

Dietary intervention with probiotics and muscadine grape extract shifts western diet-associated metabolic, microbial, and inflammatory parameters to reduce breast tumor growth

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Abstract

Background Western diet (WD) consumption is associated with increased risk and poor prognosis for breast cancer due to altered inflammation, metabolism, and microbial colonization. This study will determine whether intervention with probiotics (prbx) and muscadine grape extract (MGE) reduces WD-induced breast cancer risk factors.

Methods Female C57BL/6 mice were fed either control diet (CD) or WD (45% fat and 25% sugar) and randomized into six groups per diet: diet alone, antibiotics (abx), prbx, MGE, MGE + abx, and MGE + prbx (n=8). Prbx groups received 1×10^5 CFU of a 10-strain probiotic 3x weekly. MGE (0.1 phenolics/mL) and abx (5 mg/mL streptomycin, 1 mg/mL ampicillin, 1 mg/mL colistin) were administered in drinking water. Female BALB/c mice consuming either CD or WD, were injected with 1.0×10^6 4T1 triple negative breast cancer cells into the R4/5 mammary fat pad. Tumors progressed to 100 mm³ prior to treatment with MGE, prbx, or combined MGE + prbx. Size was monitored with calipers for 21 days.

Results MGE + prbx administration in WD-fed mice resulted in reduced body weight. All intervention groups displayed reduced visceral adiposity and mammary gland weight compared to WD-fed mice. Significant intervention-mediated gut microbial alterations were observed by fecal 16S sequencing and included changes in proportional abundance of *Bacteroidetes*, *Lactococcus*, *Lactobacillus*, and *Bifidobacterium* taxa. Interventions modulated inflammatory markers in the visceral adipose tissue and mammary gland as observed by immunohistochemistry (monocyte chemoattractant protein-1 (MCP-1) and macrophage marker, F4/80). Dietary intervention with MGE, prbx, and MGE + prbx reduced 4T1 tumor growth rate in WD-fed mice, but not in CD-fed mice.

Conclusions Our data suggests that MGE + prbx modulates diet-induced metabolic, inflammatory, and microbial factors. Further analysis of tumor tissue will determine whether MGE + prbx altered the tumor microenvironment to improve WD-associated BC prognosis.

Keywords Dietary intervention, breast cancer, nutraceuticals, probiotics