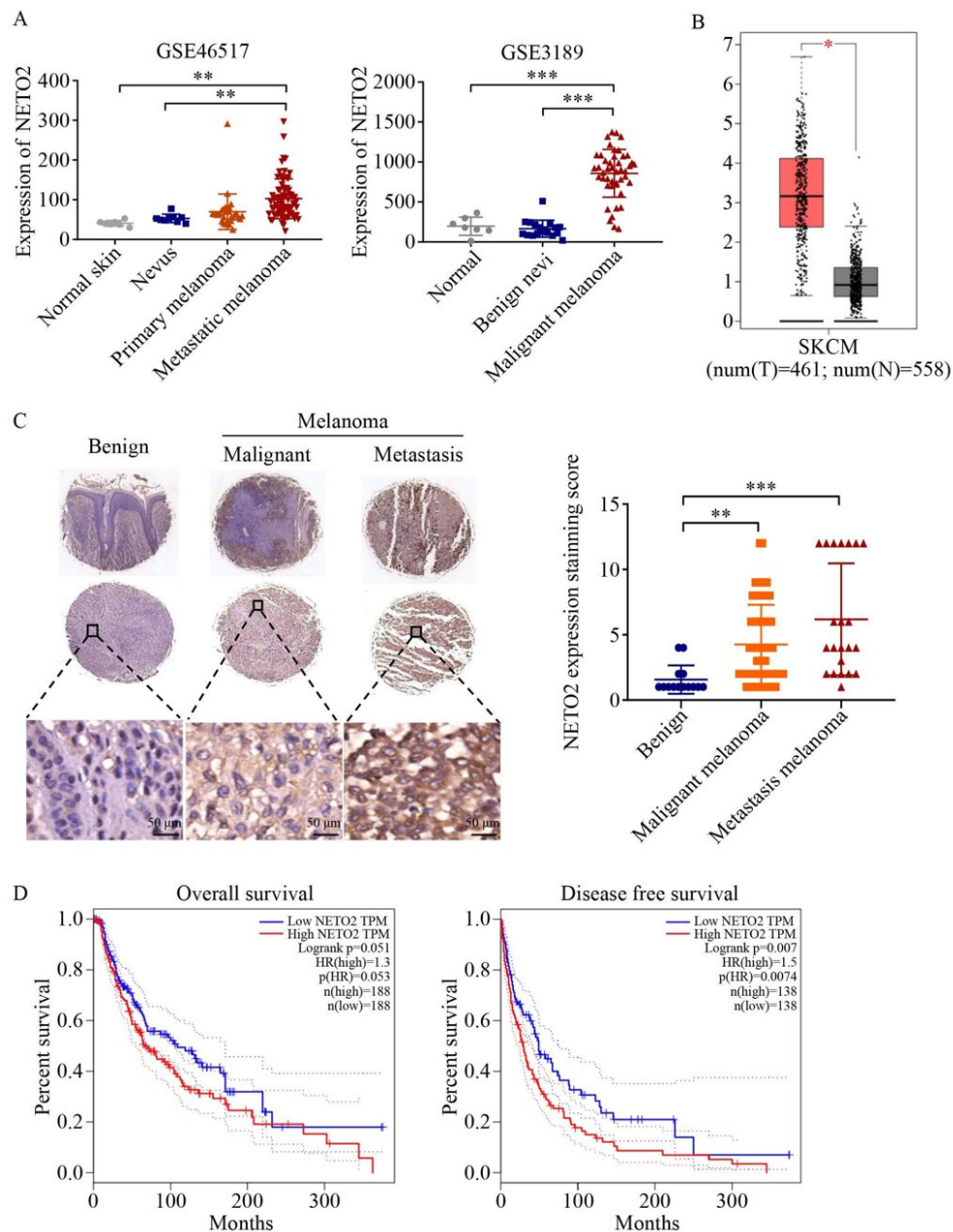


# Study uncovers the role of NETO2-mediated regulation in melanoma progression

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Credit: *Frontiers of Medicine* (2023). DOI: 10.1007/s11684-022-0935-0

Cong Peng and others at the Department of Dermatology, Xiangya Hospital, Central South University, China, conducted a study titled "[NETO2 promotes melanoma progression via activation of the Ca<sup>2+</sup>/CaMKII signaling pathway](#)," which investigated the role of Neuropilin and tolloid-like 2 (NETO2) in melanoma, a deadly form of skin cancer.

The research, published in *Frontiers of Medicine*, explores how NETO2, a membrane protein, influences the progression of melanoma through the Ca<sup>2+</sup>/CaMKII signaling pathway.

The study begins by highlighting the importance of Ca<sup>2+</sup> as a signaling ion in cellular functions such as [proliferation](#), migration, and transcription factor activation. It notes that Ca<sup>2+</sup> signaling is highly activated in melanoma, contributing to its growth and invasiveness.

NETO2, identified as an interaction partner of neuronal kainate receptors, is shown to be associated with [neuropsychiatric disorders](#) and emotional behavior regulation.

Recent studies suggest that NETO2 also plays a key role in human malignant tumors, including osteosarcoma, esophageal and gastric cancer, and pancreatic cancer.

The researchers hypothesize that NETO2 is involved in melanoma progression by activating the Ca<sup>2+</sup>-dependent CaMKII/CREB pathway. To test this, they demonstrate that NETO2 is overexpressed in melanoma and associated with the survival rate of melanoma patients.

They show that NETO2 promotes melanoma cell proliferation and migration, and increases intracellular calcium concentration, leading to increased phosphorylation of CaMKII and CREB.

The study employs various methods including cell culture, DNA plasmids, lentiviral infection, bioinformatics analysis, Western blot, proliferation and colony formation assays, migration and invasion assays, intracellular Ca<sup>2+</sup> measurement, xenograft tumor model, immunohistochemistry, and statistical analyses.

The results indicate that NETO2 overexpression in melanoma tissues is correlated with [poor prognosis](#). In vitro, NETO2 promotes melanoma cell proliferation, and in vivo, silencing NETO2 suppresses melanoma growth. NETO2 also promotes the migration and invasion of melanoma cells, potentially through the regulation of matrix metalloproteinases (MMPs).

The study concludes that NETO2 activates the calcium signaling pathway in melanoma, and its inhibition by the CaMKII inhibitor KN93 suppresses the NETO2-driven melanoma phenotype. NETO2 is suggested as a potential therapeutic target for melanoma, highlighting its role in facilitating melanoma progression through the CaMKII/CREB signaling pathway.

In summary, the study provides novel insights into the molecular mechanisms of [melanoma](#) progression and offers a feasible therapeutic target for this malignancy.

**More information:** Susi Zhu et al, NETO2 promotes melanoma progression via activation of the Ca<sup>2+</sup>/CaMKII signaling pathway, *Frontiers of Medicine* (2023). [DOI: 10.1007/s11684-022-0935-0](https://doi.org/10.1007/s11684-022-0935-0)

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