hold great promise for cancer patients, but we have an incomplete understanding of the factors that make immunotherapies successful, and of combination therapies that increase response to immunotherapy.

In work led by postdoctoral fellow Dr. Poornima Ramkumar in the Kampmann lab, we used CRISPR-based screens to elucidate cellular pathways controlling the response of multiple myeloma cells to immunotherapies targeting BCMA, a cell-surface protein. Unexpectedly, knockdown of a subunit of the protein-conducting channel in the endoplasmic reticulum, through which cell surface proteins are inserted into membranes, increased BCMA cell-surface levels in myeloma cells (while cell-surface levels of other proteins decreased). A small molecule targeting the same protein-conducting channel subunit sensitized multiple myeloma cells to BCMA immunotherapy – thus presenting a potential strategy for combination therapy.

This study was a collaboration with the labs of Arun Wiita [1], Jack Taunton [2], and Kole Roybal [3] at UCSF, as well as the UCSF Stephen & Nancy Grand Multiple Myeloma Translational Initiative [4] and Clinical team (Drs. Jeffrey Wolf, Tom Martin, Nina Shah and Sandy Wong), and Heidelberg Pharma. It was published in Blood Advances:


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