

## **Development of improved immunotherapy cancer treatments**

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Immune checkpoint blockade (ICB) has emerged as a powerful cancer treatment modality, yet other immunosuppressive mechanisms can render it ineffective. One such mechanism is the generation of metabolites that alter the tumor microenvironment such that immune cells are excluded from the tumor. Thus, the development of small molecules to counter these immunosuppressive effects is of paramount importance for effective ICB treatment. Through a complexity-to-diversity screen and further optimization of derivatives from the natural product adrenosterone, a library of bioactive compounds has been synthesized to selectively reduce immunosuppressive metabolites as demonstrated by *in vitro* enzymatic assays, cell culture, and murine tumor models. Thus, this group of molecules in combination with ICB therapy offers a promising advance in cancer immunotherapy treatments.