Faecal microbiome as determinant of the effect of diet on colorectal-cancer risk: comparison of red meat based versus pesco-vegetarian diets in rodent models.

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Background:

Colorectal cancer (CRC) is the third cause of cancer related death worldwide. The geographical variation of incidence demonstrates how environmental factors, as dietary habits, play a major role in CRC. The study is focused on the role of microbiome profile and relative metabolites on CRC risk to determine whether reduced intake of red/processed meat can reduce the level of toxic metabolites.

Methods and Results:

We compared in two colon carcinogenesis animals' models (Azoxymethane induced carcinogenesis; Pirc rats mutated in *Apc* gene) a high-risk meat-based diet (MBD) with a lower CRC risk pesco-vegetarian diet (PVD). An additional arm is a MBD diet supplemented with tocopherol (MBD-T), possibly mitigating the risk. In all animal model we found a diverse microbial community among the three diets where some genera showed the strongest inverse relation to neoplastic lesions. Performing fecal-microbiota transplant from Pirc rats into germ–free rats in which carcinogenesis was induced with Azoxymethane, we demonstrated that fecal microbiome with specific metabolomics profile were able to transmit cancer risk: rats transplanted with the MBD feces, had a significantly higher number of preneoplastic lesions related with specific microbial and metabolomic profiles.

Conclusions and Significance:

Our results thus demonstrate how the diet can modulate the gut microbiota composition and how the gut microbiota can influence the risk of colorectal cancer in different animal models of carcinogenesis.

Keywords:

Gut Microbiome; Metabolomics; Diet; Pesco-vegetarian diet; Colorectal cancer.

References:

1. **Vitali F**, Tortora K, Di Paola M, Bartolucci G, Menicatti M, **De Filippo C, Caderni G.** Intestinal microbiota profiles in a genetic model of colon tumorigenesis correlates with colon cancer biomarkers. *Sci Rep*. 2022 Jan 26;12(1):1432.
2. Sofi F, Dinu M, Pagliai G, **Pierre F, Gueraud F, Bowman J, Gerard P**, Longo V, Giovannelli L**, Caderni G, De Filippo C**. Fecal microbiome as determinant of the effect of diet on colorectal cancer risk: comparison of meat-based versus pesco-vegetarian diets (the MeaTIc study). *Trials*. 2019;20(1):688.
3. Caini S, **Chioccioli S**, Pastore E, Fontana M, Tortora K, **Caderni G**, Masala G. Fish Consumption and Colorectal Cancer Risk: Meta-Analysis of Prospective Epidemiological Studies and Review of Evidence from Animal Studies. *Cancers* (Basel). 2022 Jan 27;14(3):640.
4. Martin OCB, Olier M, Ellero-Simatos S, Naud N, Dupuy J, Huc L, Taché S, Graillot V, Levêque M, Bézirard V, Héliès-Toussaint C, Estrada FBY, Tondereau V, Lippi Y, Naylies C, Peyriga L, Canlet C, Davila AM, Blachier F, Ferrier L, Boutet-Robinet E, **Guéraud F**, Théodorou V, **Pierre FHF**. Haem iron reshapes colonic luminal environment: impact on mucosal homeostasis and microbiome through aldehyde formation. *Microbiome.* 2019 May 6;7(1):72.
5. **De Filippo C**, Cavalieri D, Di Paola M, Ramazzotti M, Poullet JB, Massart S, Collini S, Pieraccini G, Lionetti P. Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa. *Proceedings of the National Academy of Sciences USA*. 2010, 107(33):14691-6.

Listed are the five more relevant publications from the Authors participating to the study.
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Thematic Area:

- Frontiers in Microbiome Research
- Microbiome: from Research to Clinics

Infrastructures:

N.A.