IQGAP1 is a Specific Target of Haldol in Triple Negative Breast Cancer

Varun Iyer[1], Mahmood Meqdad[1] , Mahasin Osman[1*]

[1]College of Medicine and Life Sciences, 3000 Arlington Avenue, The University of Toledo, Toledo OH 43615

[2*] Corresponding author, Division of Hematology and Oncology, Department of Medicine, 3000 Arlington Avenue, The University of Toledo, Toledo OH 43615

Email: mahasin.osman@utoledo.edu

Received: 2024-08-16

Accepted: 2024-09-16

Published: 2026-06-30

Background: The triple-negative breast cancer (TNBC) is a heterogenous disease lacking hormonal and growth factor receptors, and therapeutic targets. IQGAP1 is a regulatory signaling scaffold identified as an oncoprotein and biomarker in TNBC.

Objective: was to define the mechanism of haloperidol (Haldol) inhibition of IQGAP1 signaling pathway in TNBC Methods: Cell proliferation assays and a drug screen in several TNBC cell lines identified the antipsychotic Haldol as a potential inhibitor (IC50 10-20 μM) of IQGAP1. Mass spectrometry was applied on IQGAP1 immunoprecipitates isolated from Haldol-treated and vehicle control MDA-MB-231 and MDA-MB-468 TNBC cell lines to define potential differences in signaling partners.

Results: Haloperidol inhibited cell proliferation in multiple TNBC cell lines and altered IQGAP1 signaling by modulating its interaction partners differentially in MDA-MB-231 and MDA-MB-468 cells. Untreated cells showed distinct IQGAP1 associations with proteins involved in transcription and protein trafficking, whereas Haldol treatment promoted interactions linked to transcriptional regulation and apoptosis. Additionally, Haldol significantly reduced the overall protein mass in TNBC cells, consistent with its inhibitory effects on cell proliferation.

Conclusion: We identified novel IQGAP1 partners suggesting that Haldol specifically modulate IQGAP1 signaling in cell proliferation and can potentially be re-purposed for personalized treatment of TNBC and other cancers.

Keywords: Breast Cancer, IQGAP1, Haloperidol, Triple Negative Breast Cancer

https://dx.doi.org/10.46570/utjms-2025-1392