ASX/Media Release

Benitec City of Hope Human Trial Update

9 February 2009, Melbourne, Australia: Leading developer of RNA interference (RNAi)-based therapeutics Benitec Limited (ASX: BLT) announced today that there had been unprecedented interest in the update on the City of Hope HIV trial recently presented in the USA.

Findings from the trial were presented at the Stem Cell World Congress in Palm Springs, California on 20 January 2009 by Dr David DiGiusto, Director of haematopoietic cell therapies at City of Hope Medical Centre in Duarte, California.

The presentation was entitled "A Pilot Study of Safety and Feasibility of Stem Cell Therapy for AIDS Lymphoma Using Stem Cells Treated with a Lentivirus Vector Encoding Multiple anti-HIV RNAs"

The key findings presented at the meeting were that the isolation, genetic modification (with Lentiviral vector) and infusion of CD34+ cells from ARL patients is safe and feasible. Gene marking *in vivo* was within the expected range predicted by in vitro analysis of transduced CD34+ cells and gene marked cells persist (and express siRNA) for up to 10 months post infusion.

"We are trying to prevent the immunodeficiency that is a result of HIV infection. It is still an experimental treatment at the moment, but we hope that eventually we will be able to give Aids patients just one transplant and that would then protect them for life. We have data to show that the resistant cells are persisting in our lymphoma patients" said Dr DiGiusto.

The technique involves isolating genes which curb the spread of HIV inside the body, introducing the genes into human stem cells in a laboratory, then transplanting the stem cells into a patient's bone marrow.

"What the scientist did here was to genetically modify fraction of the patient's stem cells with genes that target three different aspects of HIV that allow it to get into the immune cells and replicate. When those stem cells are transplanted into patients, they create mature immune cells that circulate in the patient and protect against HIV. This study has shown that we can deliver gene modified cells which have the potential to limit the HIV infection. If we can continue to develop this approach and successfully apply it to other AIDS patients, then genetic therapy for HIV could become a reality", said Sue MacLeman, CEO Benitec Limited

The early results have been welcomed by Aids and HIV charities who have described the experimental treatment as "promising".

Around 40 million people worldwide are infected with HIV and an estimated three million die each year with the virus. In the UK there are 73,000 people who are living with HIV and in recent years a growing number of heterosexuals have been diagnosed with the infection.

HIV, which is a sexually-transmitted infection, attacks white blood cells known as T-lymphocytes, which play a central role in the immune system by fighting other forms of infection.

Over time the number of T-lymphocytes in the body decreases as the virus spreads and the immune system stops working, leading to the condition known as Auto-Immune Deficiency, or Aids, meaning patients are no longer able to fight off infections themselves. Most Aids patients die from pneumonia or cancers such as lymphoma.

Bone marrow contains stem cells that are capable of forming all types of blood cells including the white blood cells that form part of the immune system.

By giving patients stem cells that carry these anti-HIV genes, the patients' bodies are able to produce new white blood cells that are resistant to attack from HIV and so able to defend the body from other forms of infection.

This pilot feasibility study is supported through a collaboration between Benitec and City of Hope and is Benitec's first human trial. The trial uses a triple therapy delivered using a lentiviral vector developed at City of Hope in the laboratories of Dr. John Rossi and Dr. John Zaia. The rHIV7-shI-TAR-CCR5RZ vector suppresses HIV by expressing three nucleic acids that are directed against key steps in HIV replication.

A copy of the conference poster is attached.

The Study

The study with City of Hope is entitled, "A pilot study of the safety and feasibility of stem cell therapy for AIDS lymphoma using stem cells treated with a lentiviral vector-encoding multiple anti-HIV RNA's."

The pilot study is designed to determine the safety and feasibility of RNA-based anti-HIV therapy with lentivirus-transduced hematopoietic progenitor cells (HPC) in patients undergoing autologous hematopoietic stem cell transplantation (HCT) for intermediate and high grade AIDS lymphoma.

The lentivirus vector encodes three forms of anti-HIV RNA: RNAi in the form of a short hairpin RNA (shRNA) targeted to an exon in HIV-1 tat/rev (shI), a decoy for the HIV TAT-reactive element (TAR), and a ribozyme that targets the host cell CCR5 chemokine receptor (CCR5RZ). The vector, used to transduce autologous CD34-selected HPC, is called rHIV7-shI-TAR-CCR5RZ and was manufactured by the Center for Biomedicine and Genetics at City of Hope.

Following standard mobilization of HPC and collection by apheresis (HPC-A), a portion of the cells were cryo-preserved and left unmanipulated for later use as treatment. The remaining portion of the cells were enriched for CD34+ cells, cryo-preserved, and later genetically modified by infection with rHIV7-shI-TAR-CCR5RZ.

The subjects underwent conditioning therapy and at the time of autologous HCT, the rHIV7-shI-TAR-CCR5RZ transduced cells were infused, followed 24-hrs later by the infusion of untransduced autologous HPC-A.

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Forward-looking Statements

This press release contains forward-looking statements that reflect the Company's current expectations regarding future events. Forward-looking statements involve risks and uncertainties. Actual events could differ materially from those projected herein and depend on a number of factors including the success of the Company's research strategy, the applicability of the discoveries made therein, the successful and timely completion of clinical studies and the uncertainties related to the regulatory process.

About Benitec

Benitec is an Australian biotechnology company focused on licensing its extensive intellectual property portfolio and developing therapeutics to treat serious diseases using its proprietary ddRNAi technology. For additional information, please visit www.benitec.com.

About City of Hope

City of Hope is a leading research and treatment center for cancer, diabetes and other life-threatening diseases. Designated as a Comprehensive Cancer Center, the highest honor bestowed by the National Cancer Institute, and a founding member of the National Comprehensive Cancer Network, City of Hope's research and treatment protocols advance care throughout the nation. City of Hope is located in Duarte, Calif., just northeast of Los Angeles, and is ranked as one of "America's Best Hospitals" in cancer and urology by *U.S.News & World Report*. Founded in 1913, City of Hope is a pioneer in the fields of bone marrow transplantation and genetics. For more information, visit www.cityofhope.org.

A Pilot Study of Safety and Feasibility of Stem Cell Therapy for AIDS Lymphoma Using Stem Cells Treated with a Lentivirus Vector Encoding Multiple anti-HIV RNAs

David DiGiusto Ph.D.

–Director of Hematopoietic Cell Therapies

–Beckman Research Institute

–City of Hope National Medical Center

Treatment of High Risk AIDS Lymphoma

- COH pioneered the use of dose intense chemotherapy for lymphoma for non-HIV positive patients using autologous stem cell rescue and then extended this approach to AIDS Related Lymphoma (ARL).
- The approach is as follows:
  - Standard therapy cycles are completed (e.g CHOP)
  - After the last cycle, the patient's peripheral blood stem cells are collected using G-CSF
  - After carmustine (BCNU), etoposide (VP16), and cyclophosphamide dose-intense chemotherapy,

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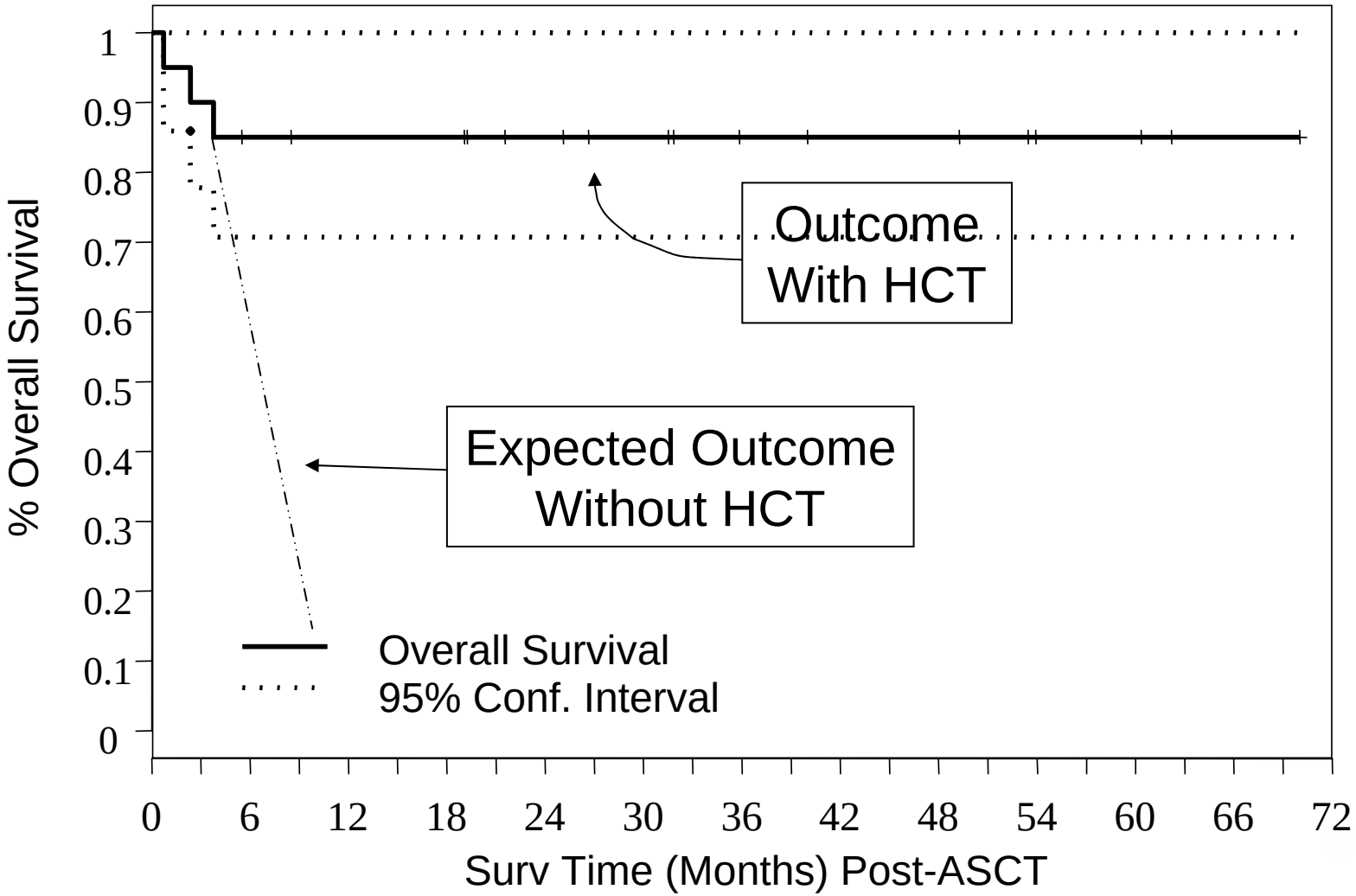
Autologous HCT for High Risk AIDS Lymphoma: COH Experience



