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Creation of a Human T-ALL Cell Line Online Database Human T-ALL cell line database

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Human cell lines are used widely in biomedical research, including oncology. Lines are often chosen for study based on their cell lineage, differentiation state, and—in the case of cancer studies—because they are believed to represent key features of a particular type of malignancy. For some studies, a cell line may be chosen due to its expression of a key gene or protein, activation of a known pathway, or because it harbors a specific genetic lesion, such as a translocation or mutation in a known oncogene or tumor suppressor. With the advent of next-generation sequencing technologies, many cell lines have now been genomically sequenced with data also available on their gene expression profiles.

T-cell acute lymphoblastic leukemia (T-ALL) is one neoplasia type for which many human cell lines exist with abundant publicly-accessible data. However, despite many T-ALL cell line resources being available, many lack certain lines and/or select pieces of information. Moreover, in some cases different sources may list contradictory data for the same cell line, either due to erroneous information, contamination by another cell line, or because cell lines may undergo genetic drift *in vitro*, creating new sub-lines with distinct features in different laboratories.(ref. 1-3) Consequently, because no single repository lists all of this data in a central location, meticulous effort is required to gather this information from multiple sources, scrutinize it, and then collate it into a meaningful format for comparing between lines. To address this deficiency, here we report the creation of a “Human T-ALL Cell Line database,” accessible at the following web portal: https://humantallcelllines.wordpress.com. Table 1 displays a greatly simplified version of one page from this database.

This comprehensive online compilation lists information in several categories for many widely-used T-ALL lines, with hyperlinks to key publications and other online sources where this data can be explored in even greater detail. Importantly, we actively curate this database, so it represents a “living document” where new information can also be deposited when it becomes available based on input from other scientists, including additional T-ALL lines or new data categories. The website provides a simple platform for users to

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communicate such requests or other suggestions to expand the database and improve its functionality.

Key elements of Table 1 (listed in greater detail online with links to references for each item in every category) include each line's surface phenotype with respect to CD3, CD4, CD8 (column B) and TCR (column C), known translocations (column D) with the oncogene(s) they impact, and each line's classification according to a schema based on oncogene expression profiling and expanded to include early T-cell precursor leukemia (ETP-ALL), a subsequently described entity (column E).(ref. 4-6) In addition, Table 1 lists the mutational status of key T-ALL oncogenes and tumor suppressors, including *CDKN2A*, *NOTCH1*, *PTEN*, *TP53*, and others (columns F-P). As mentioned above, different sources sometimes list conflicting information with regard to mutation status (e.g., for the MOLT-4 T-ALL line, *TP53* was reported to have a point mutation by one group (ref. 7), whereas a second group found a novel insertion instead).(ref. 8) In some cases, this data may be factually inaccurate. However, it is likely that many of these circumstances result from *in vitro* drift of the cell line, such that both mutational statuses are correct, depending upon the specific cell line isolate present in a particular laboratory. Due to this possibility, in such cases we list both results, to make investigators aware of this ambiguity and prompt them to determine the status of the line in their possession, if it might impact their particular research application.

Other elements available online not shown in Table 1 include patient demographic features pertaining to each line's origin, notable biologic characteristics, gene and protein expression data, sensitivity to gamma-secretase inhibitors and glucocorticoids, expanded mutation information, and hyperlinks to relevant websites and publications.

The database currently lists comprehensive data for 22 T-ALL lines for which we were able to retrieve extensive information: ALL-SIL, CCRF-CEM, D1.1, DND-41, DU.528, HPB-ALL, HSB-2, JURKAT, KARPAS-45, KOPT-K1, LOUCY, MOLT-3, MOLT-4, MOLT-14, MOLT-16, P12-ICHIKAWA, PEER, PF-382, RPMI-8402, SKW-3, SUP-T1, and TALL-1. In addition, the online database provides hyperlinks to informative manuscripts and webpages for 42 other human T-ALL lines for which only partial characterization is currently available. Ultimately, as these data become available, such lines will be added to the page detailing fully-characterized human T-ALL lines. We update and maintain this resource, with a simple online mechanism for other scientists to suggest modifications and additions, so we are hopeful that intellectual contributions from other laboratories will permit us to expand beyond the 64 T-ALL lines currently listed, as well as to the categories of information presently displayed.

