ERCC1 expression analysis in Non-Small Cell Lung Cancer (NSCLC)

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Authors' objectives
Worldwide, lung cancer accounts for approximately 1 million deaths each year, making it the most common cause of cancer-related mortality. Non-small cell lung cancer (NSCLC) accounts for approximately 85% of lung cancer cases and is often associated with a relatively poor prognosis. The majority of NSCLC patients present with advanced disease and have an average 5-year survival rate of 5%. Currently, the standard of care for NSCLC includes treatment with a platinum-based chemotherapy regimen. The cytotoxicity of platinum-based chemotherapy results from the covalent binding of platinum to the DNA within cancer cells, creating large DNA adducts. The presence of these DNA adducts activates the nucleotide excision repair (NER) pathway, and eventually triggers programmed cell death if DNA repair is insufficient. However, not all patients benefit equally from such treatment. Therefore, recent pharmacogenomic studies have been performed in order to identify specific biomarkers that may allow for patient-tailored treatment strategies.

One of the biomarkers currently being examined in NSCLC patients is expression of the gene encoding the excision repair cross-complementation group 1 protein, ERCC1. The ERCC1 gene, which is located on chromosome 19 at bands q13.2 to q13.3, encodes a key enzyme involved in the NER pathway. Specifically, ERCC1 plays a role in removing the DNA adducts induced by platinum-based chemotherapeutic regimens. As a biomarker, ERCC1 expression appears to have value as both a prognostic marker and a predictive marker. While a prognostic marker indicates prognosis regardless of treatment protocol, a predictive marker indicates the likelihood a patient will respond to a particular treatment. In the case of ERCC1, high levels appear to be associated with an improved overall prognosis in NSCLC patients. However, high levels of ERCC1 are also associated with an increased resistance to platinum-based chemotherapy regimens. Another biomarker of clinical interest for NSCLC patients is the RRM1 gene. RRM1 encodes the regulatory subunit of the ribonucleotide reductase enzyme, which also functions in the NER pathway. Like ERCC1, high levels of RRM1 expression have been associated with an improved overall prognosis for NSCLC patients, and with an increased resistance to a specific chemotherapeutic agent, namely, gemcitabine. Since NSCLC patients are typically treated with multiple chemotherapy agents that function in different manners, it is believed that the assessment of multiple biomarkers is necessary in order to select the optimal treatment regimen for a given NSCLC patient.

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