tebubio
Facilitators of Life Sciences Research

Unlocking the Power of Immunotherapy: Cutting Edge Tools for Cancer Research

Veronique Baron, PhD - HDR

BPS Bioscience

With Tebubio, advance your Research Projects faster

Thanks to our Holistic Range of Solutions

A large portfolio

Access to **over 1,300,000 standard** references and **non-catalogue** ones.

From trusted & ethical suppliers

Get solutions from **reputable global suppliers**, carefully selected for their **relevance**, **ethical** and **legal** compliance (e.g. Animal Welfare).

Dedicated scientific support

Our **Scientific Team** guides you to source, select and use solutions.

Based in Europe

Our **Teams** and **Contract Research Services Lab** are in Europe.

Team committed to success

A **PhD project manager** ensures the success of your project from A to Z.

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- **mRNA** production & delivery
- **Cell line** engineering & **protein** production
- **Cellular studies**
- **Biomarker** analysis

Reliable Supply Chain Management

- **IATA**
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Order from a single source

Consolidate your orders with us.

Tailored agreements

From specific **one-off terms** to **procure-to-pay**, supported by **e-procurement** solutions.

Our Speaker

Veronique Baron, PhD

Associate Director Marketing

- *Veronique Baron, PhD, HDR, is a cellular and molecular biologist with extensive research experience in drug discovery and development, cell signaling pathways, and cancer cell biology.*
- *Dr. Baron has worked in a variety of research environments including at INSERM, not-for-profit institutions, and biotech companies. She has published numerous patents and scientific manuscripts, trained scientists, participated in grant review panels, and helped bring a candidate drug to clinical trials.*
- *She joined BPS Bioscience in 2021 as Scientific Applications Manager and is now Associate Director of Marketing.*

Outline

1. About BPS Bioscience
2. Cancer Immunotherapy
3. Immune Checkpoint Antibodies
   Case study: PD-1 checkpoint
4. Adoptive Cell Therapy
   Case study: anti-CD19 CAR T cells
5. Custom Services

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About BPS Bioscience

Mission Statement

BPS Bioscience advances new scientific discoveries that lead to therapy by creating innovative solutions for research.

- Established in 2005 by Henry Zhu, PhD.
- Science Driven: Highly skilled and knowledgeable team of Scientists (~40% of team members have PhDs).
- We design and manufacture our products in San Diego, CA.
- Global Reach: Our extensive offering of products and services provide value worldwide.

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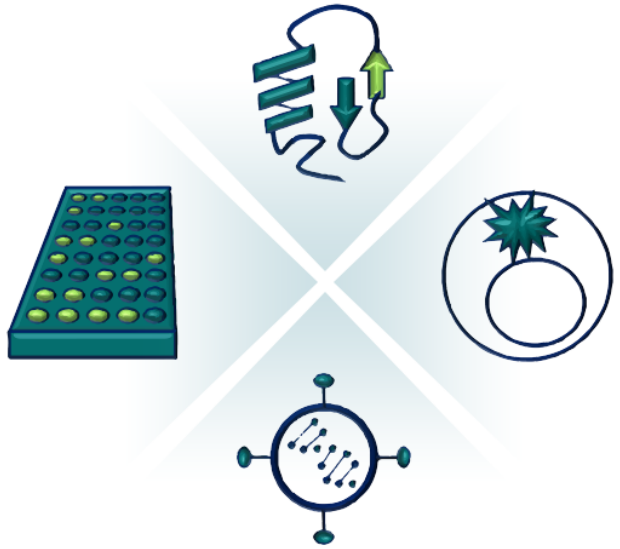
Our Products & Services

