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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	EID:964 , PMID:25939061
L718Q	C-D	Lung Adenocarcinoma	EID:8058 , PMID:32193290
L718V	C-D	Lung Adenocarcinoma	EID:8059 , PMID:32193290
M766Q	C (Case study)	Lung NSCLC	EID:7388 , PMID:31254668
EGFR Amplification	D (Preclinical)	Lung NSCLC	EID:3015 , PMID:28202511

Bypass Pathway Resistance

Gene	Mechanism	Source
BRAF V600E	Acquired after osimertinib progression	EID:11098 , PMID:29074209

Gene	Mechanism	Source
MET	Amplification (bypass)	CGI , OncoKB

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.

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