Protein Tyrosine Phosphatase PTP4A3/PRL-3 Drives Migration and Progression of T-Cell Acute Lymphoblastic Leukemia

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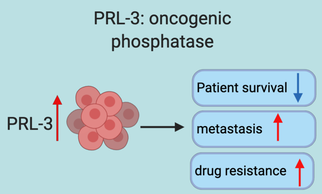
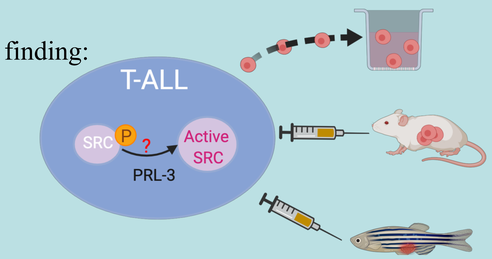
INTRODUCTION

T Hunter, Cell, 1995



Our finding:



METHODS

•**Zebrafish T-ALL model** were generated by injecting linearized Rag2: Myc + Rag2: mCherry with or without Rag2:prl3 in the embryos in the single cell stage as describe in (Blackburn et al., 2012).

• **Xenotransplantation** Jurkat cell were infected with virus encoding shRNA targeting PRL-3 or scramble shRNA (control) for 3 days and selected with puromycin (5 mg/ml) for 2 days. Live cells were sorted by FACS and injected via tail vein into NSG mice (n=9 for each group).

• **BioID2 proximal labeling** BioID2, a biotin ligase, was fused to PRL-3 (BP) and BP is overexpressed in T-ALL cells. Prior to total protein extraction, the T-ALL BP cells were cultured in biotin rich medium for 16hrs. Streptavidin pulldown assay was performed to capture biotinylated proteins, which was further determined by MS.

POSTDOC WANTED

RESULTS

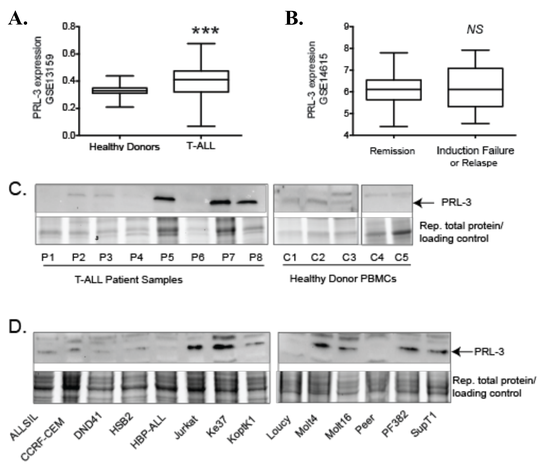


Figure 1. PRL-3 is overexpressed in human T-ALL samples and cell lines.

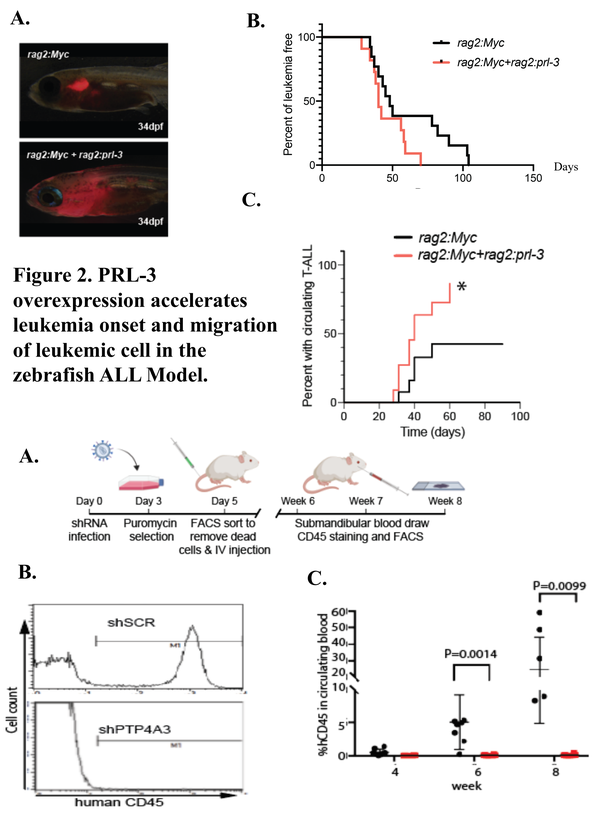


Figure 2. PRL-3 overexpression accelerates leukemia onset and migration of leukemic cell in the zebrafish ALL Model.

Figure 3 Xenotransplantation of PRL-3 knockdown Jurkat cells showed impaired engraftment and circulation in NSG mice.