Proteins/Antibodies

Assay Kits



Cell Lines

Virus-Based Tools

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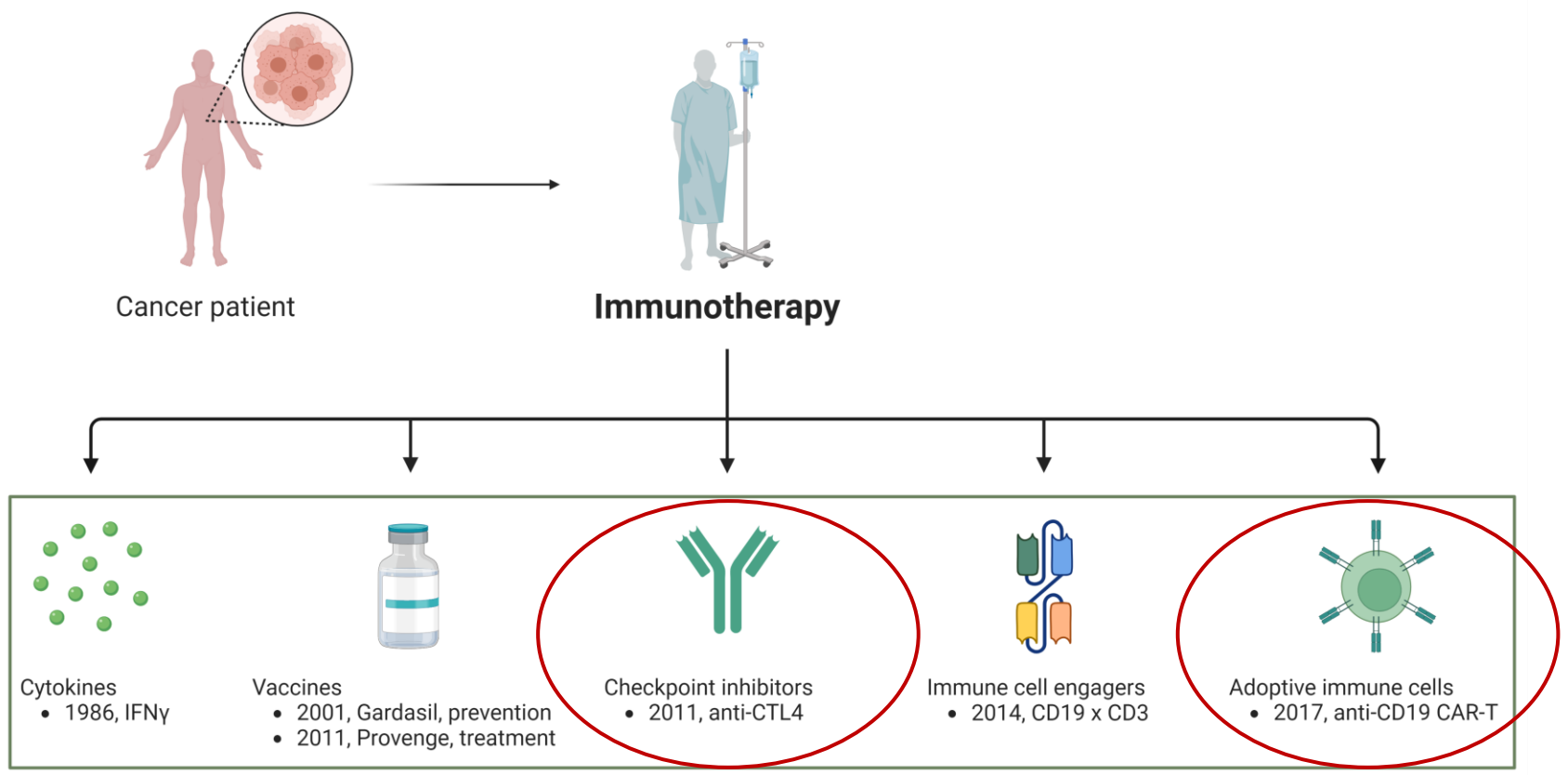
Immunotherapy in Oncology

Immunotherapy harnesses the body's own immune system to target and kill cancer cells.



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Checkpoint Immunotherapy

- What are immune checkpoints?
- Antibody drug development
- Tools for research on PD-1

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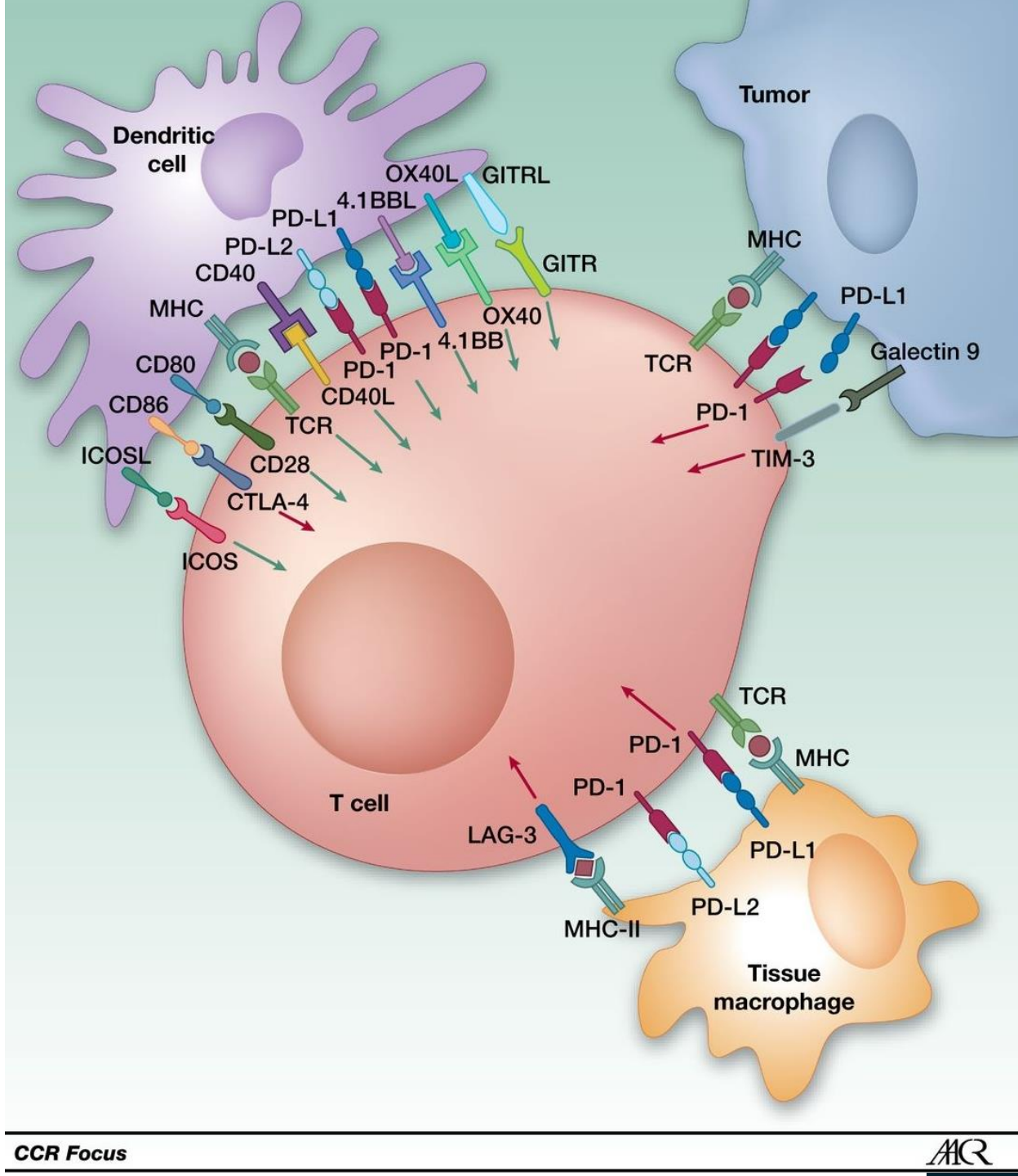
Immune Checkpoints

