Table S2. Potential clinical relevance of the less studied genes relevant to our cohort.

Gene	Subgroup	Frequency		Therapeutic Target		Drugg able*	Biomarker		Ref.
		MX	TCGA	Lung cancer	Other types of cancer		Lung cancer	Other types of cancer	
RBMX	Frequent in Mexican cohort (Not-shared)	24%	1.4%	**LUAD:** Depletion of RBMX sensitizes cells to DNA damaging agents. **LC:** Tobacco-induced mutations in RBMX may predispose smokers to develop lung cancer	**Cell lines:** Potential target of cancer therapy (Role in telomere integrity maintenance). Knockdown of RBMX impaired proliferation, migration and invasion.	No		**Esophageal:** Biomarker of poor prognosis (Higher OS in low expression group, p=0.04). **Bladder:** Prognostic biomarker (DFS, p<0.001 and OS, p=0.043, 0.0097 and 0.0099 three datasets) **Various:** Prognostic biomarker and prediction of response to immunotherapy. Higher RR in low expression group.	Tuersun H, 2023, Lui J., 2023, Sheng Y., 2024, Yang Q., 2021, Renieri A., 2014.
PDE4D	Frequent in Mexican cohort (Not-shared)	20%	1.2%	**LC:** PDE4 expression (crosstalks with HIF) and promotes progression. Role in development and progression of lung cancer.		Yes	**LUAD:** PDE4D/cAMP/IL-23 axis determines the immunotherapy efficacy.	**Pancreas:** High expression of PDE4D correlates with poor prognosis (Higher OS in low expression group, p=0.002 and RR 3.72 p<0.001)	Liu F., 2019 Feng B., 2023 Pullamsetti SS., 2013 Hsien Lai S., 2020
JAK2	Frequent in Mexican cohort (Not-shared)	16%	2.8%	**LUAD:** Overexpression, mutations and amplification of JAK2 participate in cancer progression (proliferation, migration and invasion). Target of multitarget TPX-0005 (Repotrectinib)		Yes	**LUAD:** Mutations associated with Osimertinib resistance.		Xu Y., 2017 Wang Z., 2022 Ramalingam SS.,2018
AHI1	Frequent in Mexican cohort (Not-shared)	16%	1.6%		**CML:** AHI-1 is highly deregulated and mediates TKI-resistance of stem cells	No			Liu X., 2017
GPR176	Frequent in Mexican cohort (Not-shared)	16%	1%		**Gastric:** Promotes proliferation, migration, and invasion **Colorectal:** Promotes Cancer progression in vitro and in vivo.	Yes**	**LUAD:** Unfavorable prognostic marker (Expression).	**Gastric:** High expression predicts poor prognosis (Higher OS in low expression group and HR 1.8, p-value 0.003). **Colorectal:** High expression correlates with proliferation and poor overall survival (HR = 2.68, p = 0.023). **Stomach:** Biomarker for prognosis and immune Infiltration (Higher OS in low expression group)	Zhang Y., 2023 Ni L., 2023 Tang J., 2023 Uhlen M., 2017 The Human Protein Atlas
SLC36A4	Differences in frequency (Shared)	20%	1%		**General:** Immunosuppressive tumor microenvironment mediated by kynurenine transport through SLC36A4. Role in migration. Transporters stand out as potential targets. **Cell lines:** Critical for mTORC1-regulated growth.	No	**LUAD:** Unfavorable prognostic marker (Expression).	**Colon:** High expression of SLC36A4 predicts poor relapse-free survival (p=0.005)	Chen L., 2023 Fan S-J., 2016 Goberdhan DCI., 2010 The Human Protein Atlas
AP1S1	Differences in frequency (Shared)	8%	0.2%	**LUAD:** Inhibition of AHI1 increases sensibility in resistant cells to EGFR-TKIs and causes degradation of EGFR.		No			Jeong J., 2023
NRCAM	Frequent (Shared)	24%	7.5%		**Liver:** High expression in cancer stem cells. Promotes migration and Epithelial-Mesenchymal Transition	No	**LUAD:** Differential expression between LUSC and LUAD. High expression in LUSC and Low in LUAD. **LC:** Hypermethylated	**Gastric:** High expression is associated with poor prognosis. **Liver:** High expression was associated with a poorer survival (p=0.001)	Bai C., 2022 Zhou L., 2023 Lucchetta M., 2019 Ansari J., 2016

Gene	Subgroup	Frequency		Therapeutic Target			Biomarker		Ref.
		MX	TCGA	Lung cancer	Other types of cancer	Drugg able*	Lung cancer	Other types of cancer	
TET1	Frequent (Shared)	20%	4.2%	**LC:** Proposed as oncogene. Gain function via loss of TP53. Synergistic with cytotoxic drugs. *K*nockdown confers resistance to EGFR TKIs	**TNBC:** Role in self-renewal of cancer stem cells. **Thyroid:** TET1 promotes oncogenesis and cancer progression (in hypoxia).	Yes**	**LC:** Predictive biomarker for immune checkpoint blockade. **NSCLC:** Downregulation of TET1 was correlated with poor clinical features. Mut-TET1 shows a protective effect: PFS, HR =0.46, p= 0.008 and OS, HR=0.47, p=0.019 **LUAD:** Mutations co-occur with KRAS and predicts poor survival. Higher OS in low expression group (p=0.048)	**Thyroid:** Expression is associated with poor survival (switch-hypoxia).	Yang Q., 2023 Ghazimoradi MH., 2024 Filipczak PT., 2019 Alrahali AA., 2023 Forloni M., 2016 Wu H-X., 2019 Xu Q., 2022

LC: lung cancer, NSCLC: Non-small cells lung cancer, LUAD: Lung adenocarcinoma, CML: Chronic myeloid leukemia, TNBC: Triple negative breast cancer, RR: Response rate, OS: Overall survival, HR: Hazard ratio, PFS: Progression Free Survival, DFS: Disease Free Survival.

* According to DGIbd, ChEMBL and Therapeutic Targets Database.

** Only ChEMBL