Abstract

Many studies show the ability of gut microbes to modulate the anti-tumour immune response by direct triggering the immune cells or by bacterial metabolites. Interestingly bacteria may even migrate to the tumour tissue and orchestrate the immune response on site. These anti-tumour effects can be improved by the administration of immune checkpoint inhibitors (ICI). Notably, some microbial effects occur only in the presence of ICI. On the contrary, microbiota may also promote tumour growth and negatively impact the effects of ICI therapy.

We have disrupted the gut microbiota homeostasis by antibiotics (ATB) to study the effects of gut microbiota on the ICI. This disturbance led surprisingly to reduced tumour growth and enhanced pro-inflammatory immune response not only in the gut but also within the tumour tissue, where especially IFN-γ orchestrated the anti-tumour immune response.

Importantly the anti-tumour immune response could be transferred through colonisation of germ-free mice by ATB-changed gut microbiota if concomitantly anti-programmed cell death protein 1 (αPD-1) monoclonal antibody was administrated. These mice had elevated levels of segmented filamentous bacteria (SFB), which induced systemic immune response with increased expression of IL-17 and elevated amounts of Th 17 cells, resulting in decreased tumour growth. In conclusion, this master thesis indicates the potential of gut microbiota to modulate the anti-tumour immune response and even the responsiveness to ICI.

Key words: gut microbiota, tumour, immune checkpoint inhibitors, anti-PD-1, anti-tumour immune response, colonisation, microbiota transfer, antibiotics