to a lesser degree, from endothelial cells. Given the low death rate of cardiomyocytes, the authors explored how cMacs obtain materials from these cells. They detected cardiomyocyte-derived subcellular particles (~3.5 μm in diameter and ~31 μm³ in volume), which they named ‘exophers’, and showed that ~40% of these were in contact with or inside cMacs. Transmission electron microscopy revealed that extracellular exophers contain mitochondria and fragments of sarcomeres. Of note, exopher-like structures were also detected in human cardiac tissue.

Further experiments indicated that cardiomyocytes use autophagy specifically promoted the development of mucosal T helper 1 (T₃,1) cells and CD8 T-bet T cells, but ICB therapy was required in addition to the bacterium to boost T cell effector function.

ICB therapy alters gut barrier integrity and therefore may allow translocation of bacteria or their products into the blood. In keeping with this hypothesis, serum from anti-CTLA4-treated B. pseudolongum-colonized mice, but not serum from anti-CTLA4-treated GF mice or mice colonized with control bacteria, was sufficient to reduce tumour growth and elicit strong antitumour immunity in GF mice. A network of macrophages supports mitochondrial homeostasis in the heart. Cell https://doi.org/10.1016/cell.2020.08.011 (2020)

An analysis of human serum samples revealed an abundance of the metabolite inosine, and its degradation products, in B. pseudolongum-colonized mice compared with controls. Although previous studies have described an immunosuppressive role for inosine, Magor et al. showed that inosine could enhance T₃₁ cell activation in vitro. This effect depended on signalling through its receptor adenosine 2A receptor (A2AR). Indeed, the use of Rag1-deficient mice reconstituted with A2AR-deficient T cells showed that the ICB-enhancing activity of B. pseudolongum required T cell expression of A2AR. And studies involving in vivo depletion of conventional dendritic cells indicated a requirement for these cells (mediating antigen presentation, IL-12 production and T cell stimulation) in the response to ICB–bacteria co-therapy.

Importantly, oral or systemic administration of inosine led to reduced tumour size and increased antitumour immunity when given to tumour-bearing mice together with anti-CTLA4 and CpG as a costimulus. Inosine was effective even in mice with a diverse microbiota and in other tumour models.

These data suggest that this previously unknown immune-boosting metabolite may be useful for the development of microorganism-based adjuvant therapies.

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