



Creating Greater Certainty in the
Fight Against Cancer

Poster NO. 2990
AACR 2021

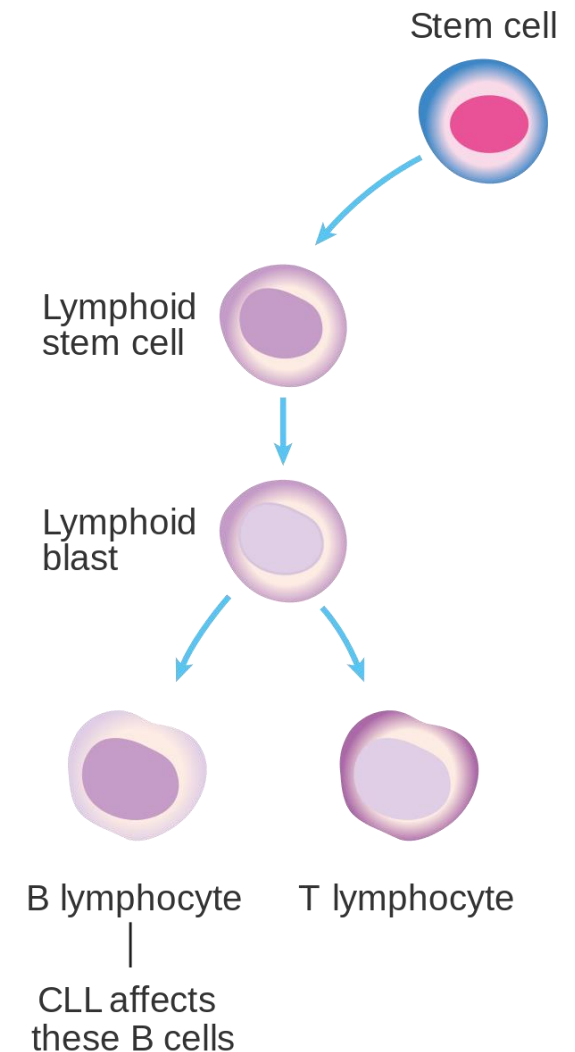
In Vitro Drug Sensitivity Screening Platform for Chronic Lymphocytic Leukemia (CLL) Patient Samples