RESULTS

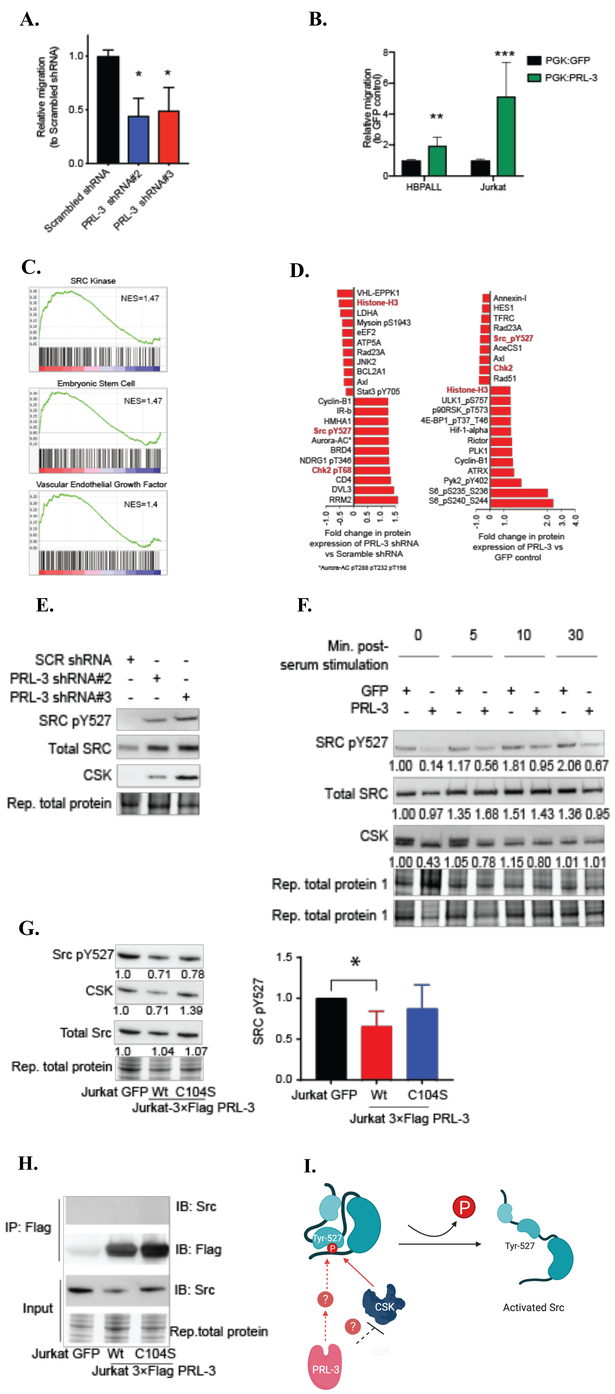
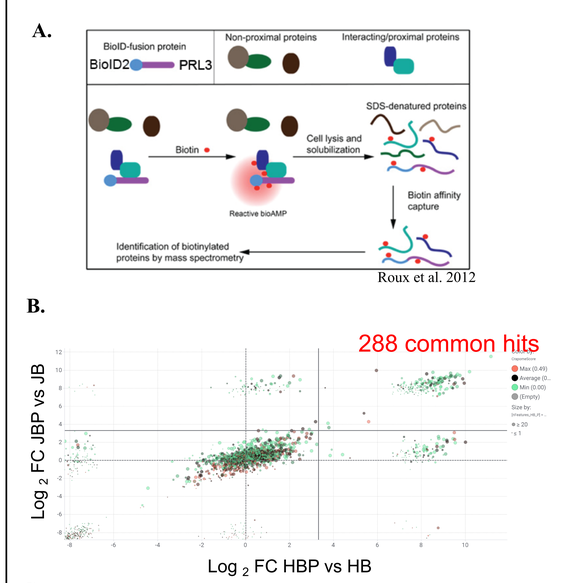


Figure 4. PRL-3 promotes migration via SRC pathway.

RESULTS



C.

KEGG 2019 Human — Bar Graph | Table | Clustergram

Hover each row to see the overlapping genes.

10 entries per page — Search:

Index	Name	P-value	Adjusted p-value	Odds Ratio	Combined score
1	Fc gamma R-mediated phagocytosis	7.543e-7	0.0002323	7.63	107.58
2	T cell receptor signaling pathway	0.000001987	0.0003060	6.88	90.27
3	ErbB signaling pathway	0.00003092	0.002381	6.54	67.87
4	Regulation of actin cytoskeleton	0.000002882	0.0002959	4.54	57.96
5	Thyroid hormone signaling pathway	0.00004665	0.002874	5.39	53.73
6	Pancreatic secretion	0.00008607	0.004418	5.67	53.06
7	Proximal tubule bicarbonate reclamation	0.004228	0.03946	9.06	49.51
8	Salivary secretion	0.0003217	0.009909	5.40	43.44
9	Inositol phosphate metabolism	0.0006903	0.01329	5.63	40.98
10	D-Glutamine and D-glutamate metabolism	0.06996	0.2449	13.89	36.94

Figure 5 BioID2- based proximal labeling identified PRL-3 interacting protein pool.

Future Directions

- Identify the mechanism by which PRL-3 modulate SRC pathway
- Validate the PRL-3 direct targets that promotes migration.

Funding

Markey Cancer Center Travel Award
University of Kentucky Biomedical Education Travel Award

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R01CA227656

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