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Report

Ls What genes interact with the drug Ibrutinib, and which of those genes have specific variants in CIViC associated with sensitivity or resistance?

I'll help you find genes that interact with Ibrutinib and then check which of those genes have variants in CIViC associated with sensitivity or resistance.

L get_gene_interactions_for_drug_list

Now let me search CIViC for evidence about sensitivity and resistance for the top interacting genes:

L get_variant_evidence

L get_variant_evidence

Now let me also check for PLCG2 variants specifically, as this was the top-scoring gene for drug interactions:

L get_variant_evidence

Let me also check for CIViC assertions to get the most validated clinical evidence:

L get_variant_assertions

Here's a comprehensive summary of what I found:

Genes That Interact with Ibrutinib

Based on DGIdb data, the top genes interacting with Ibrutinib include:

Gene	Interaction Score	Interaction Type	Key Sources
PLCG2	4.61	-	CGI , DoCM , PMID:24869598
MYD88	1.54	-	CGI , CIViC , PharmGKB

Gene	Interaction Score	Interaction Type	Key Sources
BTK	0.38	Inhibitor (inhibitory)	<u>Multiple sources</u> including CIViC, TTD, CGI, ChEMBL
Other genes: BMX, TEC, LYN, SMARCA4, CSF3R, EPHA8, etc.			

CIViC Variants Associated with Ibrutinib Response

Sensitivity/Response Variants

Gene	Variant	Disease	Evidence Level	CIViC Link
MYD88	L265P	Lymphoplasmacytic Lymphoma	B (Clinical)	EID:986 , PMID:25853747
BTK	Expression	B-cell ALL	D (Preclinical)	EID:9287 , PMID:28031181

Resistance Variants

Gene	Variant	Disease	Evidence Level	CIViC Link
BTK	C481S	CLL	B (Clinical)	EID:436 , PMID:24869598 ; EID:1770 , PMID:26182309
BTK	T316A	CLL	C (Case study)	EID:1985 , PMID:27626698
PIM1	L2V, P81S, S97N	DLBCL-ABC	D (Preclinical)	EID:9945-9947 , PMID:27904766

Key Findings

Overlapping genes (appear in both DGIdb drug interactions AND CIViC with sensitivity/resistance evidence):

1. BTK - The primary target of ibrutinib

- **Resistance:** C481S mutation (most common acquired resistance mechanism in CLL - found in ~80% of resistant cases) and T316A
- **Sensitivity:** BTK expression associated with response in B-ALL

2. MYD88 - Key interacting gene

- **Sensitivity:** L265P mutation associated with better response in Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma

PLCG2 - Although it has the highest interaction score in DGIdb and is known to be involved in ibrutinib resistance (mutations found in patients with acquired resistance), I did not find specific PLCG2 variant evidence entries in CIViC for ibrutinib at this time.

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not be accurate or up to date.