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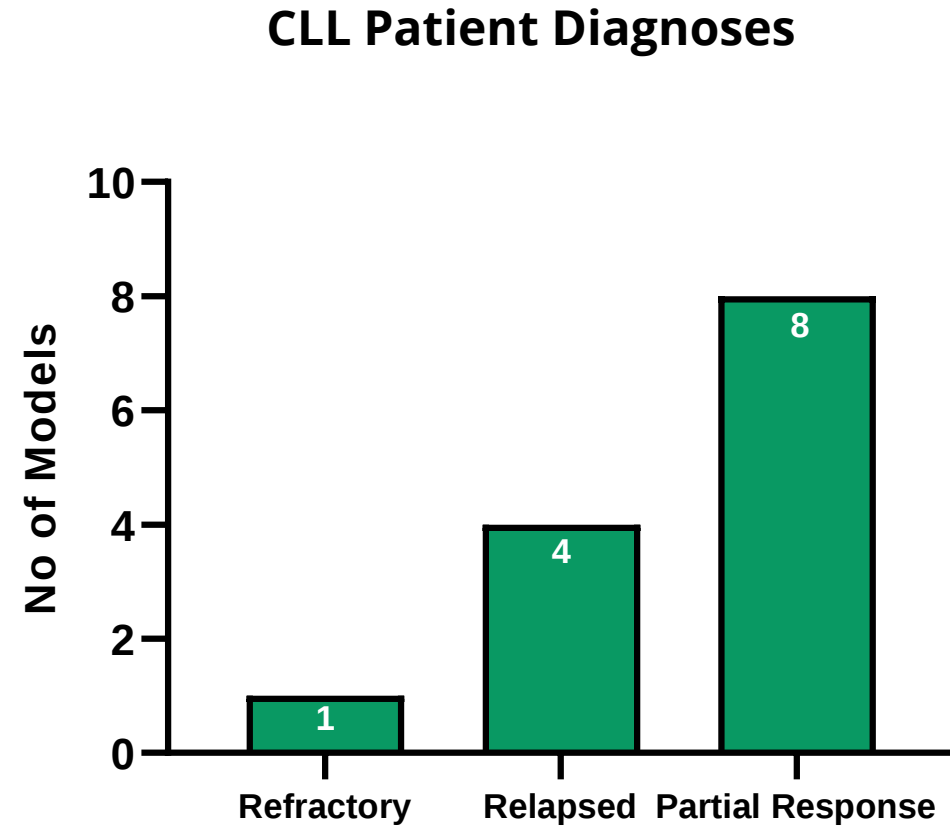
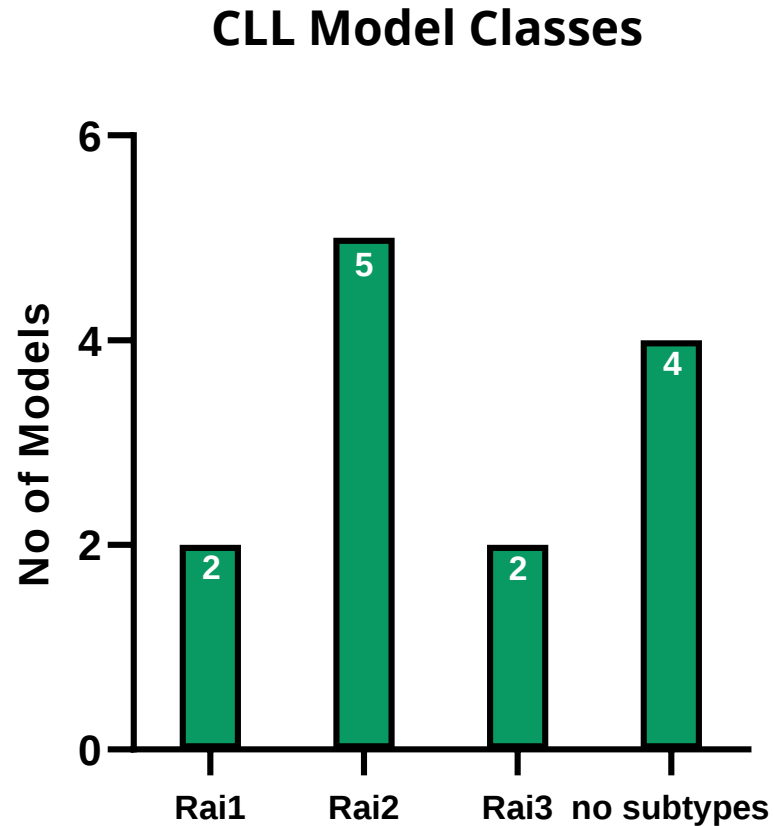
Champions Oncology, Rockville, MD

Chronic Lymphocytic Leukemia (CLL)

- Chronic lymphocytic leukemia (CLL) is a B cell malignancy.
- One of most common leukemia in adults over age 19.
- 15,000 new cases diagnosed every year with 4,500 deaths per year.
- It is a clonal B-cell neoplasm of mature cells.
- B cell receptor signaling is the central pathway in CLL pathogenesis.
- Rai/binet staging systems
- Markers with prognostic significance:
 - Del17p
 - IgVH
 - CD38



Champions' CLL Model Diversity



Expression of CLL Markers in Champions' CLL Models

Collection												
Models	ID	CD45	CD3	CD5	CD10	CD19	CD20	CD23	CD34	CD38	CD79b	Fmc7
CTG-3751	2681											
CTG-3752	3452	++	-	++	-	++	+	-	-	-	++ 96%	++
CTG-3753	4365	++	-	++	-	++	+	-	-		-	-
CTG-3754	4368	++	-	++	-	++	Low 6.8%	Low 9%	-	Low 6%	+	-
CTG-3755	4463	++	-	++	-	++	+	Low 9%	-	-	++	-
CTG-3756	4531	++	-	+	-	++	-	-	-	-	++	-
CTG-3757	4683	++	-	++	-	++	+	Low 8%	-	+	++	
CTG-3758	4827	++	-	++	-	++	++	Low 15.6%	Low 4%	Low 3%	++	++
CTG-3759	4915											
CTG-3760	4976											
CTG-3761	5076											
CTG-3762	5684	++	-	++	-	++	++	++	Low 2.41%	+	++	Low 5%
CTG-3763	6299	++	-	++	-	++	++	+	Low 4.3%-	+	+	-

