Biomarker Strategies for Cell Therapy in Autoimmune Diseases

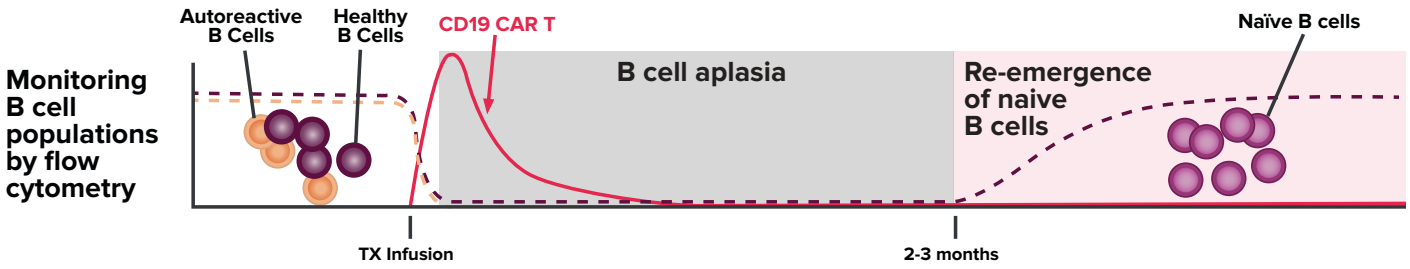
Measuring the B Cell Reset

CellCarta

B cell depleting therapies, originally developed to fight cancerous B cells, have now been redirected for therapeutic applications in autoimmune diseases, and are used to address targets such as CD20, CD19 and BAFF. This approach is now extending to cell therapies from multiple technical platforms (autologous, allogenic, and *in vivo*).[1, 2]

At the American Society for Hematology 2023, proof of concept data for treatment of various autoimmune diseases (SLE - systemic lupus erythematosus, SSc - systemic sclerosis, IIM - Idiopathic inflammatory myopathy) with MB-CART19.1, an autologous CD19 CAR T cell product, was presented.[3]

The mechanistic hypothesis supporting the repurposing of B cell-depleting cell-based therapies for autoimmune indications is referred to as **B cell reset**. The goal is to drive B cell counts to such a low level that disease causing auto-reactive B cell populations are eliminated, thereby allowing the B cell fraction to repopulate with naïve B cells devoid of pathogenic subsets, which improves disease outcomes without causing immunosuppression.



Illustrative graphic adapted from Taubmann J. et al.

[1] Lee D, Rojas OL, and Gommerman JL. Nature Reviews Drug Discovery, vol. 20, 2021, pp. 179–199.
[2] Harrison C. Nature Biotechnology, vol. 42, 2024, pp. 995–997.
[3] Mueller F,et al. Blood, vol. 142, 2023, pp. 220–221.

Assessment	Objective	Assays	Matrix	CellCarta Support
Therapeutic Cell Kinetics	Monitor therapeutic cell product kinetics in vivo (transduction, expansion, & long- term persistence)	**Genomics** ▪ WPRE by ddPCR (in silico validation of sequence compatibility) ▪ Custom ddPCR assay design and development ▪ Micro-haplotyping	▪ Cryo-preserved PBMC ▪ Fresh Whole Blood in PAXgene Blood DNA Tubes (IVD)	▪ Global PBMC processing ▪ Global support for genomics platform
		Flow Cytometry ▪ Cell therapy product enumeration panel	▪ Fresh Whole Blood ▪ Fixed Whole Blood (CytoChex BCT vacutainers) for enhanced stability	▪ Expert custom flow panel development incorporating CAR detection reagents for cell kinetics monitoring
B Cell Aplasia	Pharmacodynamic measurement of absolute target B cell depletion	**Flow Cytometry** ▪ B cell enumeration with TBNK ▪ Custom B cell panel with enumeration	▪ Fixed Whole Blood (CytoChex BCT vacutainers) ▪ Cryopreserved PBMC (no absolute counts with this matrix)	▪ OTS TBNK panels with low level of detection (1.1 cells / µL of blood). ▪ Global TBNK analysis (NA, EU, AUS, CH)
		Immunoassays ▪ Total Serum IgG	▪ Serum / Plasma	▪ Global ligand binding assay capabilities
Cellular Phenotyping	Monitor activation / exhaustion status of cell therapy product **or** Monitor B cell repopulation with naive phenotypes	**Genomics** ▪ Single-Cell RNAseq with TCR/BCR repertoire ▪ Bulk BCRseq	▪ Cryo-preserved PBMC ▪ Fresh Whole Blood in PAXgene Blood RNA Tubes (IVD)	▪ Global presence for PBMC processing. ▪ Global presence for genomics capabilities
		Flow Cytometry ▪ B cell phenotyping to quantify early naive and naive B cells, as well as B cell class switching ▪ Cell therapy product phenotyping panels	▪ Cryopreserved PBMC ▪ Fixed Whole Blood (CytoChex BCT vacutainers) for enhanced stability	▪ OTS panels for B cell and T cell phenotyping. ▪ Expert custom flow panel development incorporating CAR detection reagents for cell kinetics monitoring and phenotyping markers
Soluble Biomarkers	PD markers for evidence of cell killing cytokine release **and** Other peripheral measures of disease activity	**Immunoassays** ▪ Cytokine Analysis (MSD, Olink, Ella) ▪ Common PD Markers (IgG, BCMA, NFL, GFAP, Tau)	▪ Serum / Plasma	▪ Global ligand binding assay capabilities

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