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Modulation of Inflammatory Gene Expression by Mind-Body Transformations Therapy (MBT-T) in Breast Cancer Patients

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Introduction

Mind-Body Transformations Therapy (MBT-T) is an evidence-based therapeutic protocol designed to harness natural biological rhythms and biological plasticity in order to modulate gene expression (1). By reducing stress-induced dysfunctions, MBT-T facilitates the activation of endogenous healing mechanisms through the establishment of an optimal mind-body state (2-4). In our previous study we demonstrated that MBT-T significantly reduced the serum levels of multiple cytokines and chemokines in breast cancer patients who had completed loco-regional treatment and adjuvant chemotherapy, compared to a matched control group not exposed to MBT-T (5).

To further elucidate the molecular basis of these effects, we conducted a NanoString gene expression analysis on RNA extracted from blood samples collected from participants enrolled in the MBT-T study. This comprehensive analysis allowed us to deepen the transcriptional changes induced by the therapy, providing a detailed snapshot of gene activity related to inflammatory pathways. By examining gene expression profiles before and after MBT-T intervention, we identified specific genes and pathways that are modulated by the therapy. The insights gained from this molecular investigation are crucial for validating MBT-T as a scientifically grounded therapeutic option and for guiding future research directions in mind-body medicine and oncology.

Materials and Methods

MBT-T protocol enrolled 23 breast cancer patients who completed loco-regional treatment and adjuvant chemotherapy, randomized to Arm A (Control, n=7) candidate to a Standard follow-up only, and Arm B (Experimental, n=16) Standard follow-up plus biweekly MBT-T psychological intervention for 4 months. Blood samples were collected at five time points: before treatment (T0), 1 hour after the first session (T1), after 2 months (T2) at the end of treatment (T3) and 2 months post-(Tt) and related total RNA was extracted. Gene expression change was evaluated by analyzing the nCounter® Human Inflammation Panel, comprising 249 genes implicated in inflammatory and immune-related pathways, at the end of the treatment (Tt) compared to baseline (T0). Matched timepoints were also analyzed in control patients.

Results

MBT-T Induces a Significant Reduction of Inflammatory Gene Expression

Figure 1

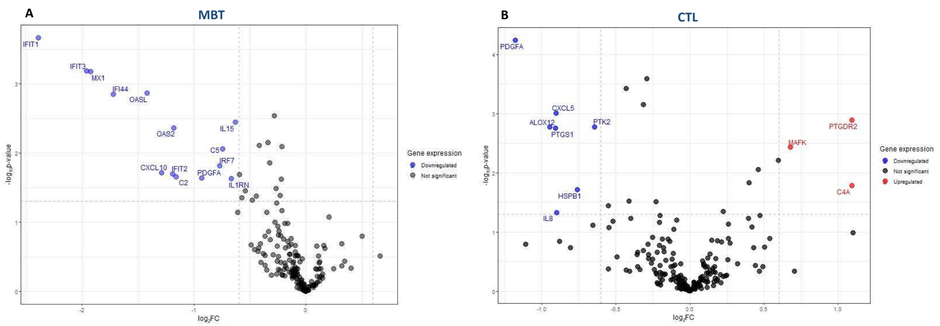


Table 1

Gene-mRNA	Log2foldchange	Std err log2	p-value	Bh p-value	pathway
IFIT1	-2.39	0.5350	**0.000215**	0.0393	Interferon Signaling
IFIT3	-1.96	0.4910	**0.000653**	0.0403	Interferon Signaling
MX1	-1.92	0.4800	**0.000661**	0.0403	Interferon Signaling
OASL	-1.42	0.3840	**0.001360**	0.0518	Interferon Signaling
IFI44	-1.72	0.4690	**0.001410**	0.0518	Interferon Signaling
IL15	-0.63	0.1920	**0.003570**	0.0933	Interleukin-2 family signaling
OAS2	-1.18	0.3690	**0.004280**	0.0979	Interferon Signaling
C5	-0.74	0.2580	**0.008750**	0.1330	Complement cascade
IRF7	-0.77	0.2920	**0.015100**	0.1970	DDX58/IFIH1-mediated induction of interferon-alphabeta, Interferon Signaling
CXCL10	-1.29	0.5060	**0.019000**	0.2090	
IFIT2	-1.19	0.4730	**0.020000**	0.2090	Interferon Signaling
C2	-1.16	0.4680	**0.021900**	0.2090	
PDGFA	-0.93	0.3800	**0.023000**	0.2090	Extracellular matrix organization, MAPK1MAPK3 signaling
IL1RN	-0.66	0.2720	**0.023400**	0.2090	Interleukin-1 signaling