++ = >50%

+ = 20% - 50%

Kinetics of an In Vitro Drug Sensitivity Screening Platform Developed for Chronic Lymphocytic Leukemia (CLL) Patient Samples

Schematic Representation of Ex Vivo Study

Patient-derived CLL
models

Drug

Applications

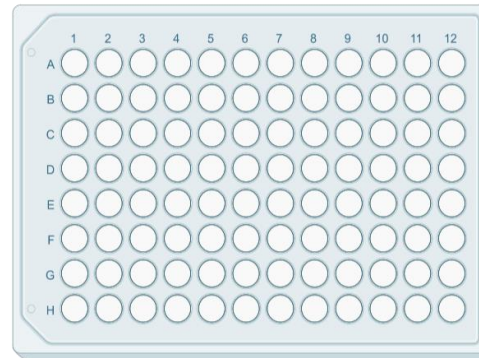
- Drug Screening
- Biomarker Discovery
- Mechanism of Action
- In Vivo Model Selection

Specimen Input:

- PBMC
- Leukapheresis
- Bone Marrow Sample
- PDX Explant



Enriched
Growth Media



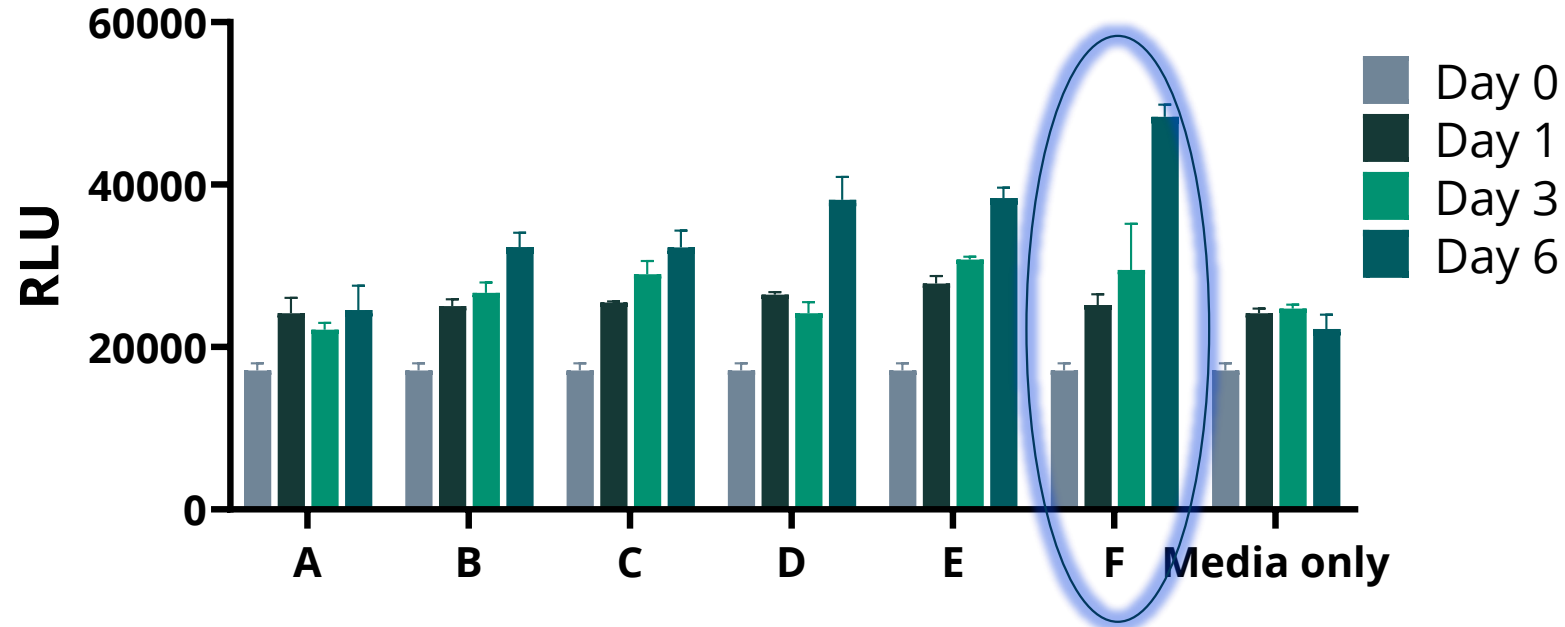
Assay format:

