

## Abstract

# Exploring the Role of N-WASP in Breast Cancer Metastasis through Mass Spectrometry and Potential Signalling Pathway Analysis <sup>†</sup>

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**Abstract: Background:** Neural Wiskott–Aldrich Syndrome Protein (N-WASP) is a key regulator of the actin cytoskeleton and is implicated in various cellular processes, including cell motility and invasion. In cancer biology, the role of N-WASP in cell motility and metastasis is of particular interest, yet its specific functions in breast cancer remain to be fully understood. **Method:** To investigate the impact of N-WASP on breast cancer cell behaviour, we employed siRNA to knock down N-WASP expression in the MDA-MB-231 breast cancer cell line. After the knockdown, proteomic changes in the cells were analysed using mass spectrometry. Notable alterations in the genes present in both total and phosphorylated proteins were further analysed. **Results:** The proteomic data analysis ranked 50 genes that exhibited the most up-regulation and down-regulation in total and phosphorylated proteins. These 200 genes were further examined using the REACTOME database to identify affected signalling pathways. Knockdown of N-WASP led to significant changes in the RHOD, RHOF, and RHOG GTPase cycles ( $p = 0.015$ ,  $p = 0.01$ , and  $p = 0.027$ ), pathways closely associated with cell motility and actin cytoskeleton organisation. These cycles are crucial in modulating cellular dynamics, impacting a range of processes from immune response to neuronal development, wound healing, and, particularly, cancer metastasis. Furthermore, the findings highlighted the role of non-integrin membrane–ECM interactions in cell motility and cytoskeleton dynamics ( $p = 0.021$ ). The altered protein expression patterns suggest a link between N-WASP, non-integrin membrane–ECM interactions, and the cytoskeletal changes essential for cell migration and invasion—key factors in cancer metastasis. **Conclusions:** Our findings reinforce the critical role of N-WASP in regulating the cytoskeleton and influencing cell motility, invasion, and metastasis in breast cancer. This study not only provides deeper insights into the molecular mechanism of breast cancer progression but also highlights N-WASP as a potential therapeutic target for intervention strategies in breast cancer treatment.

**Keywords:** N-WASP; breast cancer; cytoskeleton; cancer metastasis; cell motility



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