

This is a copy of a chat between Claude and Lars S. Content may include unverified or unsafe content

*(i)* that do not represent the views of Anthropic. Shared snapshot may contain attachments and data not displayed here.

Report

**Ls** Are there known resistance mechanisms for genes targeted by Osimertinib in DGIdb?

I'll search for information about Osimertinib's gene targets and any resistance mechanisms in the DGIdb database.

**L** get\_gene\_interactions\_for\_drug\_list

Now let me search CIViC for specific resistance evidence for Osimertinib:

**L** get\_variant\_evidence

Yes, there are well-documented resistance mechanisms for genes targeted by Osimertinib in DGIdb and CIViC. Here's a summary:

## Primary Target

EGFR is the main target of Osimertinib (inhibitory interaction), supported by multiple databases including [CIViC](#), [OncoKB](#), [CGI](#), and [COSMIC](#).

## Known Resistance Mutations

### EGFR Mutations

Mutation	Evidence Level	Disease Context	Source
C797S	B (Clinical)	Lung NSCLC	<a href="#">EID:964</a> , <a href="#">PMID:25939061</a>
L718Q	C-D	Lung Adenocarcinoma	<a href="#">EID:8058</a> , <a href="#">PMID:32193290</a>
L718V	C-D	Lung Adenocarcinoma	<a href="#">EID:8059</a> , <a href="#">PMID:32193290</a>
M766Q	C (Case study)	Lung NSCLC	<a href="#">EID:7388</a> , <a href="#">PMID:31254668</a>
EGFR Amplification	D (Preclinical)	Lung NSCLC	<a href="#">EID:3015</a> , <a href="#">PMID:28202511</a>

### Bypass Pathway Resistance

Gene	Mechanism	Source
BRAF V600E	Acquired after osimertinib progression	<a href="#">EID:11098</a> , <a href="#">PMID:29074209</a>

Gene	Mechanism	Source
MET	Amplification (bypass)	<a href="#">CGI</a> , <a href="#">OncoKB</a>

## Other Genes Associated with Osimertinib Response

DGIdb also lists interactions with **STAT3**, **CTNNB1**, **NRAS**, **PIK3CA**, **PTEN**, and **TP53**, which have been implicated in resistance mechanisms in various studies ([PMID:31839416](#)).

## Key Takeaway

The **C797S mutation** is the best-characterized resistance mechanism, discovered in patients whose tumors developed resistance to osimertinib. The L718Q/V mutations represent additional on-target resistance mechanisms, while BRAF V600E and MET amplification represent off-target bypass mechanisms.

(i) Turn on web search in Search and tools menu. Otherwise, links provided may not be accurate or up to date.

[Start your own conversation](#)