- 6 day assay

Study Endpoints:

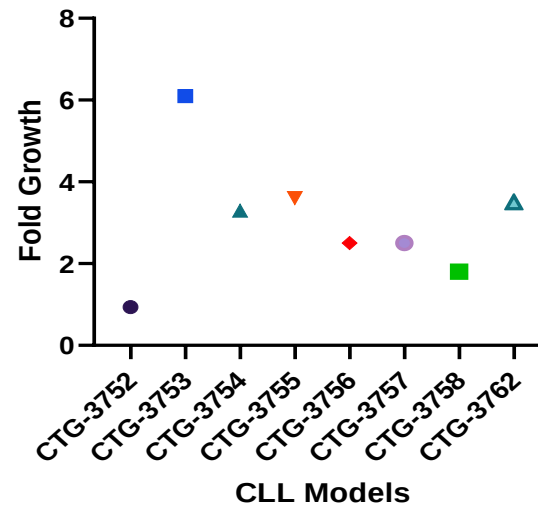
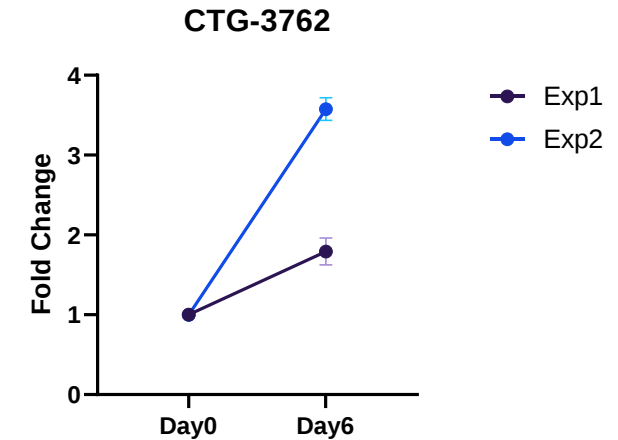
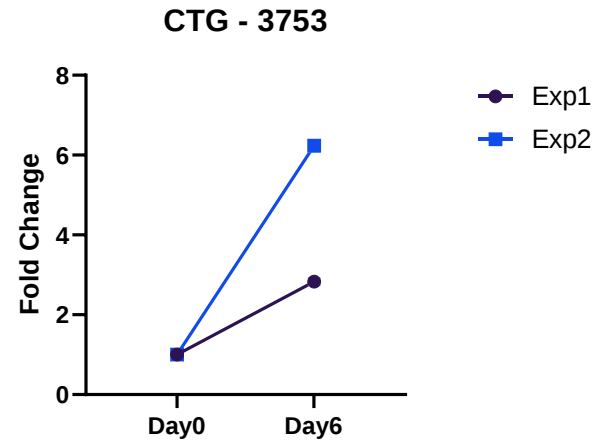
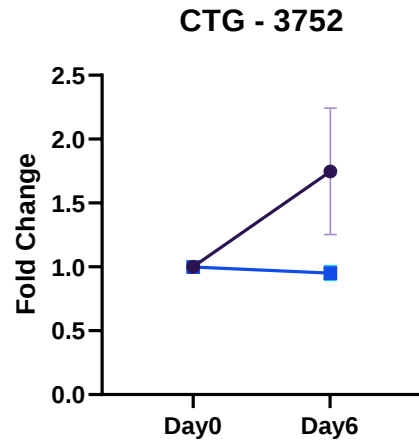
- Proliferation
- Tumor Cytotoxicity
- Apoptosis
- Phenotyping