- Regulate the immune system to promote a response and to dampen inflammation and prevent autoimmunity.
- Engage when a receptor on the immune cell binds to partner protein on another cell.
- Two types:
  - Co-stimulatory, promote immune response: CD28, ICOS, CD137
  - Co-inhibitory, inhibit immune response: PD-1, CTLA4, LAG3, CD40L, TIGIT, OX40, VISTA



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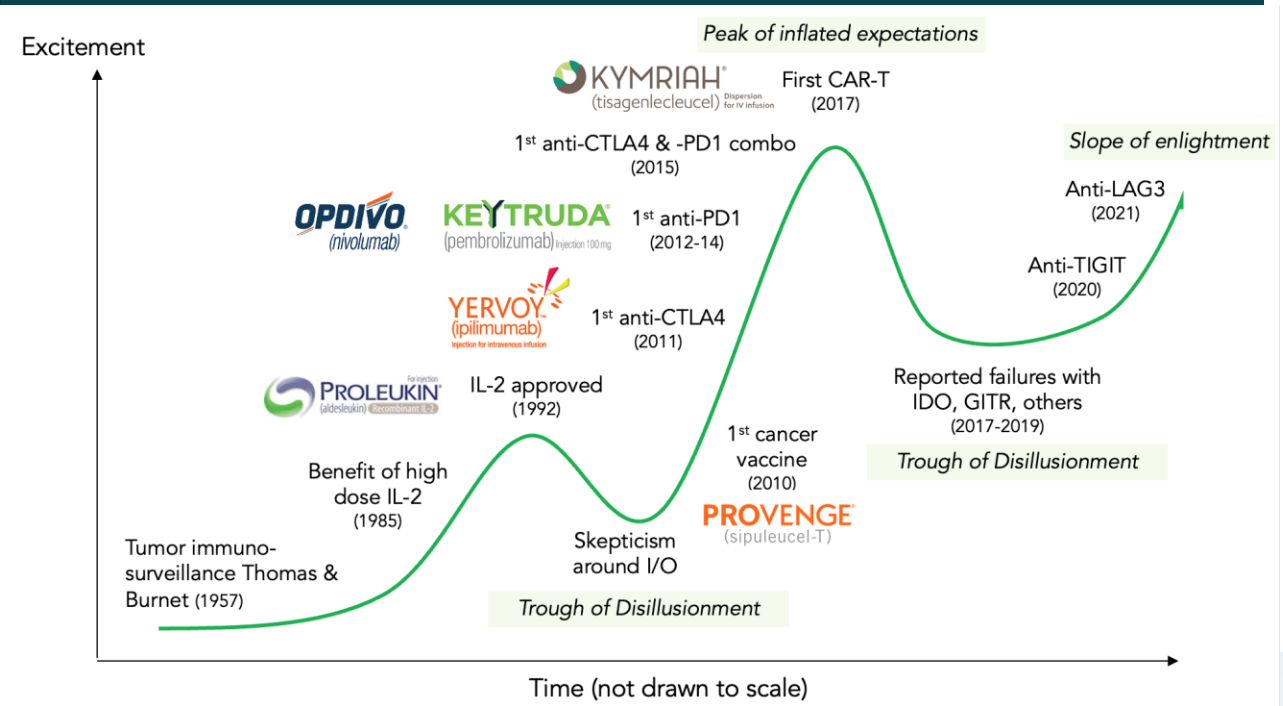
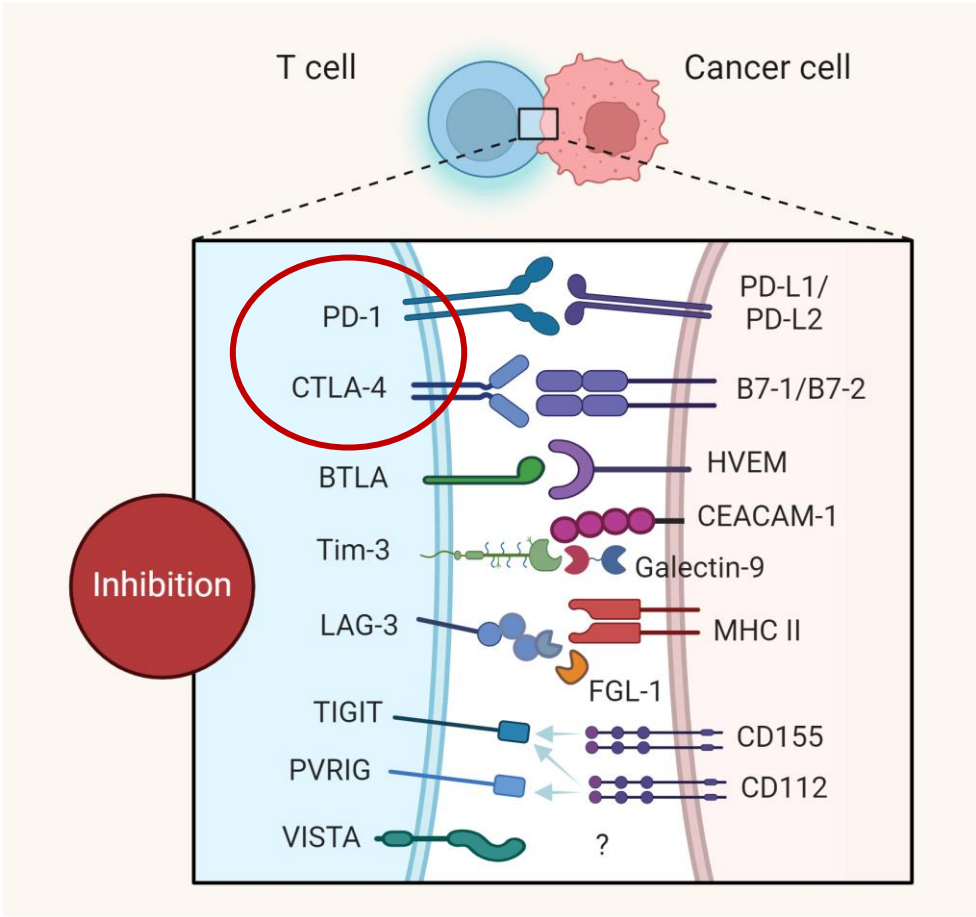
In the Clinic





