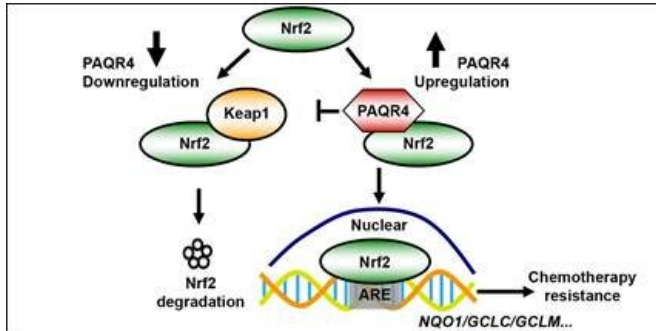


Inhibiting Nrf2 protein ubiquitination and degradation in non-small cell lung cancer

16 March 2020, by Liu Jia



PAQR4 promotes chemotherapy resistance mediated by Nrf2. Credit: CHEN Yongbin

Lung cancer is the predominant cause of cancer related deaths. Within the main types of lung cancers, small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC), NSCLC accounts for approximately 85%, with a poor five year survival of only ~15%. Despite the significant progress in treatment options, prognosis remains poor because of the locally advanced metastatic tumors in most patients at the time of diagnosis.

In a study published in *Theranostics*, a team of scientists from Kunming Institute of Zoology of the Chinese Academy of Sciences found that Progesterin and AdipoQ Receptor 4 (PAQR4) promotes chemoresistance in NSCLC through inhibiting nuclear factor erythroid 2-related factor 2 (Nrf2) protein degradation, showing PAQR4 as a potential novel biomarker and therapeutic target for non-small cell lung cancer.

The scientists provided evidence showing that PAQR4 is increased in NSCLC patients and cancer cell lines, and identified many mutations in PAQR4 in non-small cell lung cancer tissues.

They demonstrated that PAQR4 high expression correlates with worse clinical outcomes, and that

its down-regulation suppresses cell proliferation by triggering cellular apoptosis.

Importantly, PAQR4 physically interacts with Nrf2, blocks the interaction between Nrf2 and Kelch-like ECH-associated protein 1 (Keap1), and thus Nrf2 is stably expressed and accumulated in the nucleus, which activates the expression of a series of genes involved in antioxidant stress.

This study has identified a new mechanism by which PAQR4 regulates the ubiquitination and protein stability of transcription factor Nrf2, suggesting that screening and applying leading compounds that specifically inhibit PAQR4 functions, in combination with chemotherapy drugs, may lead to better clinical efficacy in future.

More information: Peifang Xu et al. PAQR4 promotes chemoresistance in non-small cell lung cancer through inhibiting Nrf2 protein degradation, *Theranostics* (2020). DOI: [10.7150/thno.43142](https://doi.org/10.7150/thno.43142)

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