Development of Assay Culture Conditions

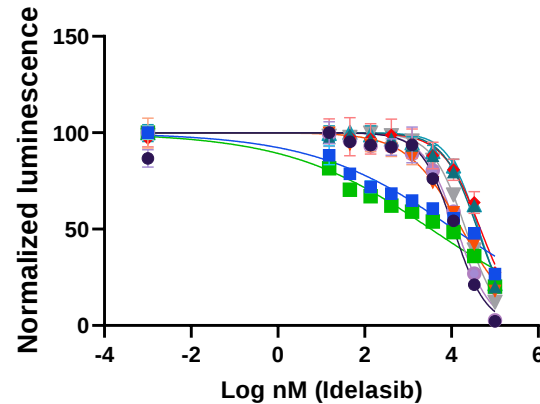


Selection of media, supplements and other culture conditions
(representative of several studies with similar results across models)

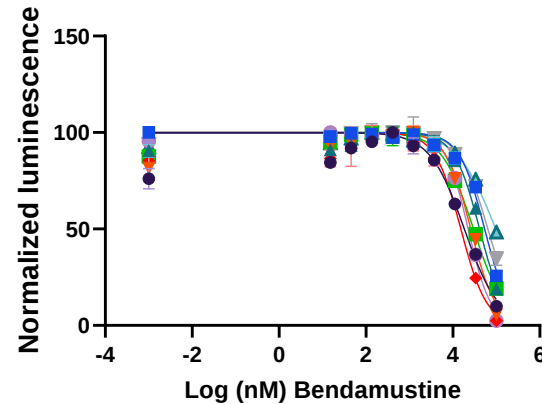
Growth in Ex Vivo Assay with Complete Cytokine Media and Reproducible Performance



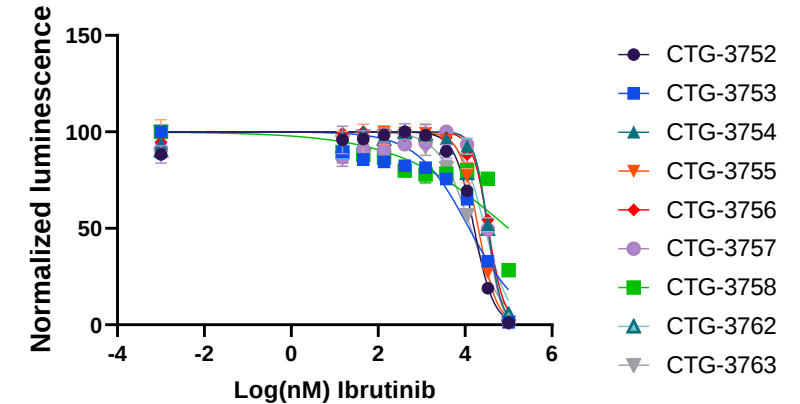
Responsiveness of CLL to SOC Treatment in Ex Vivo Platform



Idelalisib Treated Models	IC ₅₀ (nM)	R ²
CTG-3752	11256	0.96
CTG-3753	11409	0.94
CTG-3754	39647	0.96
CTG-3755	17329	0.97
CTG-3756	46609	0.91
CTG-3757	13373	0.98
CTG-3758	3368	0.95
CTG-3762	42263	0.96
CTG-3763	21287	0.99