Market revenue of existing checkpoint inhibitor antibodies estimated between $27 billion and $38 billion in 2024

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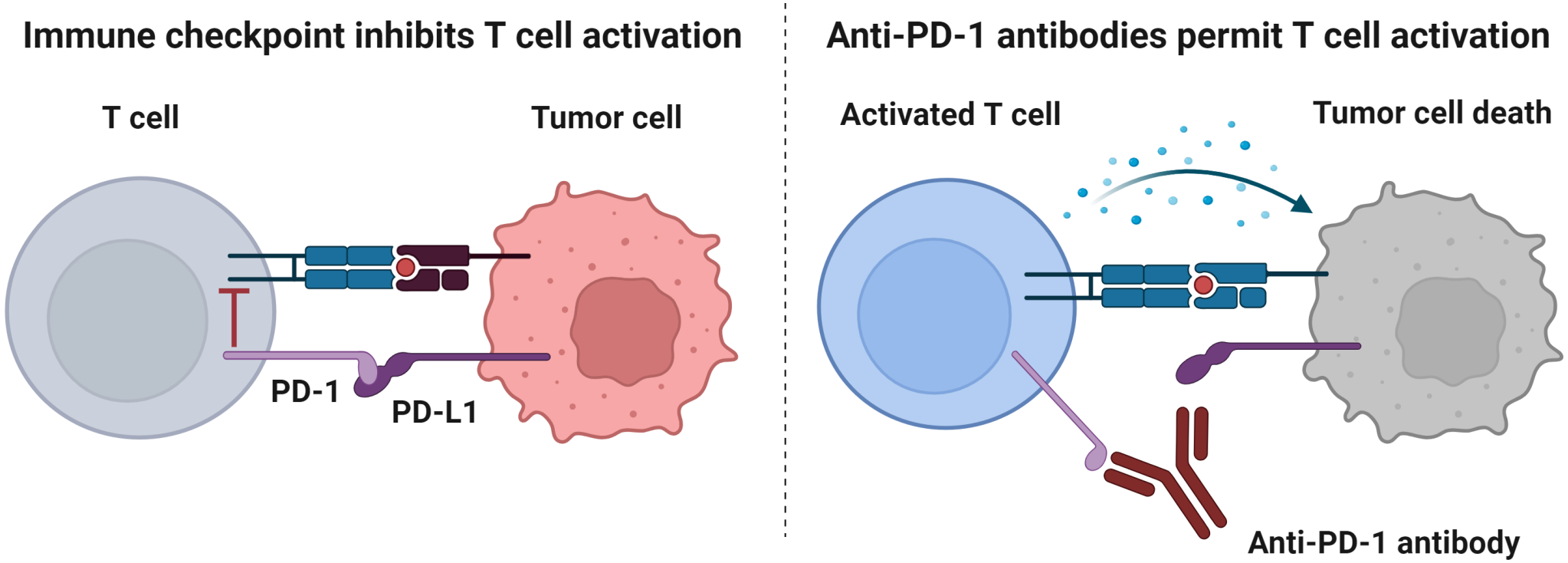
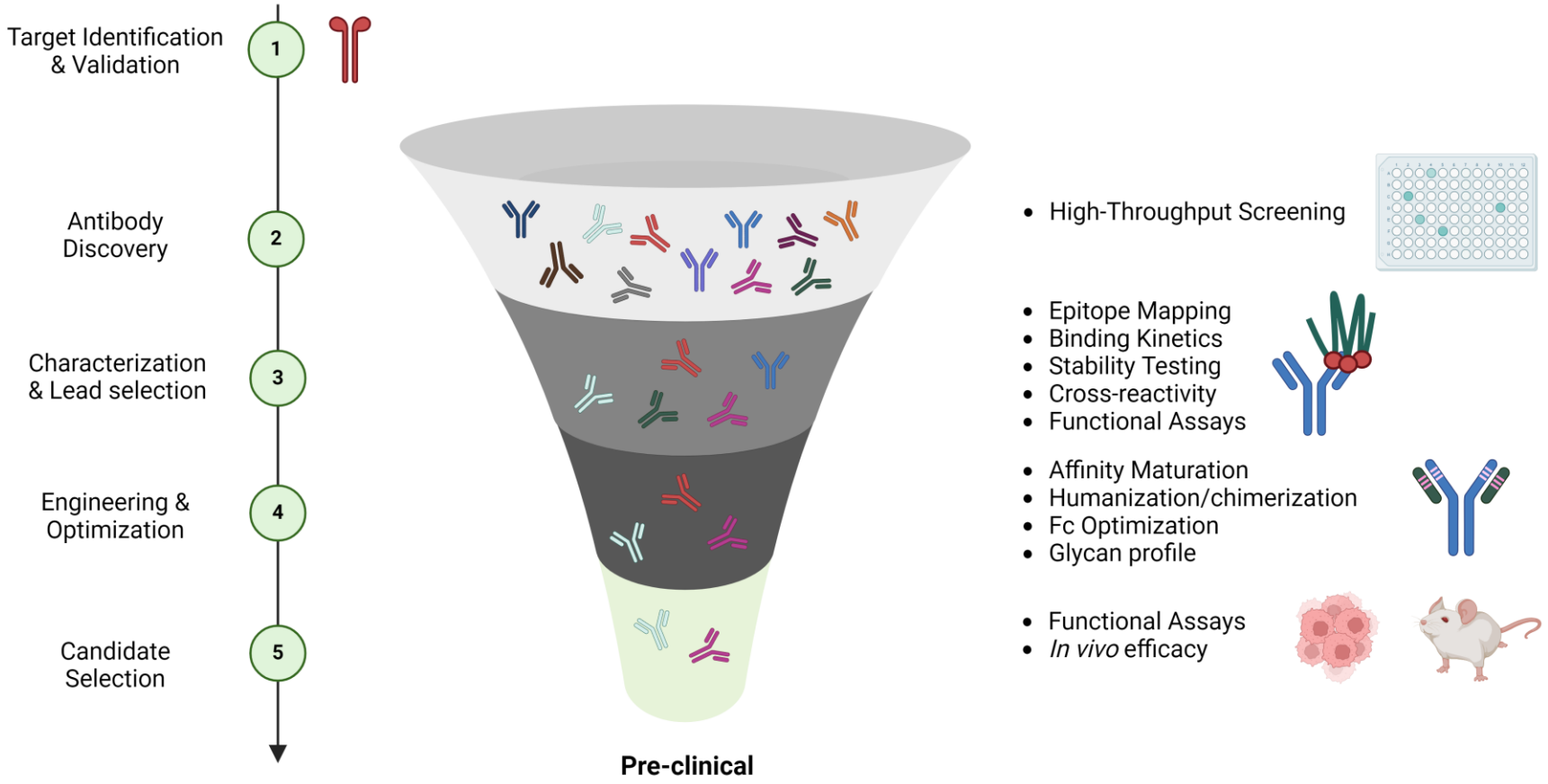
Immune Checkpoint Antibodies