Modified from A. Krishnan et al. Blood 2005; 105:874-8

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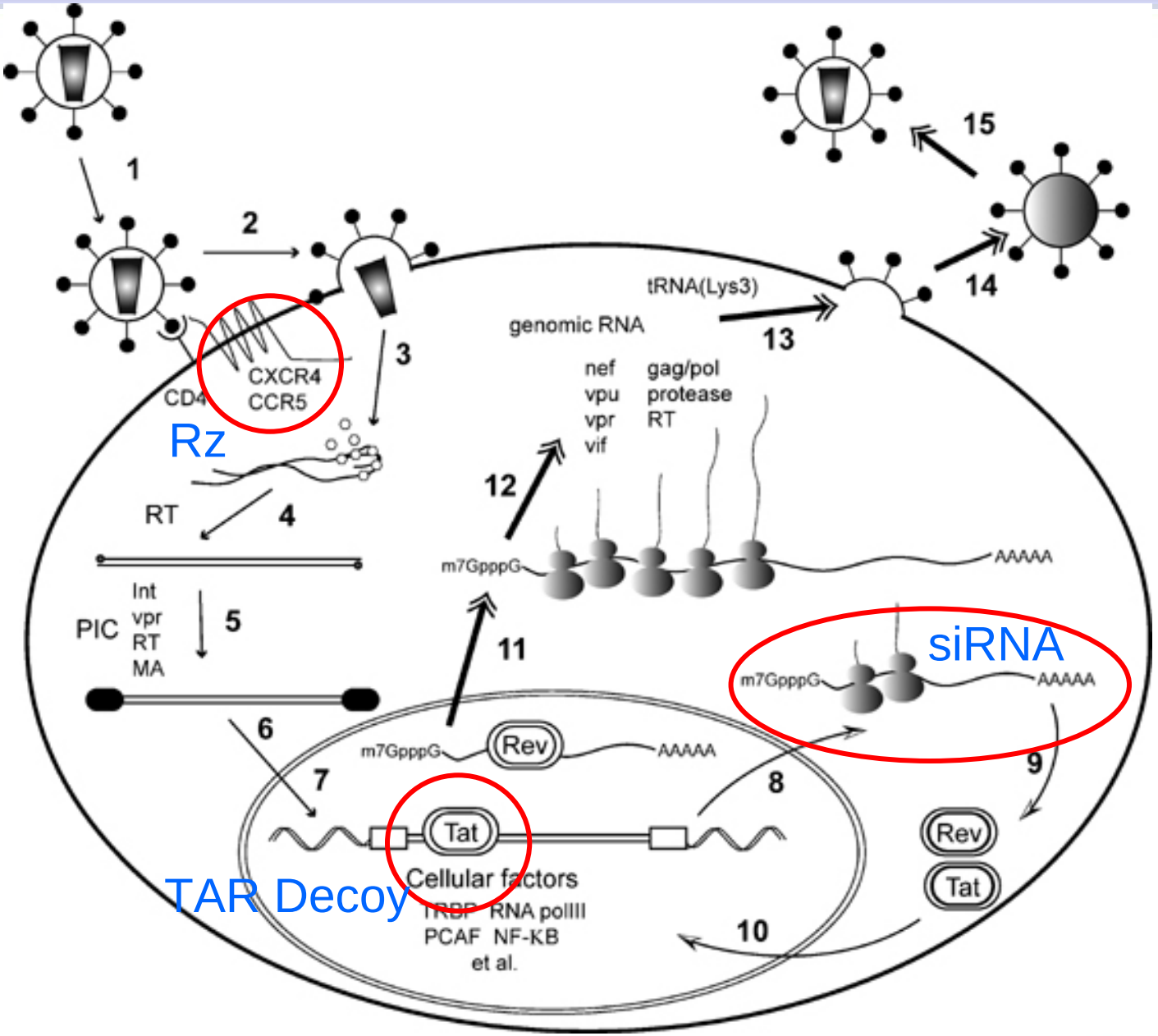
HIV Lifecycle

Progress and prospects: RNA-based therapies for treatment of HIV infection

L Scherer, J J Rossi and M S Weinberg



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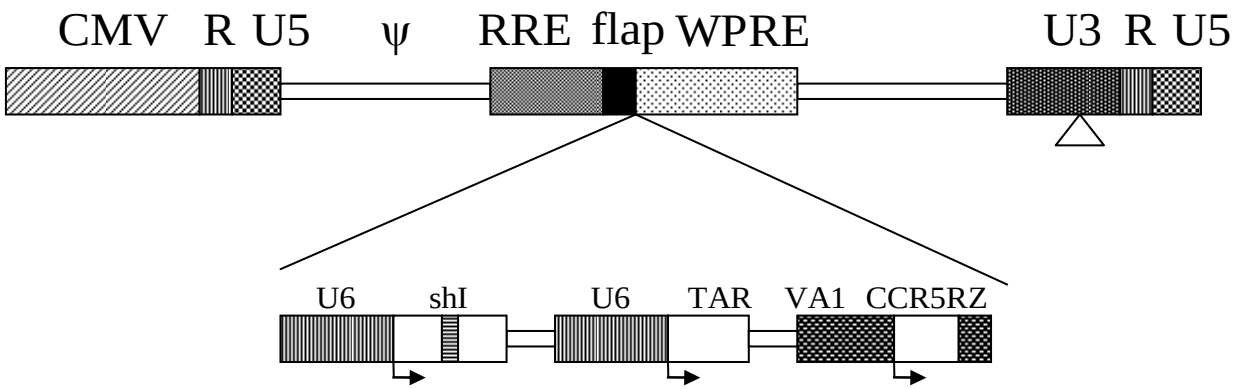
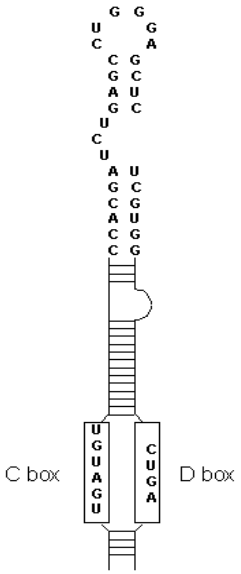
Lentiviral Vector for Clinical Trials

rHIV7-shI-TAR-CCR5RZ



shI



TAR decoy

U16 snoRNA

CCR5 mRNA

Ribozyme

by M. Li/J. Rossi

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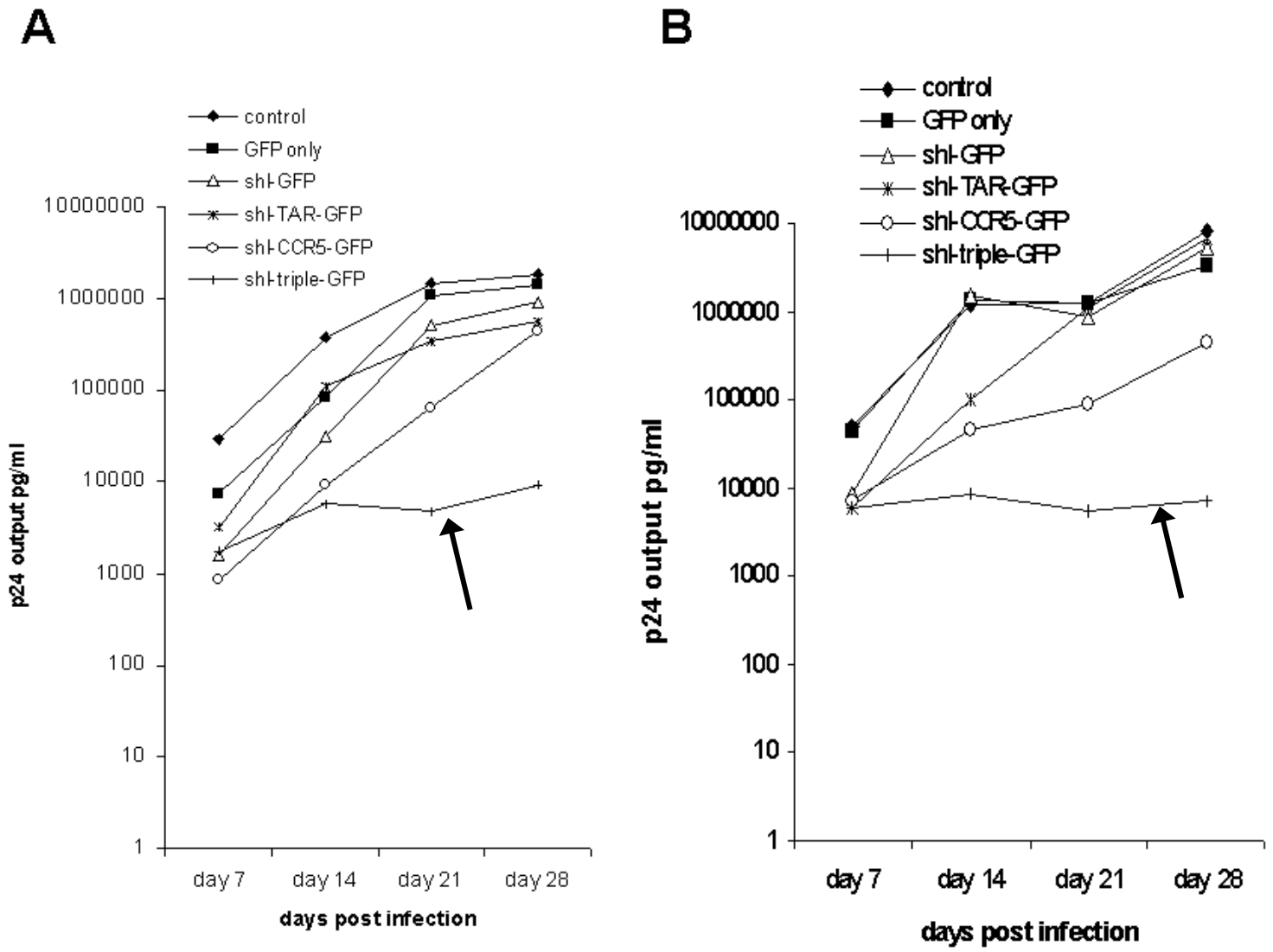
Antiviral Effect of Triple Anti-HIV RNAs in Monocytes Derived From Transduced CD34+ cells