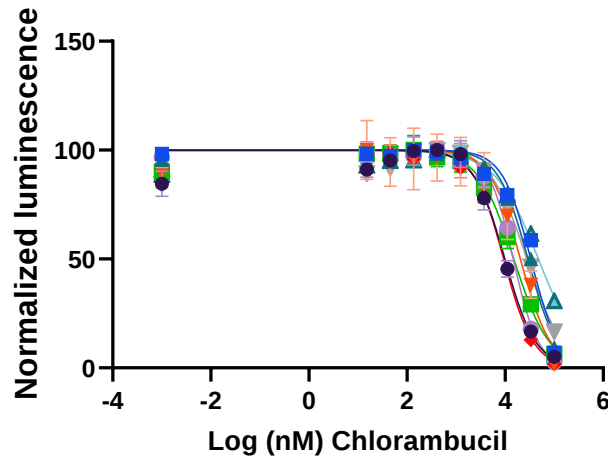


Bendamustine Treated Models	IC ₅₀ (nM)	R ²
CTG-3752	18358	0.87
CTG-3753	53802	0.88
CTG-3754	41150	0.99
CTG-3755	25783	0.99
CTG-3756	15261	0.99
CTG-3757	22478	0.98
CTG-3758	29809	0.96
CTG-3762	96917	0.93
CTG-3763	63937	0.95

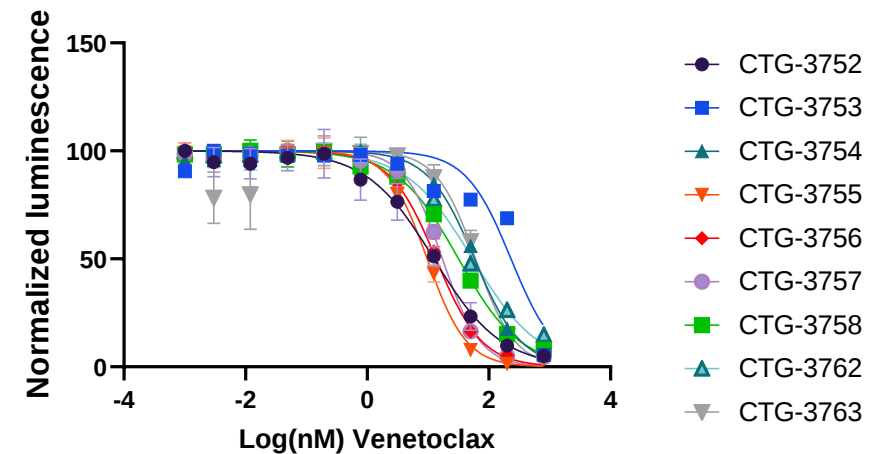


Ibrutinib Treated Models	IC ₅₀ (nM)	R ²
CTG-3752	16186	0.97
CTG-3753	12433	0.88
CTG-3754	33723	0.96
CTG-3755	20218	0.98
CTG-3756	34287	0.98
CTG-3757	32698	0.93
CTG-3758	99781	0.67
CTG-3762	28842	0.96
CTG-3763	13578	0.98

