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**Roseburia intestinalis: a new venue in immunotherapy landscape for colorectal cancer - Kang X, Liu C, Ding Y, et al.**

Kang X, Liu C, Ding Y, et al.[*Roseburia intestinalis generated butyrate boosts anti-PD-1 efficacy in colorectal cancer by activating cytotoxic CD8+T cells.*](https://gut.bmj.com/content/72/11/2112) Gut 2023; 72: 2112-2122. doi: 10.1136/gutjnl-2023-330291

Colorectal cancer (CRC) is a major cause of cancer-related mortality worldwide. Although immunotherapy has revolutionised the treatment landscape of several cancers, the benefit in CRC is limited to patients with microsatellite instability (MSI)-high subtype, which has been shown to be responsive to immune checkpoint inhibitors such as programmed cell death protein 1 (PD-1) inhibitor. The major challenge lies in the fact that most CRC tumours (~85%) are microsatellite stable (MSS) and considered to be “immune-cold”. Gut microbiome-mediated immunomodulation could be leveraged to enhance the efficacy of immunotherapy for CRC.

Kang et al., studied the role of probiotic species, Roseburia intestinalis (R. intestinalis), in colorectal tumourigenesis and immunotherapy by using multiple mouse models. R. intestinalis was found to be significantly depleted in patients with CRC compared with healthy controls. The administration of R. intestinalis was shown to inhibit tumour formation and restore gut barrier function. While MSS-type CRC models were resistant to anti-PD-1 monotherapy, R. intestinalis led to a significant reduction in tumour weight and size in these models.

Additionally, the combination of R. intestinalis with anti-PD1 synergised the anti-tumour effects of R.  intestinalis in MSS-type tumours. This tumour-suppressive function was found to be mainly mediated through butyrate; a metabolite produced by R. intestinalis. They suppressed tumour growth by inducing cytotoxic granzyme B+, interferon (IFN)-γ+ and tumour necrosis factor (TNF)-α CD8+ T cells in MSI-high and MSS CRC mouse models.  Mechanistically, butyrate directly induced the activity of CD8+ T cells by binding to toll-like receptor 5 (TLR5) and activating nuclear factor kappa B (NF-κB) signalling.

This study sheds light on the role of R. intestinalis as a potential adjuvant therapy to augment treatment efficacy in CRC, especially in patients with anti-PD1 therapy resistance.