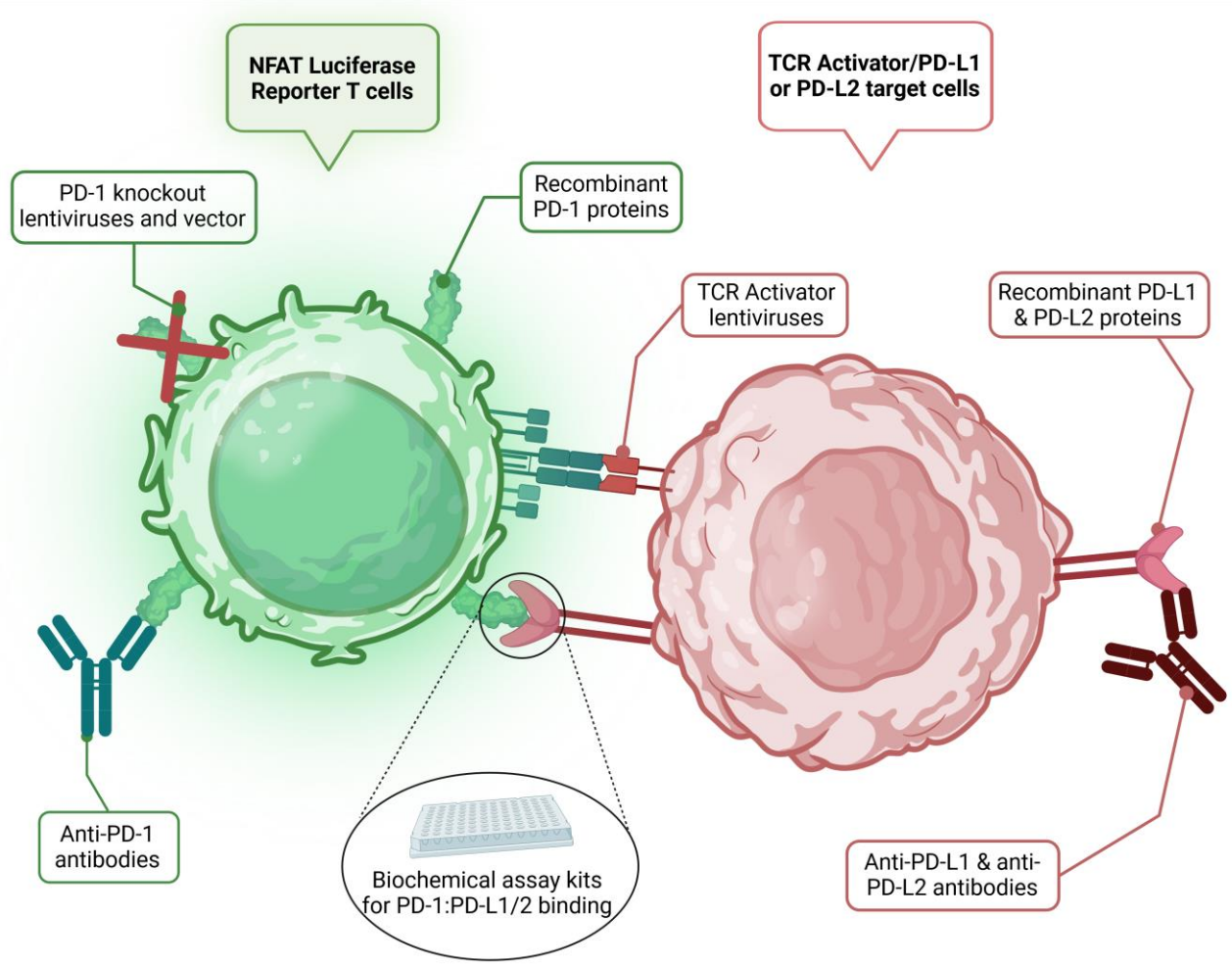
Antibody Development



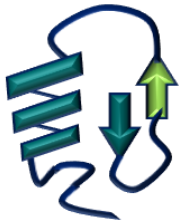
Challenges:

- Require several iterations of validation and optimization
- Functional validation use immune-related assays = relatively complex, need for advanced cellular models

Case Study: PD-1/PD-L1 or PD-L2



Proteins and Antibodies



Proteins PD-1, PD-L1, PD-L2 (51 products)

- To use as antigen/ligand for antibody production or for affinity measurement studies