Responsiveness of CLL to SOC Treatment in Ex Vivo Platform

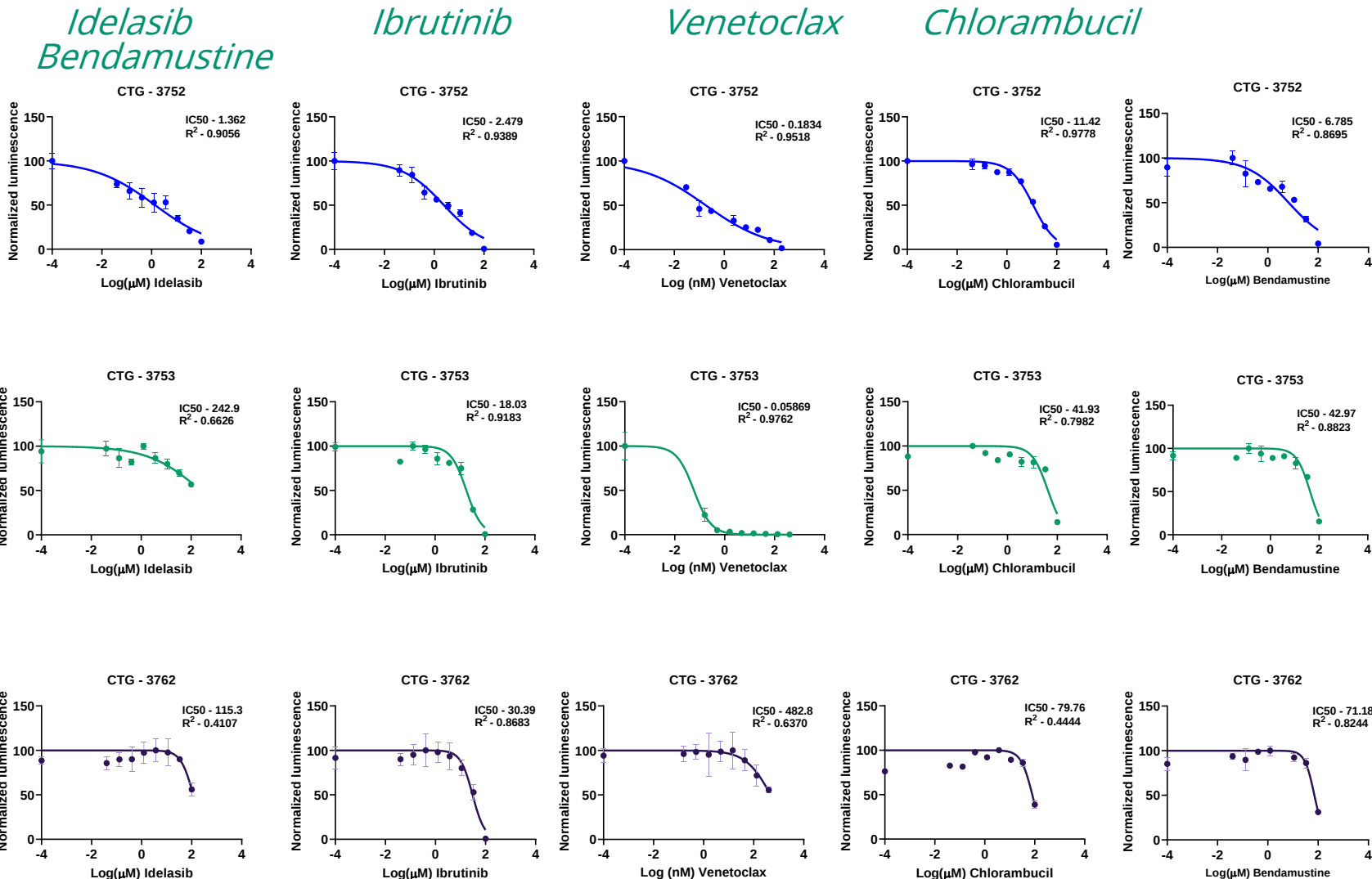


Chlorambucil Treated Models	IC ₅₀ (nM)	R ²
CTG-3752	9868	0.96
CTG-3753	33349	0.96
CTG-3754	29130	0.98
CTG-3755	20463	0.90
CTG-3756	9355	0.98
CTG-3757	14667	0.99
CTG-3758	15046	0.97
CTG-3762	47741	0.94
CTG-3763	27856	0.92



Venetoclax Treated Models	IC ₅₀ (nM)	R ²
CTG-3752	12.5	0.97
CTG-3753	231.6	0.88
CTG-3754	58.19	0.99
CTG-3755	9.679	0.99
CTG-3756	13.52	0.99
CTG-3757	17.27	0.99
CTG-3758	31.77	0.99
CTG-3762	54.16	0.99
CTG-3763	60.77	0.89

