

## Mediterranean Diet-Driven Changes in Gut Microbiota Decrease the Infiltration of Inflammatory Myeloid Cells into the Intestinal Tissue

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**Abstract :** Obesity is a high-priority health problem worldwide due to its high prevalence. The proportion of obese and overweight subjects in industrialized countries exceeds half of the population in most cases. Beyond the metabolic problem, obesity boosts inflammation levels in the organism. The gut microbiota, considered an organ by itself, controls a high variety of processes at a systemic level. In fact, the microbiota interacts closely with the immune system, being crucial in determining the maturation state of neutrophils, key effectors of the innate immune response. It is known that changes in the diet exert strong effects on the variety and activity of the gut microbiota. The effect that those changes have on the axis microbiota-immune response is an unexplored field. In this study, 10 patients with obesity (weight  $114,3 \pm 14,5$  Kg, BMI  $40,47 \pm 3,66$ ) followed a Mediterranean-hypocaloric diet for 3 months, reducing their initial weight by  $12,71 \pm 3\%$ . A transplant of microbiota from these patients before and after the diet was performed into wild type "germ-free" mice (n=10/group), treated with antibiotics. Six weeks after the transplant, mice were euthanized, and the presence of cells from the innate immune system were analysed in different organs (bone marrow, blood, spleen, visceral adipose tissue, and intestine) by flow cytometry. No differences were observed in the number of myeloid cells in bone marrow, blood, spleen, or visceral adipose tissue of mice transplanted with patient's microbiota before and after following the Mediterranean diet. However, the intestine of mice that received post-diet microbiota presented a marked decrease in the number of neutrophils (whose presence is associated with tissue inflammation), as well as macrophages. In line with these findings, intestine monocytes from mice with post-diet microbiota showed a less inflammatory profile (lower Ly6G<sup>low</sup> proportion of cells). These results point toward a decrease in the inflammatory state of the intestinal tissue, derived from changes in the gut microbiota, which occurred after a 3-month Mediterranean diet.

**Keywords :** obesity, nutrition, Mediterranean diet, gut microbiota, immune system

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