Supplementary Material

**The Complex Puzzle of Interactions among Functional Food, Gut Microbiota and Colorectal Cancer**

Lígia Aurélio Bezerra Maranhão Mendonça\*1, Rosângela dos Santos Ferreira 2\*, Rita de Cássia Avellaneda Guimarães 2, Alinne Pereira de Castro1, Octávio Luiz Franco1,3, Rosemary Matias4,5, Cristiano Marcelo Espinola Carvalho1,5

**\* Correspondence:** Lígia Aurélio Bezerra Maranhão Mendonça lmendoncanutri@gmail.com

# 1 Supplementary Table 2

**Table 2.** Functional foods, BFC constituents, used in the treatment of CRC

|  |
| --- |
| **Biological assay** |
| * **Functional Food**
 | * **Bioactive Substance**
 | **Probable bioactive effect** | **Population** | * **Ref.**
 |
| Flaxseed | * Polyunsaturated fatty acid (n-3)
 | Inhibition of angiogenesis caused by CRC | Nude (nu/nu) | * [95]
 |
| * Increased expression of FFAR4 in colon
 | Sprague–Dawley rats | * [96]
 |
| Phytic AcidInositol Hexaphosphate (IP6) | Inhibition of development of metastatic progression of CRC | BALB/c(n = 48) | * [97]
 |
| Lignan | Decreased proliferation and increased apoptosis of tumor cells - CRC | * Caco-2 colon cancer cells
 | * [98]
 |
| Oat | *β* glucan | Prevention of CRC | * Kunming Mice
 | * [92]
 |
| Phenolic amides (Avenanthramides) | Reducing the risk of CRC | Caco-2 and HT29 colon cancer cells | * [99]
 |
| Induction of apoptosis of colon cells | HCT-116 human colon cancer cells | [7] |
| Soy | Isoflavone (Genistein and daidzein) | Suppression of colon cancer growth | Sprague–Dawley rats | * [100]
 |
| * Reducing the risk of CRC - Anti-cancer
 | Women(n = 68.412) | * [101]
 |
| * Patients with CRC (n = 901)
 | * [102]
 |
| * Patients with CRC (n = 101)
 | * [93]
 |
| **Reviews and Other Studies** |
| * **Functional Food**
 | * **Bioactive Substance**
 | **Probable bioactive effect** | * **Ref.**
 |
| Flaxseed | * Polyunsaturated fatty acid (n-3)
 | Blocks tumor formation | * [103]
 |
| Deregulates the expression of genes involved in the CRC and alters the membrane lipid composition of tumor cells.Reduction of proliferation and induction of apoptosis. | * [104]
 |
| IP6 | Inhibition of the metastatic process in CRC | * [96]
 |
| Lignanas* (Secossolariciresinol diglucoside)
 | Reduction of proliferation and induction of tumor cell apoptosis | * [103]
 |
| Modulates cellular signaling pathways | * [105]
 |
| Antiproliferative and anti-angiogenesis protection | * [106]
 |
| Phenolic amides (Avenanthramides) | Reducing the risk of CRC | * [107]
 |
| Oat | *β* Glucan | Formation of short chain fatty acids (SCFA) that decrease intra-colonic pH, inhibiting pathogenic and toxic proliferation (Figure 2) | * [108]
 |
| Soy | Isoflavone (Genistein and daidzein) | Inhibit cell proliferation and induce apoptosis; Decrease GLI1 expression | * [109] [110]
 |
| Inhibition of MMP-9 (Matrix metallopeptidase 9) responsible for tumor progression | * [111]
 |
| Saponins | Inhibition of MMP-9 and gelatinase B, responsible for tumor progression | * [111]
 |