Differential Drug Response of Primary CLL Cells based on Pretreatment

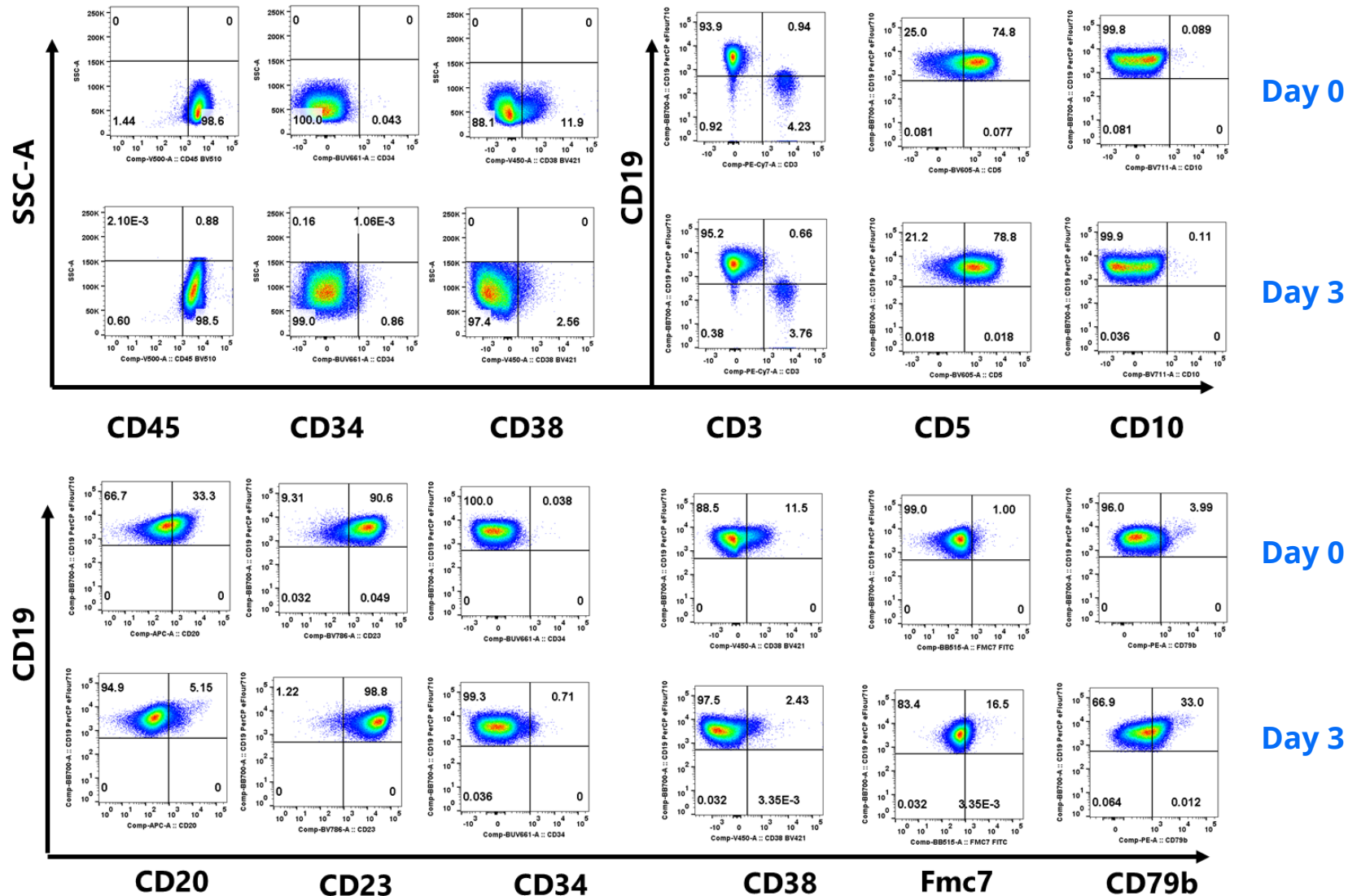


Relapsed
Bendamustine
treated

Relapsed
Ibrutinib
treated

Refractory

Representative Phenotyping Pre/Post Culture



Conclusions

- Patient-derived primary CLL cells survived and proliferated in enriched media.
- CLL models showed responsiveness to standard of care drugs in ex vivo platform. Interestingly, differential response observed based on pretreatment.
- Expression of CLL markers are retained in ex vivo culture.
- The ex vivo drug screening assay developed is a robust platform for evaluation of novel therapeutics of CLL.
- WES and RNA-Seq is in progress for all models.



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