1329 THE USE OF NOVEL MICROBIAL-BASED THERAPEUTICS IN THE TREATMENT OF CANCER

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Background Accumulating evidence has emerged highlighting the importance of the gut microbiota in relation to cancers distant from the gastro-intestinal tract.[1 2] Certain members of the gut microbiota, such as strains belonging to the genus *Bifidobacterium* and *Lacticaseibacillus*, have been shown to modulate host-immune responses as well as synergising with immune checkpoint inhibitor therapy.[3] In addition, loss of these protective species through antibiotic-induced disturbances accelerated breast tumour growth in murine models.[4] Research conducted in the Robinson lab has focused on manipulating the gut microbiota using a newly discovered live biotherapeutic product (LBP) to improve cancer outcomes.

Methods and Results In various orthotopic mouse models of breast cancer (BRPKp110, PyMT-BO1, and 4T1), the administration of a specific microbial strain has been found to reduce primary tumour growth compared to control (PBS-treated) mice. Long-term administration of the microbial strain also significantly delayed tumour onset time and overall tumour burden in a genetically engineered spontaneous murine breast cancer model (MMTV-PyMT). Flow cytometric analysis of tumours has shown increased infiltration and activity of CD8+ T cells as well as increased polarisation to a $CD44^{hi}CD62L^{lo}$ CD8+ memory T cell subset in the blood after LBP-supplementation, suggesting the induction of systemic immunological memory.

We have also shown that the therapeutic potential of this microbial strain is not limited to administration of the live bacteria. Previous work demonstrated that intravenous administration of purified bacterial extracellular vesicles (BEVs) significantly reduced melanoma tumour volumes in a B16-F10 mouse model. Observed immunomodulatory properties of BEVs include strong activation of toll-like receptor (TLR)-2 (as determined by TLR-2 reporter HEK293 cells) as well as increased infiltration of tumour-associated neutrophils *in vivo*.

Conclusions Utilising specific members of the microbiota and microbial-derived extracellular vesicles to adapt host-tumour immune responses could offer a novel approach to accompany conventional cancer treatments. Future work to assess efficacy in humans, who display large inter-individual microbiome variation, is integral for future development.

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Ethics Approval All animal experiments were performed in accordance with UK Home Office regulations and the European Legal Framework for the Protection of Animals used for Scientific Purposes (European Directive 86/609/EEC).

http://dx.doi.org/10.1136/jitc-2023-SITC2023.1329