From M. Li et al Mol Ther 2005

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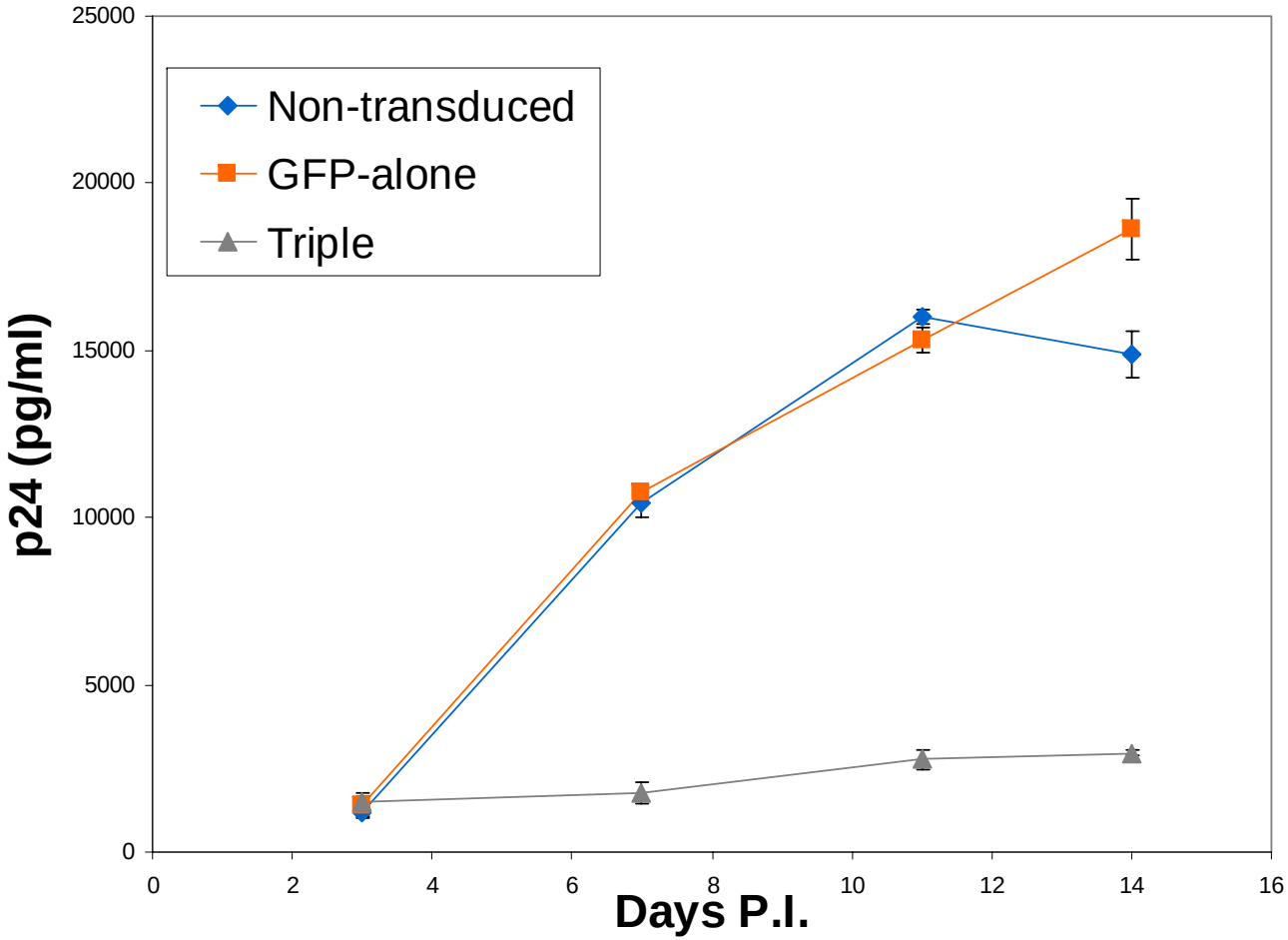
Antiviral Effect of Triple Anti-HIV RNAs in Thymocytes Derived From Transduced CD34+ cells



Anderson et al. Mol Ther 2007; 15: 1182-88

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Clinical Trial: IRB-04047/BB-IND 13283

Specific Aims:

The primary objective is to determine **safety and feasibility** of lentivirus-transduced hematopoietic stem cells in the setting of autologous HCT for the treatment of AIDS lymphoma

The secondary objective is to determine the **quantity and duration of vector-marked** peripheral blood cells after marrow engraftment