- Conjugated: biotin for pull-down, or fluorescence-labeled
- Choice of tags
- Various species: Human, Mouse, Woodchuck, Monkey,

Neutralizing antibodies (6 products)

- To use as internal positive control
- Customers are designing new assay or testing new antibody candidates and need control(s) they know work

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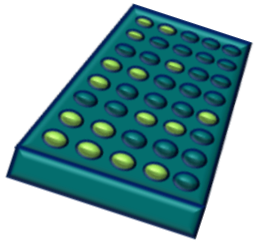
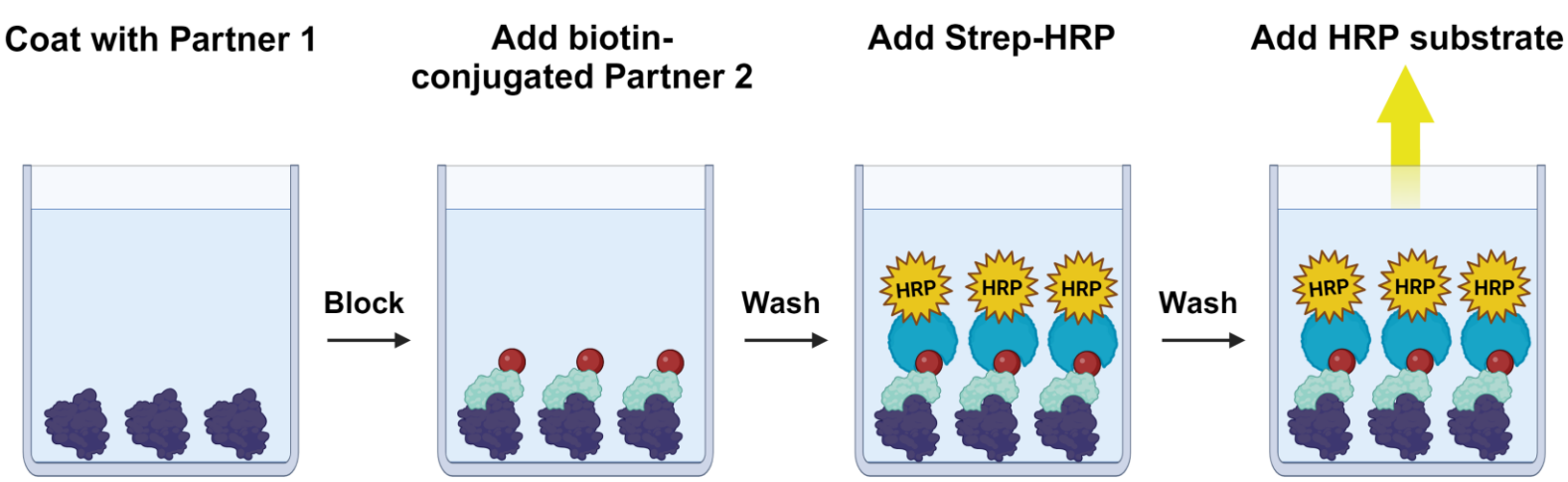
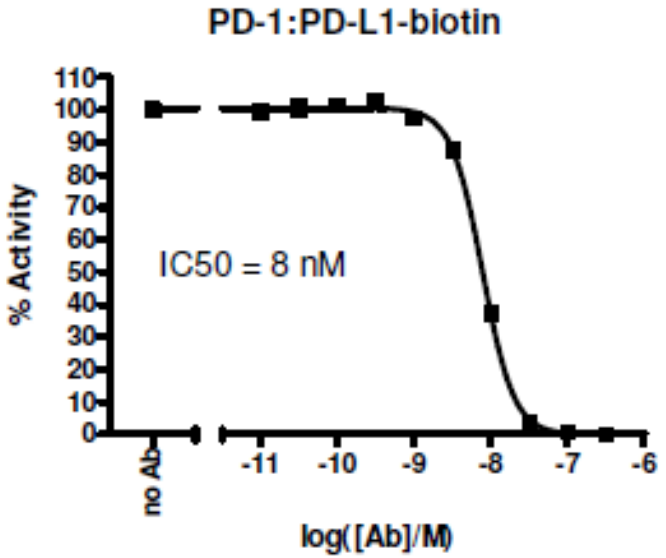
PD-1 Biochemical Assays



