

CHEMOTHERAPY-INDUCED FATIGUE INDUCES A SPECIFIC GENE EXPRESSION PROFILE IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF BREAST CANCER PATIENTS RECEIVING ADJUVANT OR NEOADJUVANT CHEMOTHERAPY

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INTRODUCTION

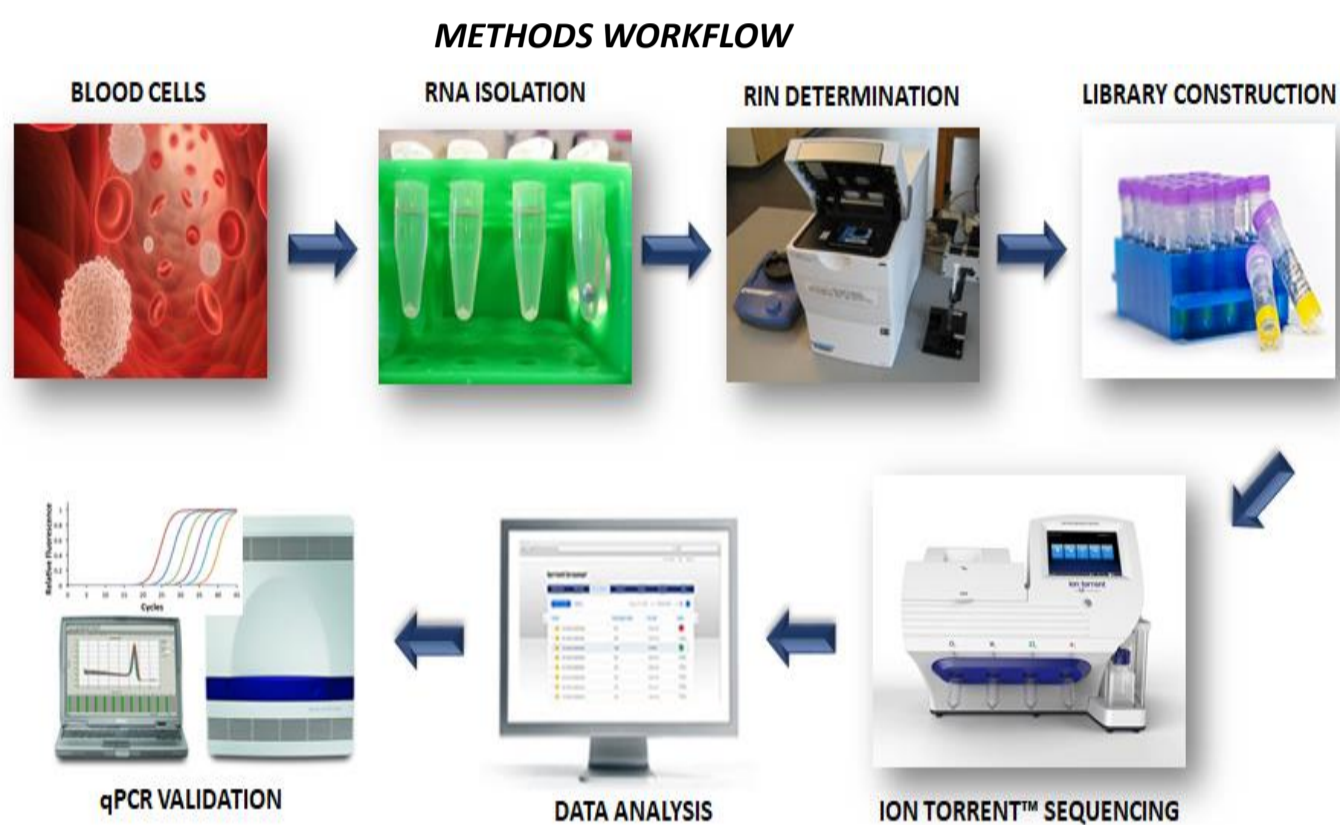
Chemotherapy induced fatigue (CIF) is a frequent and potentially debilitating side effect of chemotherapy that affects approximately 40% of patients and is severe in approximately one-fourth of those affected.¹ In addition to anemia, chemotherapy may induce fatigue through several mechanisms, including stimulation of the inflammatory response mediated by changes in cytokine levels, hormonal deregulation, or muscular toxicity.²⁻³

In this work, we aimed to evaluate whether CIF can induce a specific gene expression profile in peripheral blood mononuclear cells (PBMNC) of patients with locoregional breast cancer (LRBC) who are receiving chemotherapy through RNA-seq analysis.



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PATIENTS AND METHODS

Patients with stage I, II and III breast cancer undergoing adjuvant systemic chemotherapy based on the use of anthracyclines were screened before the start of their treatment. We assessed CIF according to the BFI and Chalder Questionnaires. Total RNA was isolated from blood samples. RNA-seq was performed in an Ion Torrent™ System. The RNA-seq results were validated by RT-qPCR in a different group of 28 patients with LRBC who developed CIF after their first cycle of chemotherapy and in 06 patients who also received chemotherapy but did not develop CIF (controls).

RESULTS

A total of 12,345 transcripts were sequenced, of which 26 were selected out of 71 that had significantly different expression before and after chemotherapy. These 26 genes as well as their expression fold change obtained by RNA-seq and validated by qPCR can be found in Table 1. We observed a significant increase in expression of DUSP18 and RHOTB1 and decreased expression of NCAN and RAET1G in patients who developed CIF after chemotherapy. Control patients only exhibited a significant decrease in NCAN expression.

CONCLUSION

CIF induces specific changes in gene expression in the PBMNC of LRBC patients. Some of these changes, such as down-regulation of NCAN expression, may reflect direct effects of chemotherapy since they are also observed in the controls. Furthermore, CIF may involve down-regulation of skeletal muscle genes (RHOTB1, DUSP18) and immune systems (RAETG1), whereas NCAN down-regulation may underlie the adverse cognitive effects of chemotherapy.

REFERENCES

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Table 1. Genes differentially expressed in CIF

Gene	RNA-seq	qPCR	
		FATIGUE	Control
MRPS11	5,7	16,2	0,84
LPIN1	5,87	14,22	2,98
HTLF	5,96	1,38	53,13
TAF1A	6,10	34,8	629,76
ZNF3	7,53	4,56	2,75
DUSP14	8,52	36,9	1,15
DUSP18	6,52	8,12	0,85
TAF9B	9,20	1,30	1,91
HIP1R	5,65	0,19	1,68
PAICS	6,83	0,83	0,47
NAA30	6,15	1,33	0,39
SFT2D2	7,71	3,57	1,11
GOLM1	7,76	7,4	0,8
SLC37A4	-7,93	0,6	0,03
RHOTB1	7,5	1,7	1,23
BST1	7,5	2,8	1,37
PIK3R4	9,1	1,0	2,29
MS4A6A	8,06	0,44	0,33
CHRNA	-5,3	0,28	0,91
NCAN	-8,1	0,2	0,37
NBPF14	9,57	0,6	1,89
CGB8	-8,5	1,0	1,3
CCL25	-7,21	0,81	0,87
RAET1G	-8,02	0,97	0,82