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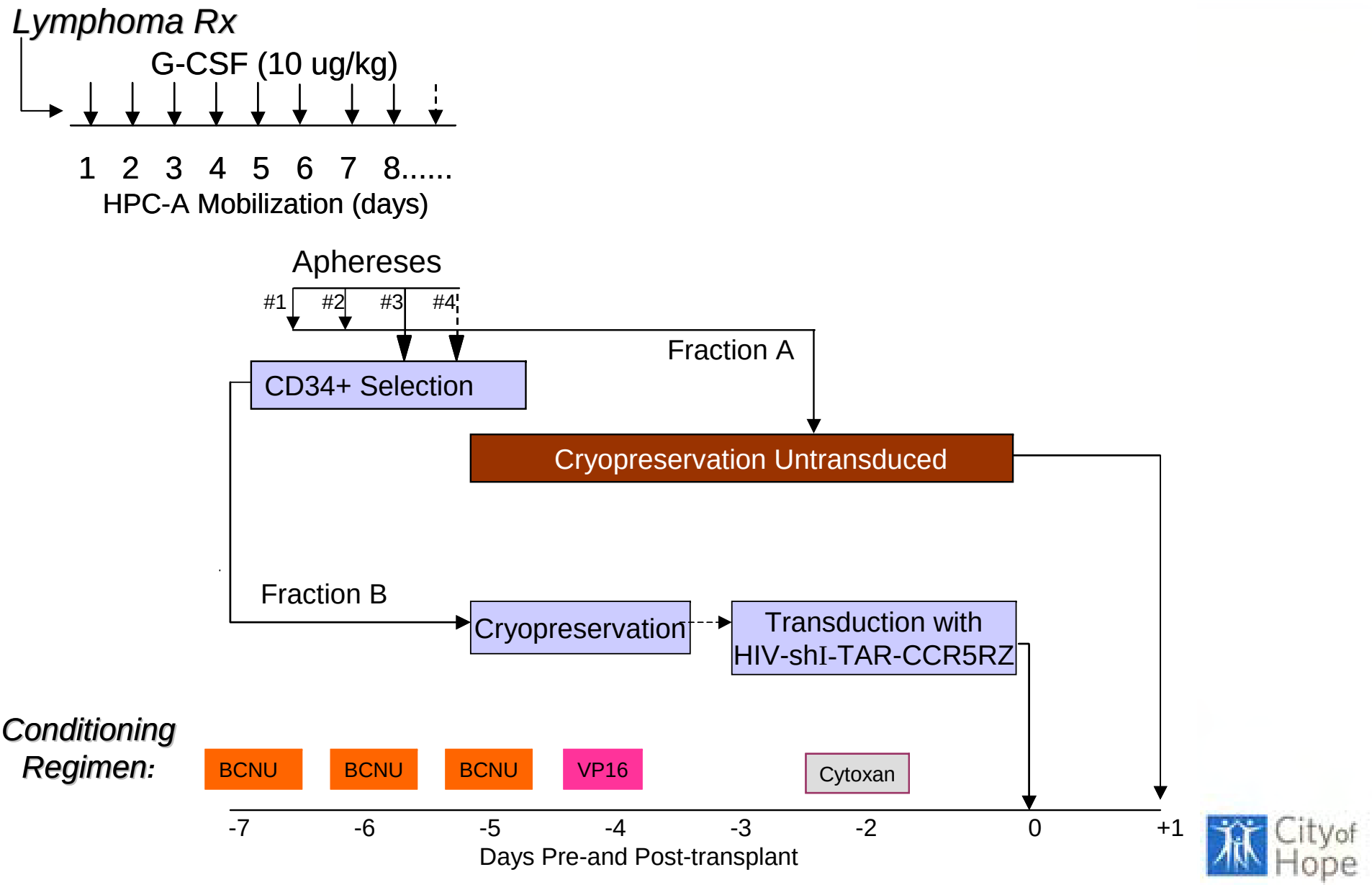
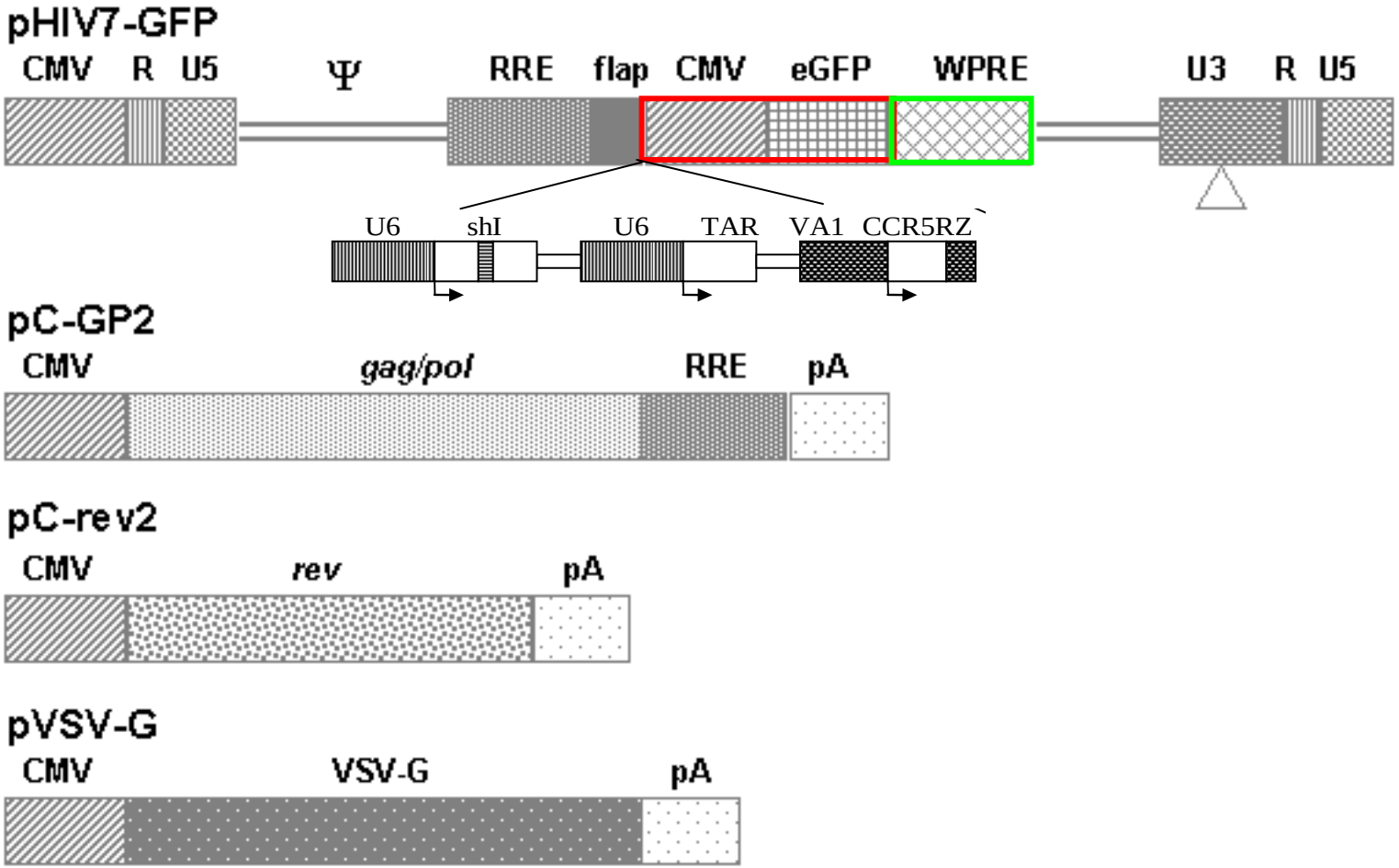
Study Design: AIDS Lymphoma



4 Plasmid Production System



WPRE - woodchuck hepatitis post-transcriptional regulatory element

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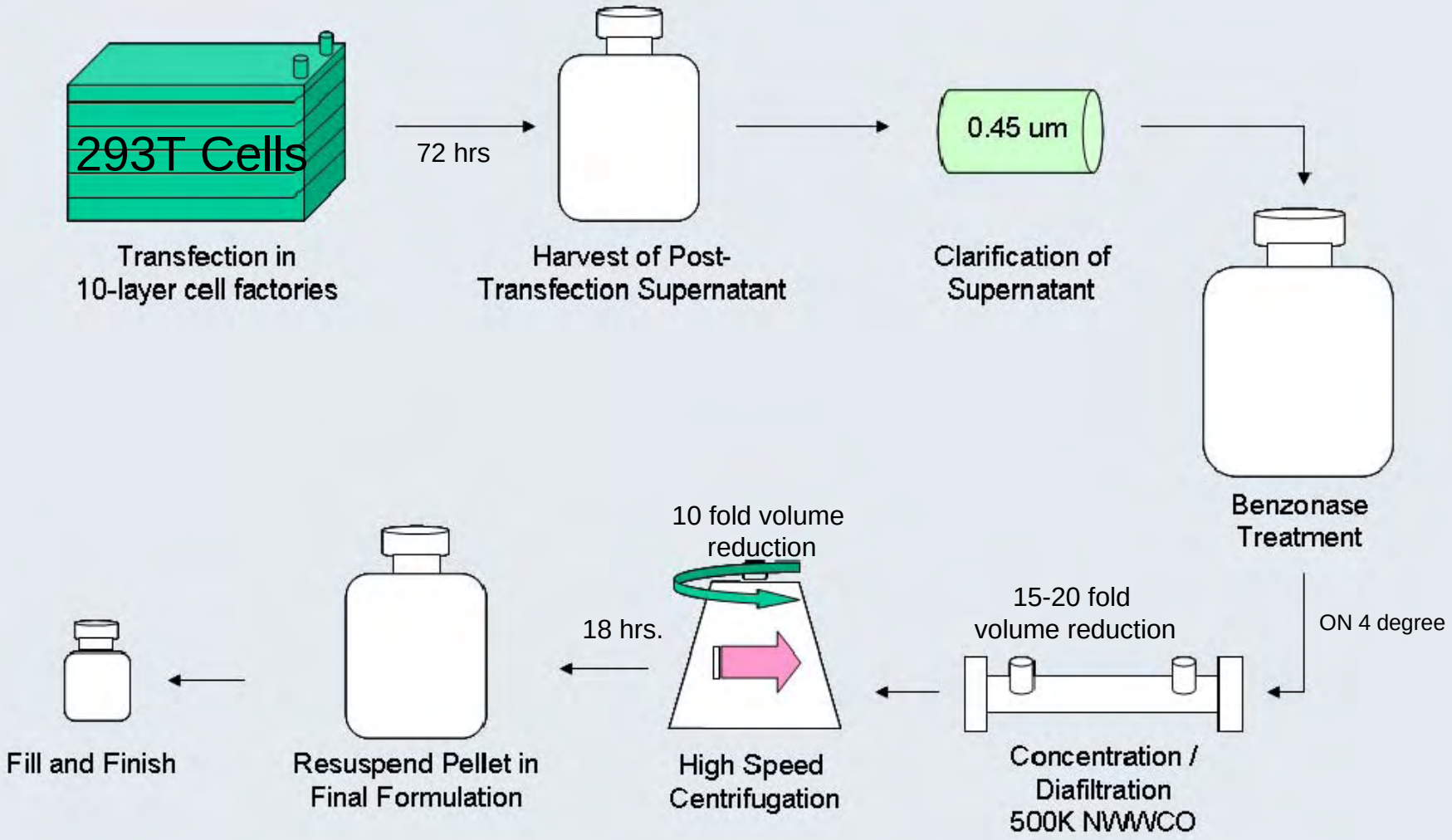
Lentiviral Vector Production

COH Center for Biomedicine and Genetics



by D. Hsu/L. Couture

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Patient Accruals

UPN	Sex	Age at Transplant	Diagnosis	Months Post transplant
304	M	55	Diffuse Large Cell Type (Immunoblastic Plasmacytoid)	11.0
305	M	45	Diffuse Large B-Cell (Anaplastic)	10.2
306	M	45	Plasmablastic Lymphoma	5.0
307	M	25	Diffuse Large B Cell Lymphoma	3.6

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HSC Products Collected and Infused

UPN #	RX Collected (CD34+/kg)	Exp Collected (CD34+/kg)	Exp Infused (CD34+/kg)	Total CD34+ Cells Infused/Kg
304	3.9E+06	3.6E+06	7.7E+05	4.7E+06
305	3.4E+06	3.8E+06	7.3E+05	4.1E+06
306	5.6E+06	8.8E+06	1.2E+06	6.8E+06
307	6.5E+06	1.3E+07	1.6E+06	8.1E+06

