patients. Parental formulation is expensive during transportation and storage and inconvenient for patients. The goal of this project is to develop oral cancer-specific bacteria-based immunotherapy to address the unmet needs of parental immunotherapy.

Materials and Methods Bacteria are bio-engineered to specifically target cancers after oral administration. Bacteria are further bio-engineered to deliver an ICI, cytokine and other diagnostic and therapeutic agents. Mice carrying syngeneic bladder cancers and patient-derived bladder cancer xenografts as well as transgenic mice with spontaneous bladder cancer were used to determine the anti-cancer efficacy and perform molecular correlative studies.

Results After oral administration, bioengineered bladder cancer-specific bacteria (BCSB) are delivered to bladder cancer tumors. On average, BCSB in subcutaneous tumors was 4,469 times (median: 777, ranging from 35 to 46,360 times) higher than the colonies in vital organs, including the heart, lung, liver, spleen, and kidney at 48 and 72 hours after oral administration. In SV40T/Ras double transgenic mice with spontaneous bladder cancer, cancer-specific delivery to the bladder cancer is between 33,793 to 205,172 times that of the normal bladder. BCSB can induce macrophage M1 differentiation in tumors, deliver chemokine CXCL11 and induce CD8 T cell infiltration to tumors. Using a chimeric anti-PD1-green fluorescent protein, the expression of anti-PD1 protein is confirmed within tumors starting at 24 hours after oral administration and peaked at 72 and 96 hours. Oral BCSB carrying an anti-PD1 protein is at least as effective as anti-PD1 antibody through intraperitoneal injection.

Conclusions We have developed an oral cancer-specific platform for cancer immunotherapy. After oral administration, BCSB confers cancer-specific delivery, alters tumor microenvironment and can potentially be developed for cancer immunotherapy in humans.

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Plenary session 9: Immuno-monitoring

09.03 CHARACTERIZATION OF T CELL SPECIFICITY AND EXERCISE-INDUCED DYNAMICS OF SOLUBLE IMMUNOLOGICAL MARKERS BEFORE AND AFTER HIGH-INTENSITY AEROBIC EXERCISE (INHALE)

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Background Exercise enhances immune surveillance and prevents the development and recurrence of several cancers. It has been well studied that acute exercise induces mobilization of lymphocytes into the peripheral blood, predominantly comprising of NK cells and antigen-experienced T cells.[1] However, the mechanisms underlying these clinical benefits are still unclear. The antigen specificity of exercise-mobilized T cells,[2] and the associated secreted markers have only recently attracted research attention.[3 4] Thus, this study aims to comprehensively understand the characteristics of exercise-mobilized T cells at a mechanistic level, which is highly needed to optimize the effects of exercise in cancer patients.

Materials and Methods 23 healthy participants enrolled in our INHALE study (NCT05826496, Capital Region's Ethics Committee approval H-23006672) underwent a single session of supervised high-intensity exercise on bicycle ergometers in May 2023, with peripheral blood samples collected before exercise (bsl), at 2 minutes post-exercise (ex02), and 60 minutes post-exercise (ex60).

Results The mean age of our cohort was 37 years, with a mean BMI of 23,37 kg/m^2 and a physical activity level of 3585 MET-min/wk assessed by IPAQ-SF. The participants completed the high-intensity exercise session at a mean of 96,4% of their maximal heart rate and 118,1% of the maximal power on VO_2 max test, respectively. We observe a strong mobilization of NK, T and B cells at ex02, which correlates strongly with adrenaline levels. All cell subsets fall below baseline counts at ex60. Exercise-mobilized CD8$^+$ T cells show a higher proportion effector memory and terminally differentiated effector memory (TEMRA) T cells, in line with higher frequencies of CD57$^+$, CD95$^+$ and PD-1$^+$ CD8$^+$ T cells post-exercise. To assess the dynamics of T cell specificity against a panel of common viral epitopes following high-intensity exercise, we conducted a DNA-barcoded peptide-MHC multimer assay; the data will be presented at ITOC 2024.

Conclusions The INHALE study provides valuable data from a relatively large cohort of 23 healthy participants on the effects of exercise specifically in the T cell compartment. In addition, this investigation serves as an important physiological reference for our ongoing clinical exercise study in NSCLC patients (HI AIM). Prospectively, understanding exercise-triggered circulating tumor-associated antigen-specific T cells may be used to enhance the anti-tumor immune response. This work is funded by the German Research Foundation (DFG) - project number 505368854.

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