Aberrant KIF11 induction is a potential driver of aggressiveness in ER-α positive breast cancer

Yisun Jeong[1,2*], Sun Moon Yang[3*], Sun Young Yoon[1,5], Ji Young You3, Eun-Shin Lee[3], Harim Oh[4], Jongmin Sim[4], Seung Pil Jung[3], Sangmin Kim[1,2], and Jeong Eon Lee[1,2,5]
[1]Department of Breast Cancer Center, [2]Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine,
[3]Department of Surgery, [4]Department of Pathology, Korea University Anam Hospital, [5]Department of Health Sciences and Technology, SAIHST, Sungkyunkwan University, Seoul, Korea.

San Antonio Breast Cancer Symposium
December 9-12, 2025

Abstract

- Kinesin family member 11 (KIF11) is a motor protein for mitotic spindle formation and proper cell division.
- In this study, we investigated the regulation of KIF11 expression and assessed the therapeutic potential of its specific inhibitor, ispinesib, in breast cancer models.
- Analysis of the GSE4922 dataset revealed that estrogen receptor-positive (ER+) breast cancer patients with high KIF11 expression exhibited significantly poorer survival compared to those with low expression. Moreover, KIF11 levels were elevated in lymph node-positive (LN+) patients and those with advanced-stage disease, suggesting its potential role in tumor progression.
- We further found that KIF11 expression was positively correlated with MAPK1 expression and negatively correlated with STAT3 expression. Pharmacological inhibition of MEK1/2 using binimetinib significantly reduced KIF11 expression.
- Finally, we evaluated ispinesib induced G2/M phase arrest and completely inhibited cell growth in ER+ breast cancer cells. These findings support KIF11 as a prognostic marker and potential therapeutic target in ER+ breast cancer.

Introduction

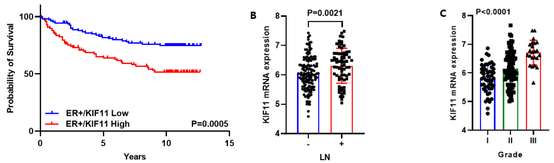
- In ER+ breast cancer, resistance and recurrence remain clinical challenges. Therefore, identifying the regulation of downstream signaling pathways and the discovery of alternative therapeutic targets is essential to improving long-term outcomes in ER+ cancer.
- KIF11, also known as Eg5, is a motor protein critical for mitotic spindle formation and proper cell division. While KIF11 has been implicated in promoting cell proliferation and invasion in various cancer types, its regulatory mechanisms in breast cancer remain poorly understood.
- In this study, we investigated the clinical relevance of KIF11 expression in relation to survival outcomes in ER+ breast cancer patients, as well as its underlying regulatory mechanisms.

Methods and Materials

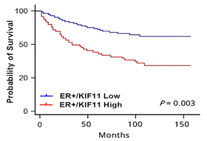
- We examined the regulatory effect of KIF11 on various signaling pathways.
  - Levels of mRNA and protein expression were analyzed by real-time PCR and western blot.
  - Cell proliferation and invasiveness were analyzed by the colony-forming assay
- We analyzed the relationship between KIF11 expression and disease free survival in GSE4922 dataset and 254 ER+ breast cancer patient who were treated in Korea University Anam Hospital.

Results I

- The levels of KIF11 expression is associated with poor prognosis in ER+ breast cancer patients.
  - we analyzed the GSE4922 dataset from the GEO database. As shown in Fig. 1A, ER+ breast cancer patients with high KIF11 expression exhibited significantly lower disease-free survival (DFS, P = 0.005).
  - KIF11 expression was significantly higher in lymph node-positive (LN+) patients compared to LN− patients (P = 0.0021).

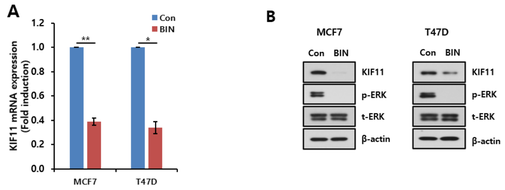


- We collected clinical information from 254 ER+ breast cancer patients and performed immunohistochemical (IHC) staining to assess KIF11 expression on tissue microarray (TMA) slides from Korea university Anam hospital
  - DFS was significantly different between patients with low and high KIF11 expression. The mean DFS was 206.3 months (95% CI, 192.9–219.6) in the KIF11-low group and 159.4 months (95% CI, 135.8–183.0) in the KIF11-high group.