Table 2

Gene-mRNA	Log2foldchange	Std err log2	p-value	Bh p-value	pathway
PDGFA	-1.180	0.177	**0,000576**	0.0111	Extracellular matrix organization, MAPK1MAPK3 signaling
CXCL5	-0.905	0.197	**0,00988**	0.0373	
PTK2	-0.643	0.151	**0,00161**	0.0373	Apoptosis, MAPK1MAPK3 signaling, Signaling by VEGF
ALOX12	-0.946	0.223	**0,00169**	0.0373	Metabolism
PTGS1	-0.908	0.215	**0,00175**	0.0373	Metabolism
HSPB1	-0.759	0.273	**0,0193**	0.2480	Signaling by VEGF
IL8	-0.901	0.397	**0,0466**	0.4470	
PTGDR2	1.090	0.247	**0,00128**	0.0373	Eicosanoid ligand-binding receptors
MAFK	0.677	0.180	**0,00371**	0.0712	
C4A	1.090	0.378	**0,0164**	0.2250	Complement cascade

Figure 1 A-B show Volcano Plots illustrating the differential gene expression between the end of treatment (Tt) and basal (T0) time points in MBT patients **(A)** and CTL patients **(B)**, respectively. The horizontal line on each plot indicates the False Discovery Rate (FDR) threshold, marking the most highly statistically significant genes that fall at the top. The vertical lines represent the logarithmic fold-change threshold (p-value < 0.05). Significantly differentially expressed genes are colored if their resulting p-value is below the threshold. Tables 1 - 2 list the most statistically significant genes ($p < 0.05$) and their associated functional pathways.

MBT-T Reduces Interferon Signaling

Figure 2

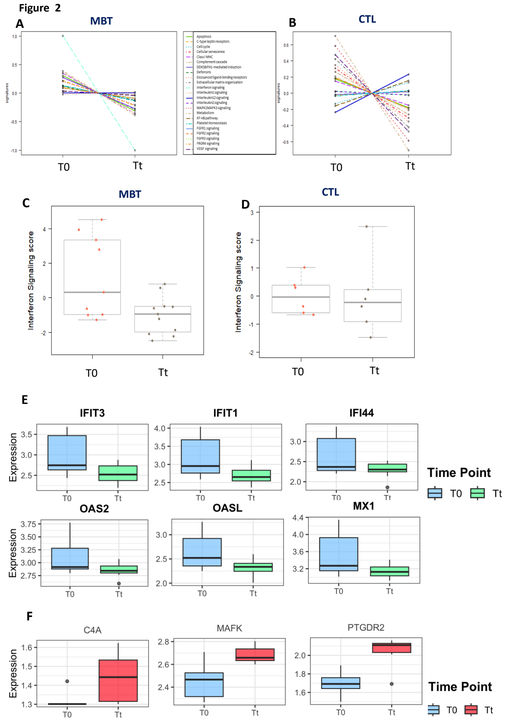
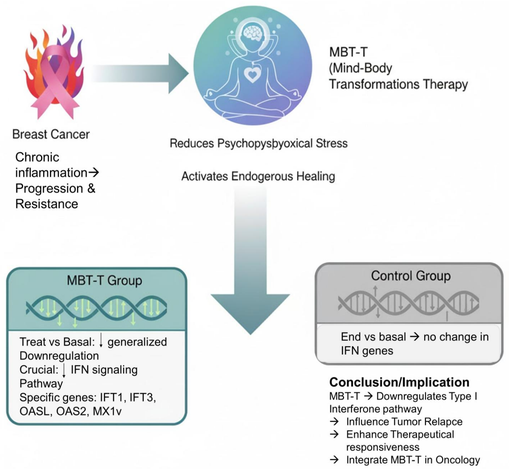


Figure 2 A-B The pathway scores are plotted to show how they vary across different conditions Tt and T0 in MBT (A) and CTL (B) respectively. Lines show each pathway's average score across values. **C-D** Plots Interferon Signaling pathway scores against conditions Tt and T0 in MBT (A) and CTL (B) respectively. **E-F** The box plots show the change in gene expression levels between the basal time point (T0) and the end of treatment (Tt) in MBT (E) and CTL (F) respectively.

Conclusions

MBT-T Modulates Inflammatory Gene Expression by downregulating the interferon signaling pathway



Conclusion/Implication

MBT-T → Downregulates Type I Interferone pathway
- → Influence Tumor Relapce
- → Enhance Therapeutical responsiveness
- → Integrate MBT-T in Oncology

MBT-T specifically induces a generalized down-regulation of gene expression in treated patients, most notably suppressing the Interferon (IFN) Signaling Pathway (e.g., IFIT1, IFIT3, MX1), a change not observed in the control group. These findings are particularly meaningful given the complex role of the IFN pathway within the tumor microenvironment, where it influences immune cell dynamics, tumor cell behavior, and response to therapy. Collectively, our data suggest that MBT-T, through the reduction of psychophysiological stress, can downregulate key inflammatory signaling pathways, particularly those mediated by type I interferons. This modulation may influence tumor progression, reduce the risk of relapse, and enhance therapeutic responsiveness in breast cancer patients. These findings support the integration of mind-body interventions as adjunctive strategies in oncological care, with potential biological impact at the molecular level.

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