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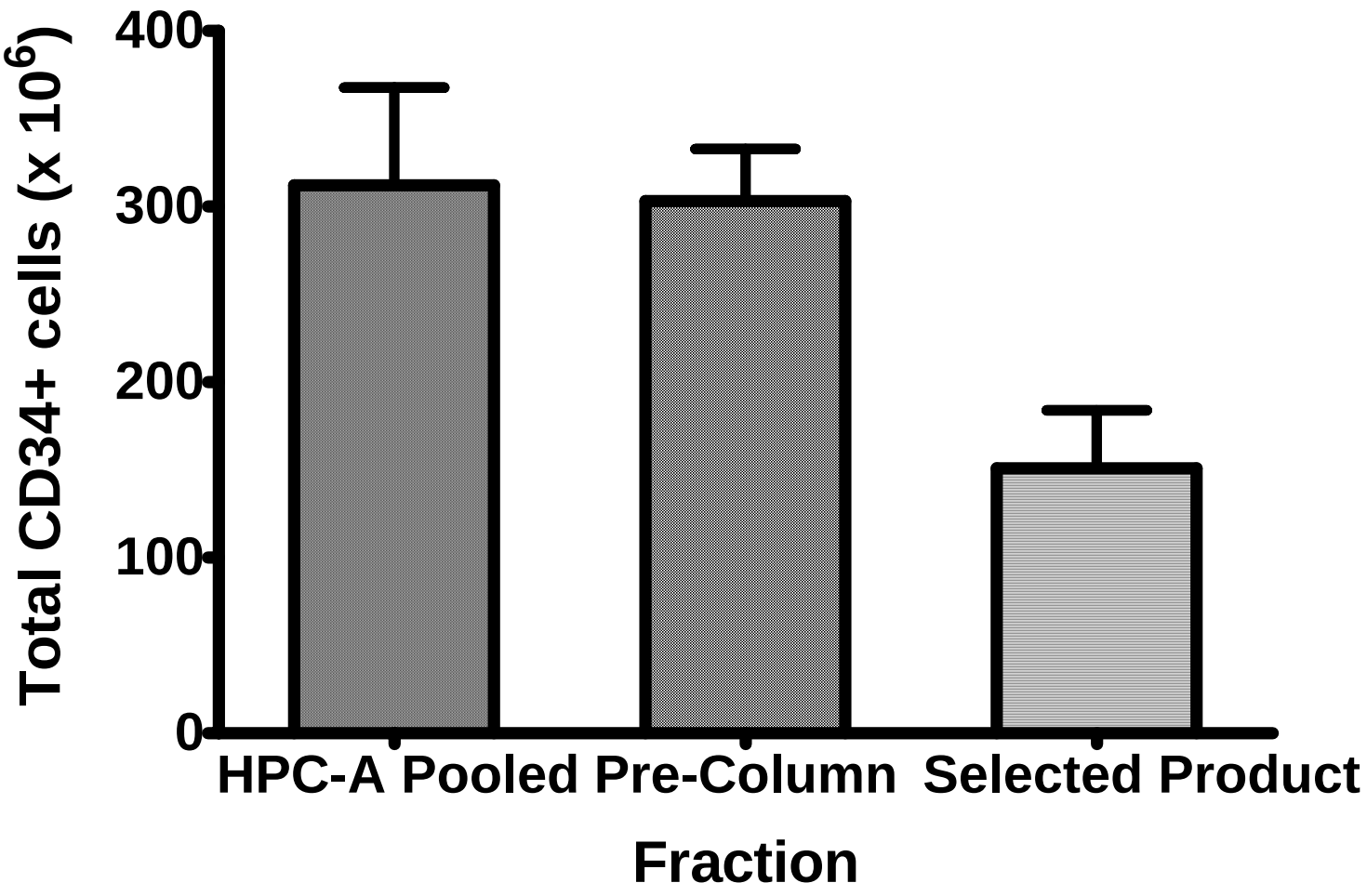
Summary CD34 Recovery



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Infusion outcome

- Three of four gene modified products did not meet viability requirements (70%).
  - Products Infused with FDA Approval.
- Minimal AE and no SAE observed
- Engraftment (ANC>500) at mean of 11 Days (similar to non-HIV Lymphoma transplant)

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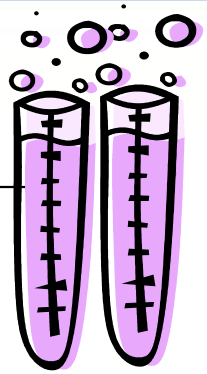
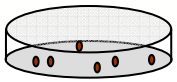
In Vitro Correlative Studies

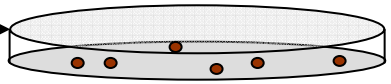


Transduced/Non-TD Cell Samples



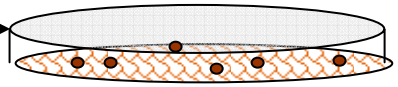
14 Day Clonogenic assay (CFU)

Liquid Culture



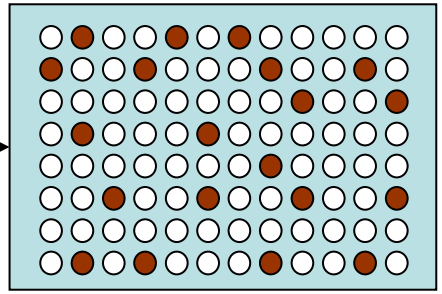
Flt-3L, SCF, TPO, IL-3, IL-6, GM-CSF, Epo

Stromal Co-Culture



SCF+IL-6

Limiting Dilution Plating



Flt-3L, SCF, TPO, IL-3, IL-6, GM-CSF, Epo

Assay Schedule

D7 PCR Phenotype	D14 PCR Phenotype Sorting	D21 PCR Phenotype	D28 PCR Phenotype Sorting
D7 PCR Phenotype	D14 PCR Phenotype Sorting	D21 PCR Phenotype	D28 PCR Phenotype Sorting
			D28 PCR

28 Day Culture with weekly demi-depletion of media

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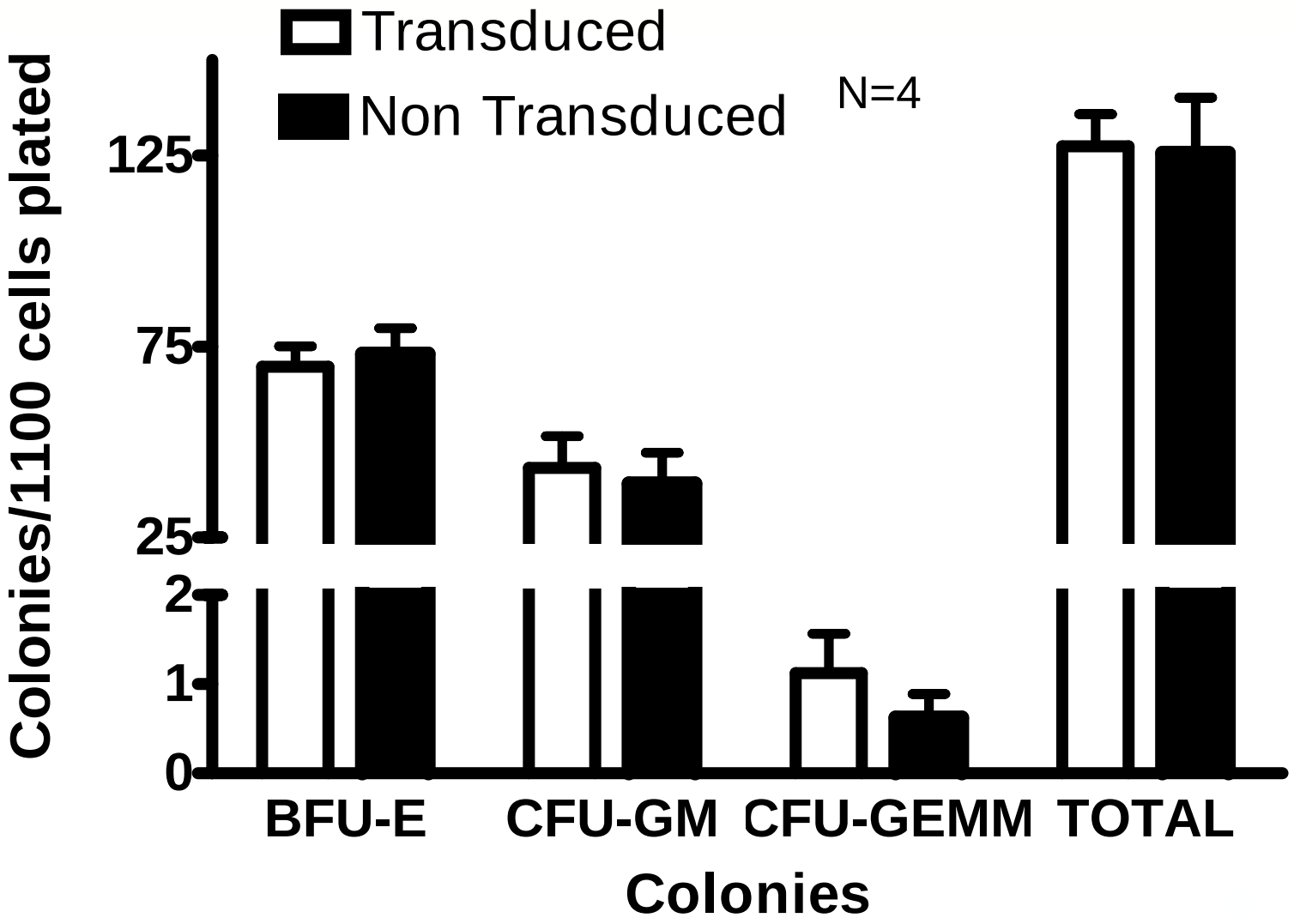
CFU-Assay