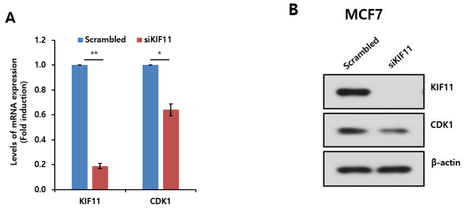
Results II

- KIF11 expression is positively correlated with MAPK1 expression.
  - Treatment with binimetinib, a selective inhibitor of MEK, significantly reduced KIF11 mRNA and protein expression levels in both MCF7 and T47D cells.



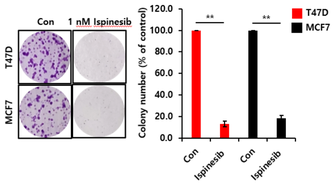
Results III

- KIF11 inhibition causes cell cycle arrest at the G2/M phase in MCF7 cells
  - KIF11 and CDK1 expression levels were reduced following KIF11 siRNA treatment. These results suggest that KIF11 promotes cell proliferation in MCF7 cells, at least in part, through the regulation of CDK1, a key mediator of G2/M phase progression.



Results IV

- A selective KIF11 Inhibitor, ispinesib, suppresses cell growth in ER+ breast cancer cells
  - ispinesib treatment completely inhibited cell growth. Collectively, these findings suggest that targeting KIF11 with ispinesib may represent a promising therapeutic strategy for the treatment of ER+ breast cancer.



Conclusions

- in ER+ breast cancer, high KIF11 levels are associated with reduced disease-free survival, lymph node metastasis, and advanced tumor stages, making it a potential prognostic biomarker.
- This study found a positive correlation between MAPK1 and KIF11 expression. Targeting the MEK/ERK pathway (upstream of MAPK1) with binimetinib decreased KIF11, while CA-MEK1 overexpression increased it.
- KIF11 knockdown led to G2/M phase arrest and decreased CDK1 expression, reinforcing KIF11's role in regulating mitosis and cell cycle progression.
- This study demonstrates that ispinesib treatment induces G2/M arrest and effectively halts cell proliferation in ER+ breast cancer cells, similar to KIF11 knockdown.
- These findings suggest that KIF11 may serve as a prognostic and predictive biomarker and a promising therapeutic target, particularly in endocrine therapy-resistant ER+ breast cancer.

Contact

SeungPil Jung
Division of Breast and Endocrine Surgery, Department of Surgery, Korea University Anam Hospital,
Korea University College of Medicine, Seoul, Republic of Korea
Email: jungspil@korea.ac.kr
Phone:82-10-9045-0083

References

1. Miziak P, Baran M, Blaszczak E, Przybyszewska-Podstawka A, Kalafut J, Smok-Kalwat J, et al. Estrogen Receptor Signaling in Breast Cancer. Cancers (Basel). 2023;15(19).
2. Castillo A, Morse HC, 3rd, Godfrey VL, Naeem R, Justice MJ. Overexpression of Eg5 causes genomic instability and tumor formation in mice. Cancer Res. 2007;67(21):10138-47.
3. Purcell JW, Davis J, Reddy M, Martin S, Samayoa K, Vo H, et al. Activity of the kinesin spindle protein inhibitor ispinesib (SB-715992) in models of breast cancer. Clin Cancer Res. 2010;16(2):566-76
4. Jungwirth G, Yu T, Cao J, Eddine MA, Moustafa M, Warta R, et al. KIF11 inhibitors filanesib and ispinesib inhibit meningioma growth in vitro and in vivo. Cancer Lett. 2021;506:1-10.
5. Klimaszewska-Wisniewska A, Neska-Dlugosz I, Buchholz K, Durslewicz J, Grzanka D, Kasperska A, et al. Prognostic Significance of KIF11 and KIF14 Expression in Pancreatic Adenocarcinoma. Cancers (Basel). 2021;13(12).

This presentation is the intellectual property of the author/presenter. Contact them at jungspil@korea.edu for permission to reprint and/or distribute.

© POSTER TEMPLATE BY GENIGRAPHICS® 1.800.790.4001 WWW.GENIGRAPHICS.COM