Our compendium assembles and organizes data from over 130 publications and 14 web resources, but we recognize this represents a small fraction of the work that has been done using these lines and information known about them. Our continued curation and input from other scientists will allow us to develop it into an even more comprehensive resource. In general, key uses of the database are that it provides: (1) a succinct reference to compare phenotype, genotype, maturation state, and other salient biologic features between different human T-ALL lines, as depicted in Table 1, (2) more detailed topics like gene and protein expression, drug sensitivities, and mutation status of key genes with direct links to data

sources for verification and further reading, and (3) an exhaustive list of every human T-ALL line for which useful information are available, with links to other laboratories and biorepositories such as the American Type Culture Collection (ATCC) and Leibniz-Insitut Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DMSZ) to facilitate their distribution to interested parties. Ultimately, we aspire to amass complete information for all 64 human T-ALL lines currently listed, as well as other lines we are not aware of. Moreover, we hope this database may also serve as a useful template for other hematologic malignancies besides T-ALL where large numbers of human cell lines exist and are used experimentally.

Like our online database, many web resources used to assemble it are constantly evolving, with new findings in T-ALL published regularly. This creates challenges to maintaining a detailed, yet “up-to-date” anthology. Likewise, because it is impossible to successfully identify—much less thoroughly review—each manuscript involving human T-ALL lines, our database undoubtedly omits potential sources, and may perpetuate previously published factual inaccuracies. By maintaining this as a public information portal, we can rectify such deficiencies and expand the utility and functionality of this database so that it meets the needs of the T-ALL scientific community, however they may evolve in the future.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table I