- **Purpose:** make sure the antibody blocks the binding of PD-1 to ligand
- **Drug development phase:** high-throughput screening in discovery; validate effect; determine IC_{50} for antibody effect
- **Assays Principle:** Measure PD-1 binding to its ligands (PD-L1, PD-L2, B7-H1)
- **Available Formats:** ELISA (colorimetric or chemiluminescent) or no-wash AlphaLISA™ and TR-FRET assays (23 assay kits available)



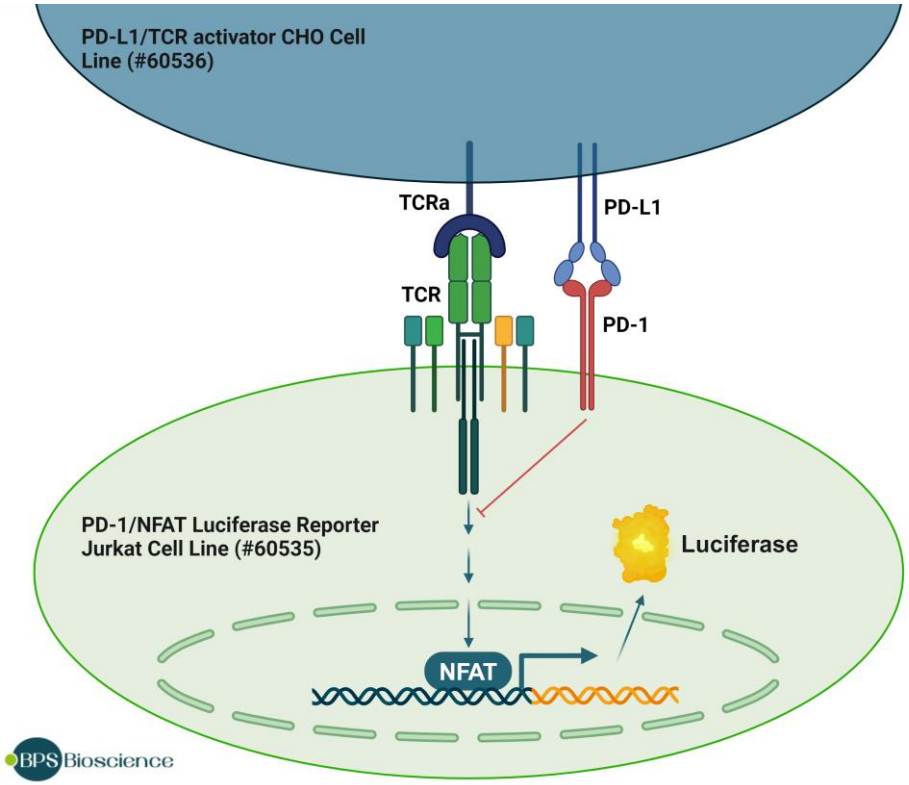


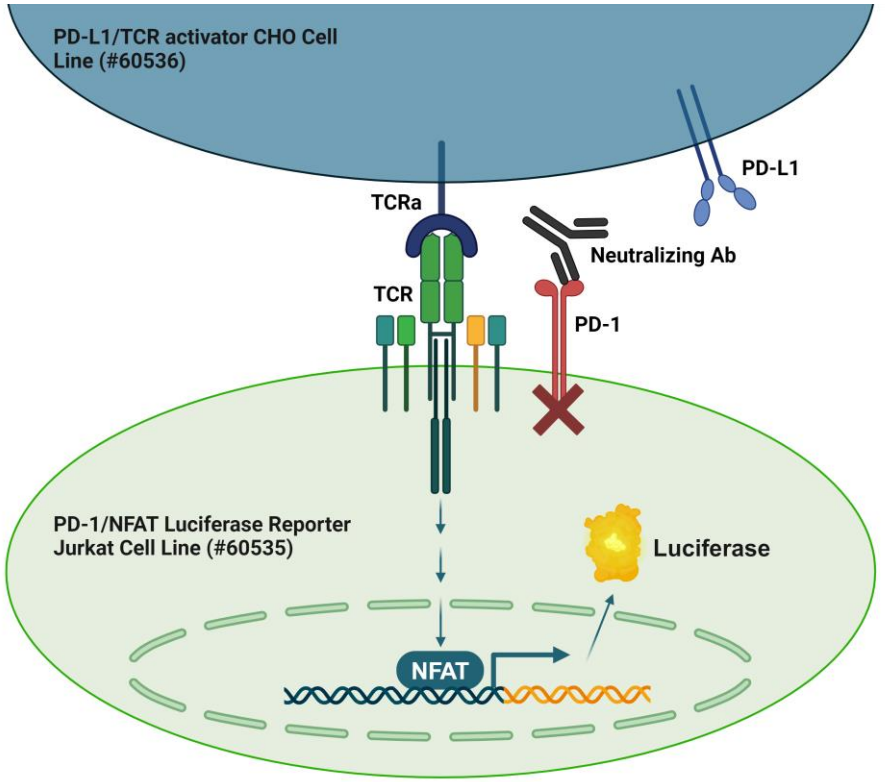
Cell Lines for Functional Assays

Purpose: make sure the antibody reactivates PD-1 expressing immune cells

Application: Use for functional assays (co-culture)

