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Title: Neuropilin-1 knockout and rescue confirms its role to promote metastasis in MDA-MB-231 breast cancer cells

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Breast Cancer (BC) metastasis remains a leading cause of female mortality. Neuropilin-1 (NRP-1) is a glycoprotein receptor that plays ligand-dependent roles in BC. Clinical studies indicate its correlation with metastatic disease; however, its functional role in BC metastasis remains uncertain. CRISPR-Cas9 was used to knockout the NRP-1 gene in MDA-MB-231 BC cells and the effects on metastasis were determined using an orthotopic mouse engraftment model. NRP-1 expression in knockout cells was rescued using a recombinant cDNA with a silent mutation in the sgRNA target-adjacent PAM sequence. Differentially expressed genes between NRP-1 knockout and control cells were determined using whole-transcriptome sequencing and validated using real-time PCR. NRP-1KO cells showed a pronounced reduction in the metastasis to the lungs. KEGG pathway analysis of the transcriptome data revealed that PI3K and ECM receptor interactions were among the top altered pathways in the NRP-1KO cells. In addition, reduction in metastasis enhancer's proteins, Integrin-ß3 and Tenascin-C and genes CCL20 and FN1 and up-regulation of metastasis suppressor genes, ACVRL and GPX3 in NRP-1KO were detected. These findings provide evidence for a functional role for NRP-1 in BC metastasis, supporting further exploration of NRP-1 and the identified genes as targets in treating metastatic BC.

Biography

Sirin A Adham Graduated from the University of Leon, Spain, in 2002 with a PhD degree in Biological Sciences/molecular biotechnology. She worked at the Department of Biology, University of Waterloo, Canada as a postdoctoral fellow on a project funded by Genome Canada from 2003-2006. From 2006-2009 she joined the Department of Biomedical Sciences at the University of Guelph, Canada as a Postdoctoral fellow and held the Associate Scientist's title in Cancer Research. In 2010, she joined the Department of Biology, College of Science, SQU, Oman. She was promoted to Associate Professor in May of 2019. Her research is focused on Cancer Molecular Biology to investigate the molecular basis of drug resistance in breast cancer. She has published her research in several highly ranked peer-reviewed international journals and was awarded research funds from SQU, Oman's Research Council (TRC) and the international Terri Fox foundation fund. Finally, she built her cancer research laboratory and supervised PhD and MSc. students at the Department of Biology (SQU).