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**Immunosuppressive CD29+ Treg accumulation in the liver in mice on checkpoint inhibitor therapy**

Green B, Myojin Y, Ma C, et al. [Immunosuppressive CD29+ Treg accumulation in the liver in mice on checkpoint inhibitor therapy.](https://gut.bmj.com/content/73/3/509) Gut 2024; 73: 509-520. doi: 10.1136/gutjnl-2023-330024.

The development of immune checkpoint inhibitors (ICI) has led to improvements in survival from many cancers. ICI work by disinhibiting the immune system to attack cancerous cells. However, liver tumours both primary and metastatic respond poorly to ICI. Regulatory T cells (Tregs) are implicated in this. The presence of intra-tumoural Tregs inversely correlates with survival from both primary and metastatic cancer in the liver but the mechanism of resistance is not understood.

Green et al., used mouse models of metastatic cancer to investigate the role of Tregs in the response to ICI. They compared mice injected with tumour cells subcutaneously and intra-hepatically and found that although ICI were able to inhibit growth of subcutaneous tumours, there was no response for intra-hepatic tumours. Flow cytometry was used to characterise the immune cells in the liver, and they found an increase in Tregs in resistant tumours. Depletion of Tregs was able to rescue the anti-tumour effect of anti-PD-1 (Programmed cell death protein 1) treatment.

To define the Treg subpopulation most responsive anti-PD-1 therapy they used single cell RNA sequencing. This identified a new Treg population which were CD29+ that actively proliferate in response to anti-PD-1 therapy. CD29 expression was found to be correlated with Ki-67 (Antigen Kiel 67) positivity a cell proliferation marker. In vitro suppression assays demonstrated that this liver specific Treg subset has enhanced suppressive capacity and Green et al., proposed that this as the mechanism for ICI-resistance.

Green et al., concluded that CD29 may be used as a biomarker to predict response of a tumour to ICI and suggested the development of CD29-targeting agents as a means of overcoming Treg-mediated ICI resistance in liver tumours.