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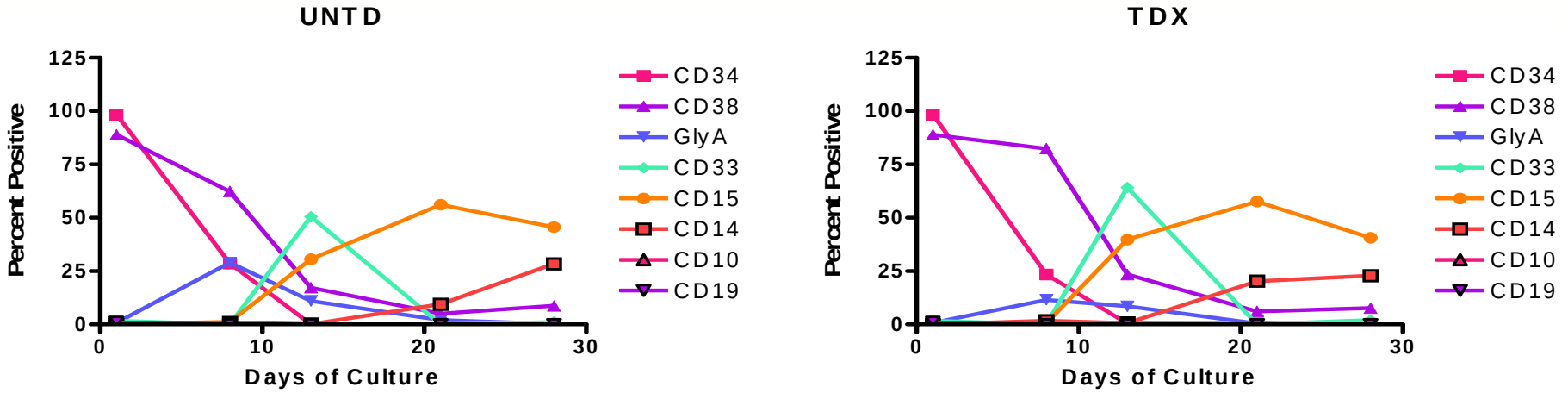
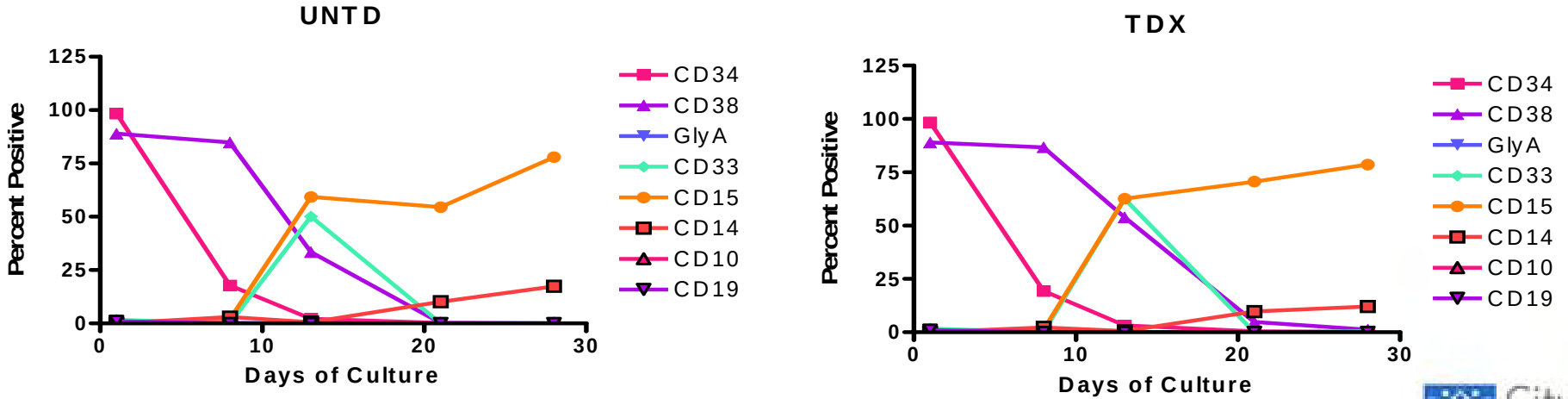
Phenotype Kinetics from 28D Culture of CD34+ Cells

Liquid Culture



Stromal Culture



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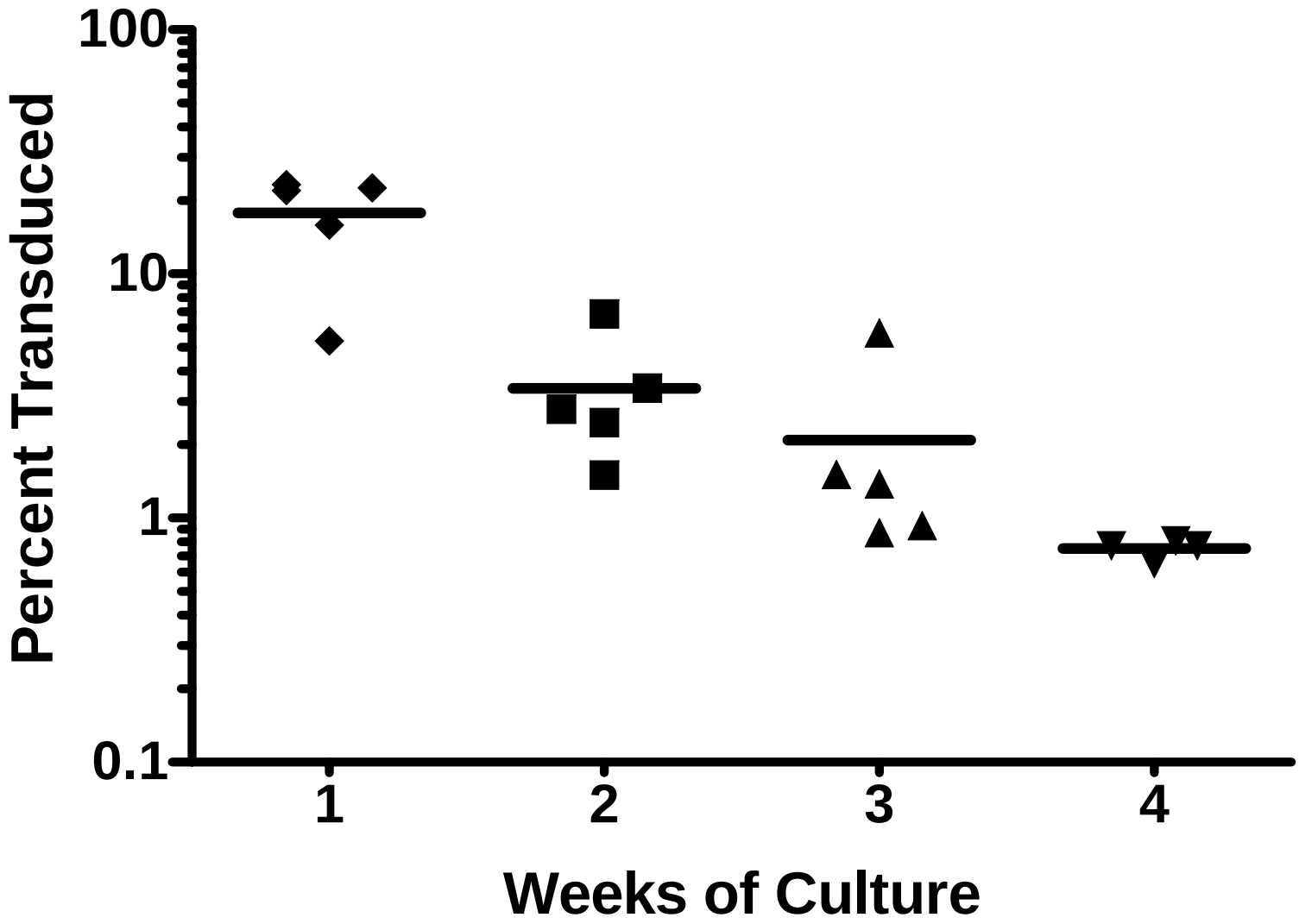
Gene Marking Kinetics in Liquid Culture



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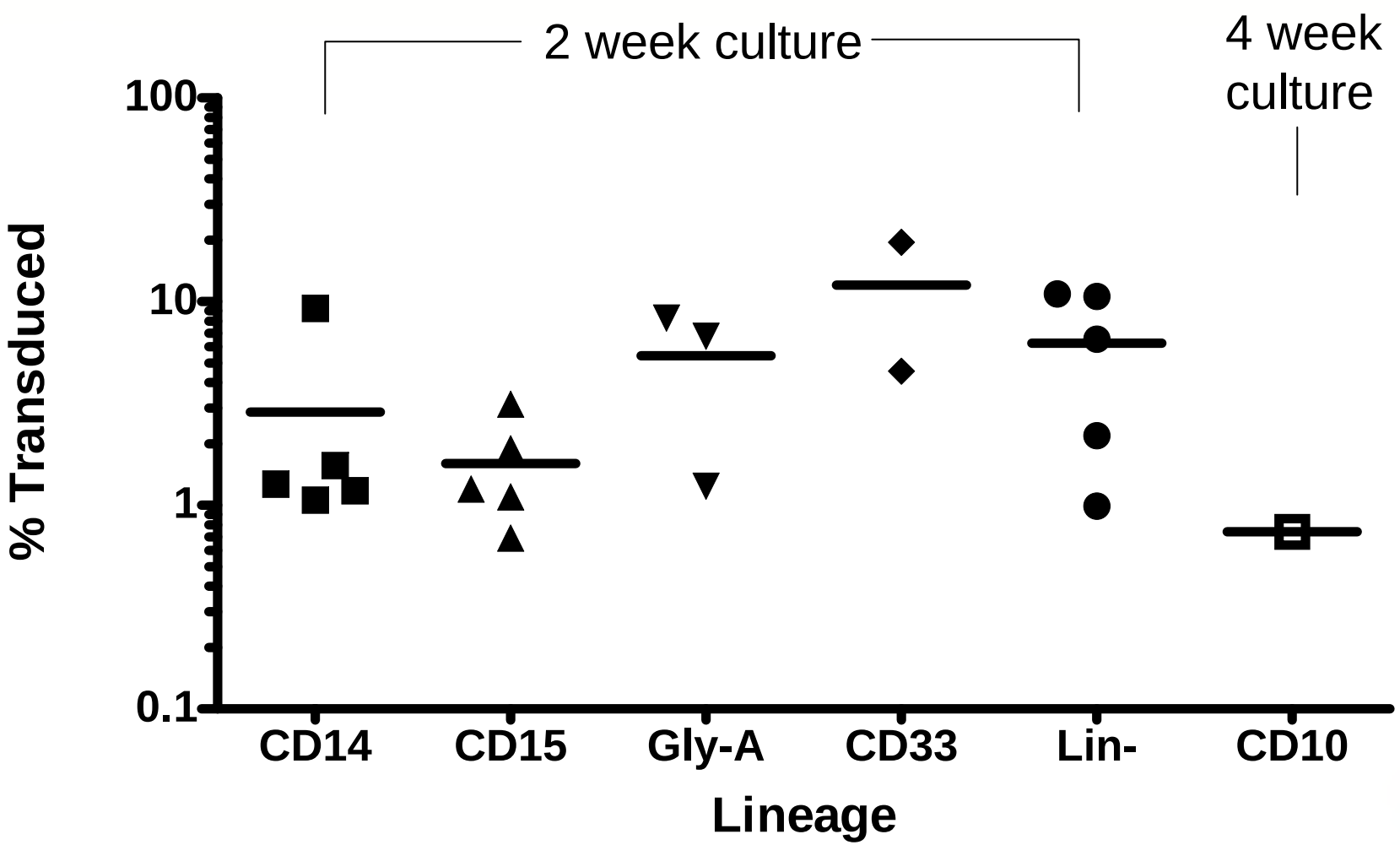
Lineage Specific Marking Data