Key Features of 22 Well-Characterized Human T-ALL Cell Lines

CELL LINE	IMMUNOPHENOTYPE	TCR STATUS	TRANSLOCATIONS	ONCOGENE GROUP	*CDKN2A*	*CREBBP*	*FBXW7*	*HRAS*	*JAK1*	*KRAS*	*MYB*	*NOTCH1*	*NRAS*	*PTEN*	*TP53*
ALL-SIL	CD3- CD4+ CD8+	TCR-	NUP214-ABL1 t(10;14) (q24;q11.2)TRAD-TLX1	*TLX1*	MUT		WT		MUT		MUT	MUT HD & PEST		WT	
CCRF-CEM	CD3- CD4+ CD8- CD3+ CD4+ CD8-	αβ mTCR- iTCRβ+	[t(5;14) (q35;q32.2)] BCL11B-(TLX3/NKX2-5) SIL-TAL1	*TAL1*	MUT		MUT			MUT	MUT	HD MUT, PEST WT/MUT		MUT	MUT
D1.1	CD3+ CD4- CD8-														
DND-41	CD3+ CD4+ CD8- CD3+ CD4- CD8-	γδ / βδ / TCR-	[t(5;14) (q35.1;q32.2)] BCL11B-TLX3	*TLX3*	WT/MUT	MUT	WT		MUT	MUT		MUT HD & PEST	MUT	WT/MUT	MUT
DU.528	CD3- CD4- CD8-	TCR-	[t(1;14) (p32;q11)]TCRδ-TAL1 [t(1; 14) (p33;q11)]	*TAL1*			MUT				MUT	WT HD & PEST		WT	WT
HPB-ALL	CD3+ CD4+ CD8+	αβ TCRαβ iTCRβ+	[t(5;14) (q35;q32.2)] BCL11B-TLX3	*TLX3*	MUT	MUT	WT/MUT	MUT	MUT			MUT HD & PEST		WT/MUT	MUT
HSB-2	CD3- CD4- CD8-	TCR-	SIL-TAL1 [t(1;7) (p34;q34)]LCK-TCRβ	*TAL1*	MUT		MUT		MUT			WT/MUT HD & PEST	MUT	WT	WT
JURKAT	CD3+ CD4+ CD8-	αβ TCRαβ iTCRβ+		*TAL1*	MUT	MUT	MUT		MUT	WT	WT	WT/MUT HD & PEST		MUT	MUT
KARPAS-45	CD3-CD4-CD8-	αβ	[t(X;11) (q13;q23)]KMT2A-FOXO4 (aka, MLL-AFX) [t(1;5) (q21;q12.2)]		WT/MUT	MUT	MUT				MUT	MUT HD		MUT	MUT
KOPT-K1			[t(11;14) (p13;q11)]LMO2-TCRγ	*TAL1*	MUT	MUT	WT				WT/MUT	MUT HD & PEST		WT	MUT
LOUCY	CD3+ CD4- CD8-	γδ	[t(16;20) (p12;q13)]	*ETP*	MUT	WT	WT		MUT		WT/MUT	WT HD & PEST		MUT	MUT
MOLT-3	CD3- CD4+ CD8- CD3- CD4+ CD8+	TCR- mTCR- iTCRβ+	[2der(7)t(7;7) (p15;q11)]	*TAL1* *LMO2*	MUT							MUT HD & PEST	MUT	MUT	WT
MOLT-4	CD3- CD4+ CD8+	TCR-	[2der(7)t(7;7) (p15;q11)]	*TAL1*	MUT	MUT	WT	MUT	MUT		MUT	MUT HD & PEST	MUT	MUT	WT/MUT
MOLT-14	CD3+ CD4- CD8-	γδ	[t(X;11) (q25;p13)]LMO2-STAG2		MUT		MUT		MUT			MUT	MUT		MUT
MOLT-16	CD3+ CD4- CD8-	αβTCRαβ iTCRαβ+	[t(8;14) (q24;q11)]TCRα-MYC [t(3;11) (q25;p13)]MO2-MBNL1	*TAL1*	MUT		WT		MUT		WT/MUT	WT HD & PEST		WT/MUT	WT/MUT
P12-ICHIKAWA	CD3- CD4+ CD8+	TCR-	[del(11) (p13p13)]LMO2 rearrangement	*LMO2*	MUT	WT	MUT		MUT	WT	MUT	MUT HDWT PEST	MUT	MUT	
	CD3- CD4+ CD8-														
PEER	CD3+ CD4+ CD8-	γδ	[t(5;14) (q35.2;q32.2)] NKX2-5-BCL11B NUP214-ABL1		MUT	WT	WT/MUT		MUT			WT/MUT HD & PEST		WT	MUT
	CD3+ CD4+ CD8+														
PF-382	CD3- CD4+ CD8+	TCR-		*TAL1*		MUT	WT	MUT	MUT		WT	MUT HD & PEST	MUT	MUT	MUT
RPMI-8402	CD3- CD4- CD8-	TCR-	SIL-TAL1 [t(11;14) (p15;q11)]LMO1-TRAD	*TAL1 LMO1*	MUT	MUT	MUT	MUT	MUT		MUT	MUT HD WT PEST		MUT	WT/MUT
SKW-3 (KE-37) *	CD3- CD4+ CD8+ CD3- CD4+ CD8-	TCR-	[t(8;14) (q24;q11)]TCRα-MYC		MUT						MUT	WT HD MUT PEST		MUT	

CELL LINE	IMMUNOPHENOTYPE	TCR STATUS	TRANSLOCATIONS	ONCOGENE GROUP	*CDKN2A*	*CREBBP*	*FBXW7*	*HRAS*	*JAK1*	*KRAS*	*MYB*	*NOTCH1*	*NRAS*	*PTEN*	*TP53*
SUP-T1	CD3- CD4+ CD8+	β (α non-functional) TCR- mTCR- iTCRβ+	[(t7;9)(q34;q34)]TCRß-NOTCH1 [inv(14)(q11;q32)]Igh-TCRα			MUT	WT		MUT			WT		WT/MUT	MUT
TALL-1	CD3+ CD4+ CD8+	αβ					WT					WT HD WT PEST	MUT	WT	MUT

*Originally obtained from a T-CLL patient, DNA fingerprint & cytogenetic analyses show some SKW-3 isolates are contaminated or replaced by KE-37, a T-ALL line.

WT: wildtype; **MUT**: mutated; **m**: membrane surface; **i**: intracellular