Abstract IDDF2021-ABS-0166 Figure 1

Abstract IDDF2021-ABS-0166 Figure 2

modulation of the gut microbiota composition, induction of oncogenic and pro-inflammatory factors and impairment of epithelial barrier. This study provides new insight into obesity-promoting colorectal carcinogenesis, at least in part by causing gut microbiome dysbiosis.

IDDF2021-ABS-0178 ASSOCIATION OF COFFEE INTAKE WITH REDUCED CANCER-RELATED MORTALITY AMONG DIAGNOSED PATIENTS WITH COLORECTAL CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background Colorectal cancer (CRC) is the third most common cancer and the fourth most common cause of cancer mortality globally. Recent advances have in diagnostic and treatment options have reduced CRC-related mortality. Coffee consumption has been studied to decrease mortality in colon, liver and pancreatic cancer.

Methods A comprehensive, computerized literature search from the electronic database of MEDLINE, Google Scholar, Cochrane Library and OVID was performed with the following search terms: colorectal cancer, coffee, and mortality. Three cohort studies were selected and validated using the Newcastle-Ottawa criteria. Multivariate results were combined under a random-effects model using pooled adjusted hazards ratio (HR). The Cochrane Review Manager Software version 5.4 was used for all analyses.

Results Three cohort studies comprising of 3723 patients were analyzed by pooling adjusted hazards ratio using the random-effects model. Coffee consumption was beneficial in reducing cancer-related mortality among CRC patients. Consumption of four or more cups of coffee per day resulted in a decrease in CRC-related mortality (RR 0.59, 95% CI 0.46-0.76, $I^2 = 0\%$) (IDDF2021-ABS-0178 Figure 1. Forest Plots - Four or More Cups of Coffee Per Day vs Non-Coffee Drinkers). Consumption of 2-3 cups per day was showed to also reduce cancer-related mortality among colorectal cancer patients (RR 0.77, 95% CI 0.66-0.91, $I^2 = 0\%$) (IDDF2021-ABS-0178 Figure 2. Forest Plots - Two to Three Cups of Coffee Per Day vs Non-Coffee Drinkers).

Conclusions Coffee consumption is beneficial in reducing cancer-related mortality among diagnosed patients with CRC.

Abstract IDDF2021-ABS-0178 Figure 1 Four or more cups of coffee per day vs non-coffee drinkers

Abstract IDDF2021-ABS-0178 Figure 2 Two or three cups of coffee per day vs non-coffee drinkers

Abstract IDDF2021-ABS-0183 Figure 1

IDDF2021-ABS-0183

SLC25A22 DRIVES IMMUNE SUPPRESSION IN KRAS-MUTANT COLORECTAL CANCER

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Background Direct targeting of KRAS is challenging and represents an unmet need. We identified SLC25A22, a mitochondrial glutamate transporter, as a potential therapeutic target in KRAS mutant colorectal cancer (CRC). In this study, we reveal that SLC25A22 underlies mutant KRAS-induced immune suppression in CRC.

Methods Immune cell infiltration was determined by flow cytometry. The immunosuppressive effect and migration of MDSC were estimated by T cell suppression assay and transwell assay, respectively.

Results Tumors from *Apc^{Min/+} Kras^{G12D} Villin-Cre* mice demonstrated marked infiltration in immunosuppressive myeloid-derived suppressor cells (MDSC) ($P < 0.001$), but reduced T-cells ($CD4^{+}/CD8^{+}$) ($P < 0.05$) (IDDF2021-ABS-0183 Figure 1. *Kras*-mutated tumors exhibit an immune-suppressive microenvironment). Tumor organoids derived from *Apc^{Min/+} Kras^{G12D} Villin-Cre* with or without SLC25A22 were injected into C57 mice. SLC25A22 knockout severely impaired tumor growth, with reduced MDSC ($P < 0.05$) but increased $CD4^{+}/CD8^{+}$ T-cells ($P < 0.05$, $P < 0.01$). Consistent data were obtained from the syngeneic mouse models of murine CRC cell lines with *Slc25a22* knockout. And there was a negative correlation between the percentage of MDSC and that of $CD8^{+}$ T-cells in the xenograft tumour tissues ($R^2 = 0.592$, $P < 0.001$). Indeed, T cell proliferation was impaired after being co-cultured with MDSC in Vitro. These results suggested that knockout of *Slc25a22* reversed mutant KRAS-driven immune suppression, especially reduced the immunosuppressive MDSC infiltration (IDDF2021-ABS-0183 Figure 2. SLC25A22 knockout impaired tumor growth and reversed mutant KRAS-driven immune suppression in syngeneic mice, IDDF2021-ABS-0183 Figure 3. SLC25A22 knockout impaired tumor growth and reversed mutant KRAS-driven immune suppression in syngeneic mice).