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TDX analysis of LDA derived samples

UPN#	Description	50 cells/well	10 cells/well	5 cells/well	All wells
304	# of +ve growth	84	34	ND	118
	% of wells plated	95%	39%	ND	
	# of wells TG positive	0	0	ND	0
	% TG positive	**0%**	**0%**	ND	**0%**
305	# of +ve growth	86	83	ND	169
	% of wells plated	98%	94%	ND	
	# of wells TG positive	2	0	ND	2
	% TG positive	**2.33%**	**0%**	ND	**1.18%**
306	# of +ve growth	77	10	13	100
	% of wells plated	88%	11%	15%	
	# of wells TG positive	1	0	0	1
	% TG positive	**1.30%**	**0%**	**0%**	**1.00%**
307	# of +ve growth	75	24	26	125
	% of wells plated	85%	27%	30%	
	# of wells TG positive	1	2	0	3
	% TG positive	**1.33%**	**8.33%**	**0%**	**2.40%**

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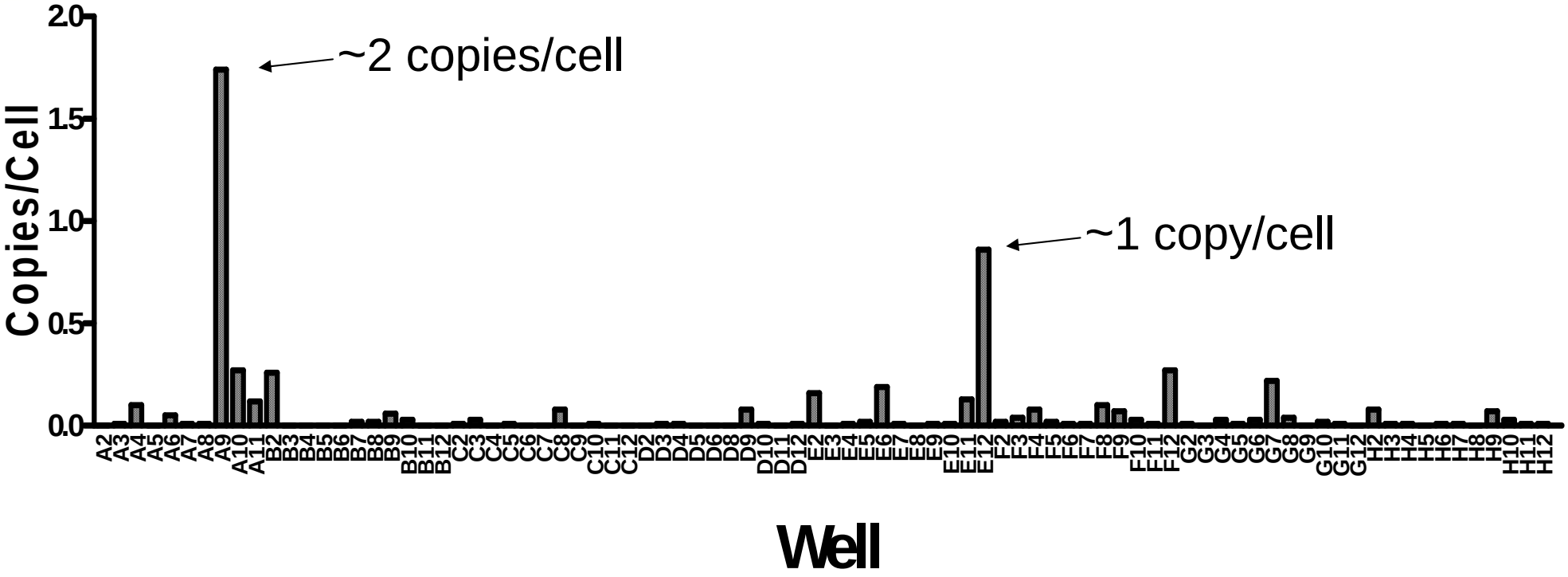
Copies per cell of integrated vector



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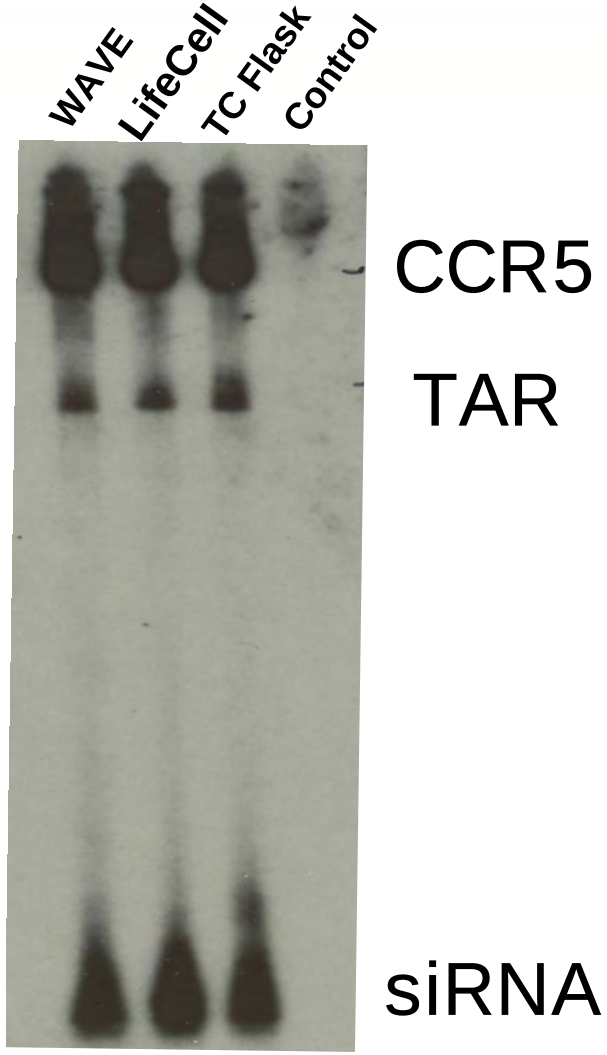
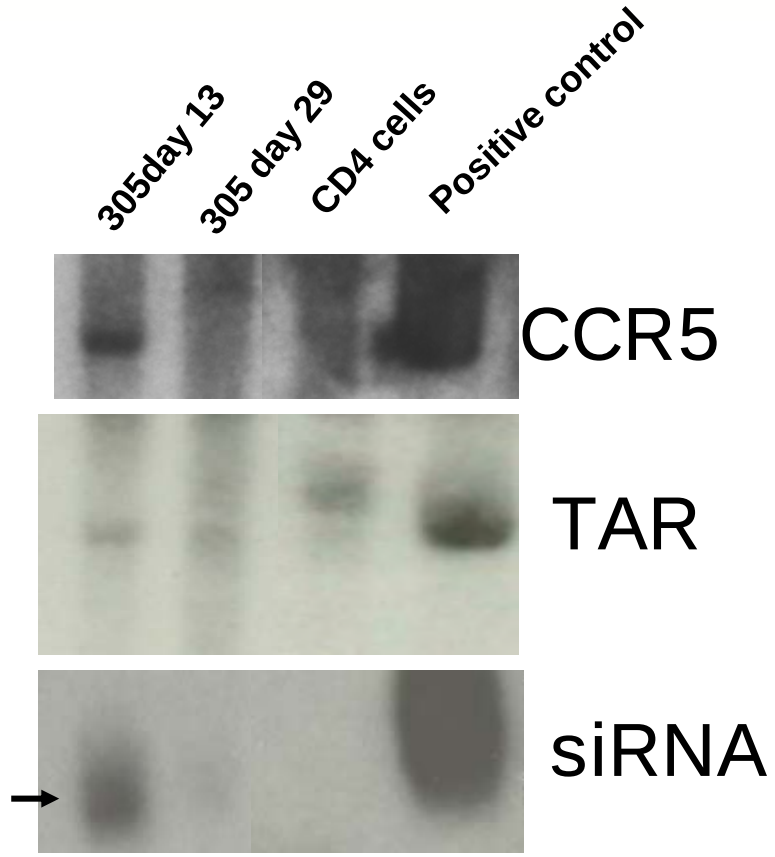
Northern Analysis of RNA Expression in Cells from *In Vitro Cultures (UPN0305)*



Highly Transduced Primary T-cells



UPN305 in vitro culture of TD CD34^{+} cells

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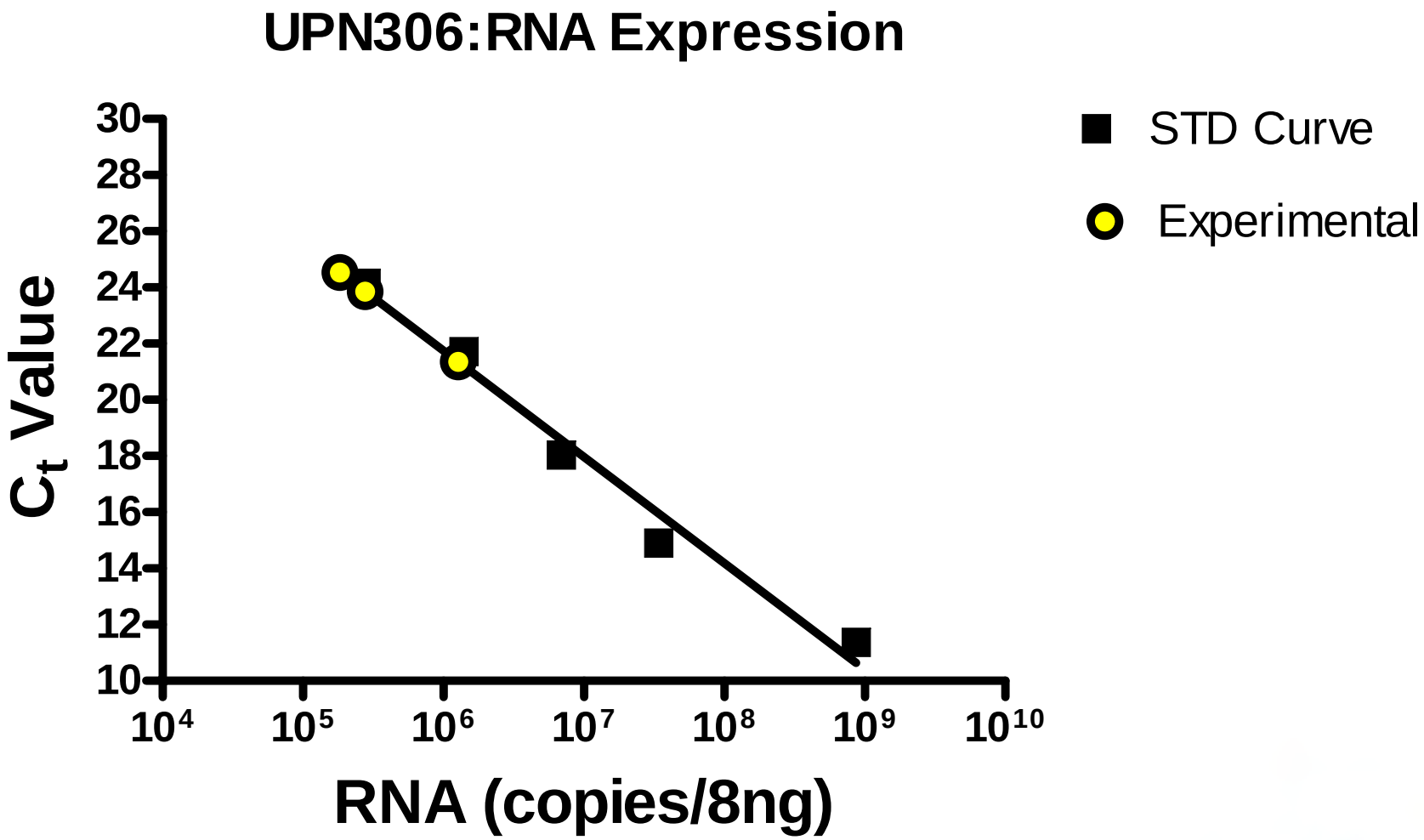
shRNA Expression in Cells from *In Vitro* Cultures by RT PCR Analysis



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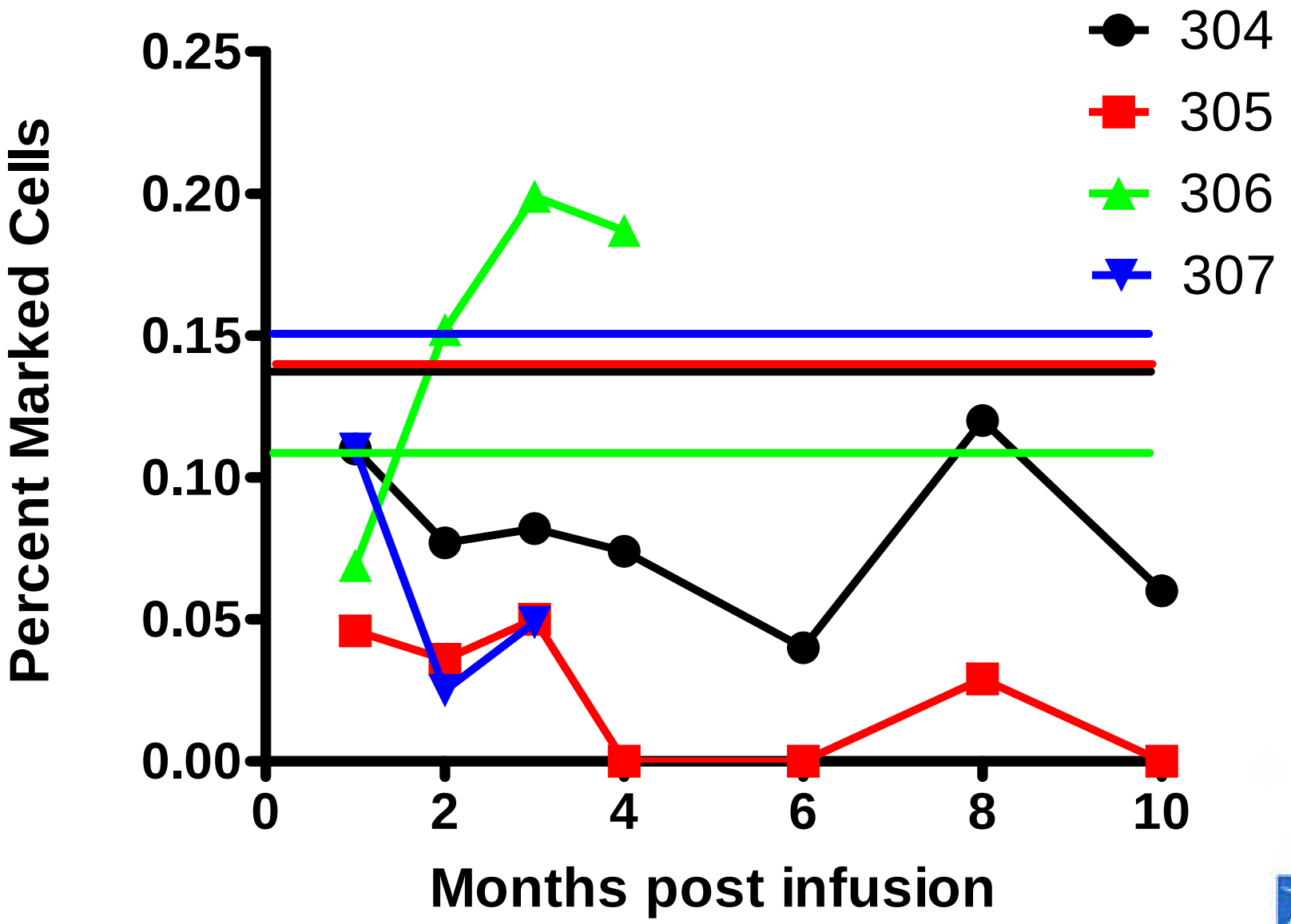
Kinetics of Gene Marking in PBMC



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shRNA Expression in Peripheral Blood and Bone Marrow.

		shRNA Copies/8ng RNA						
UPN	Population	Day 1	1M	2M	3M	4M	6M	8M
304	PBMC	9*	1420**	220*	406**	146*	15.4*	82
	PBGC	N/A	1420**	71*	N/A	N/A	N/A	76
	BMMC			159**				
	BMGC			45**				
305	PBMC	N/A	220**	N/A	N/A	N/A	N/A	N/A
	PBGC	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	BMMC			87*				
	BMGC			N/A				
306	PBMC	166**	1112**	232**	226*			
	PBGC	93**	73*	70*	21200**			
	BMMC		1018**					
	BMGC		66**					
307	PBMC	1450**	83*					
	PBGC	4950**	N/A					
	BMMC							
	BMGC							
	*	1 out of 3 wells positive						
	**	≥2 out of 3 wells positive						

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Conclusions

- The isolation, genetic modification (with Lentiviral vector) and infusion of $CD34^+$ cells from ARL patients is safe and feasible.
- Gene marking *in vivo*, while low, was within the expected range predicted by in vitro analysis of transduced $CD34^+$ cells.
- Gene marked cells persist (and express siRNA) for up to 10 months post infusion.
- Improvements in transduction efficiency and transplant regimen may lead to higher levels of engraftment of marked cells.

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Acknowledgements

Pre-Clinical Research

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Jiing-Kuan Yee Research Laboratory

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Regulatory Affairs

Broyer, Suenell; Stan, Rodica

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