- Reporter effector cells: PD-1/NFAT Luciferase Reporter Jurkat Cell Line
- Target cells: PD-L /TCR Activator CHO Cell Line





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Adoptive Cell Therapy

- Introduction, charts and numbers
- CD19 therapeutic target
- Workflow
- CD19 research tools

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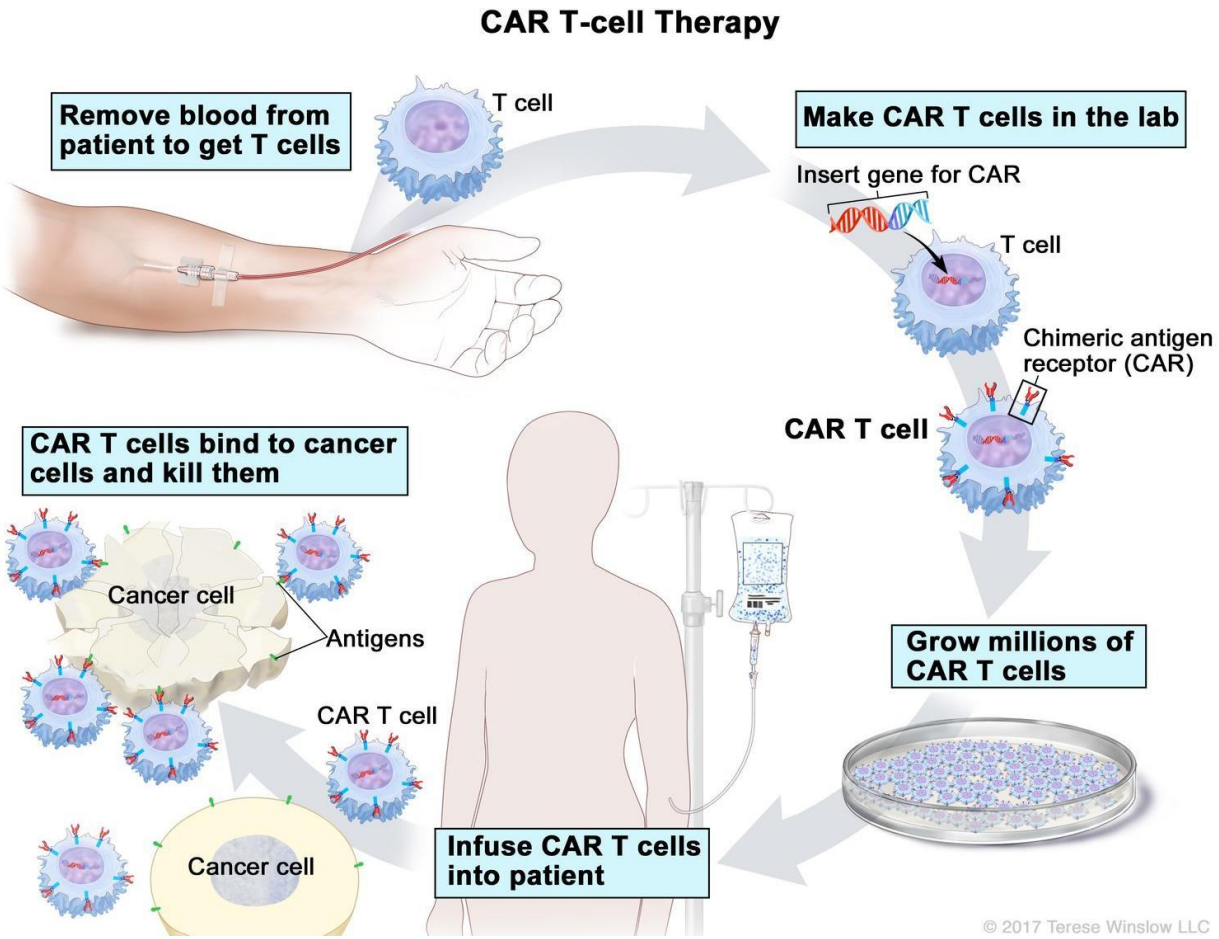
Adoptive Cell Therapy

- Immune cells: tumor-infiltrating lymphocytes (TIL) engineered T, NK, or B cells, stem cells HPS or iPSC
- Allogenic or autologous
- Express an engineered molecule that recognizes the tumor cells and activates immune cell proliferation and function
  - CAR: chimeric antigen receptor
  - TCR: T Cell Receptor

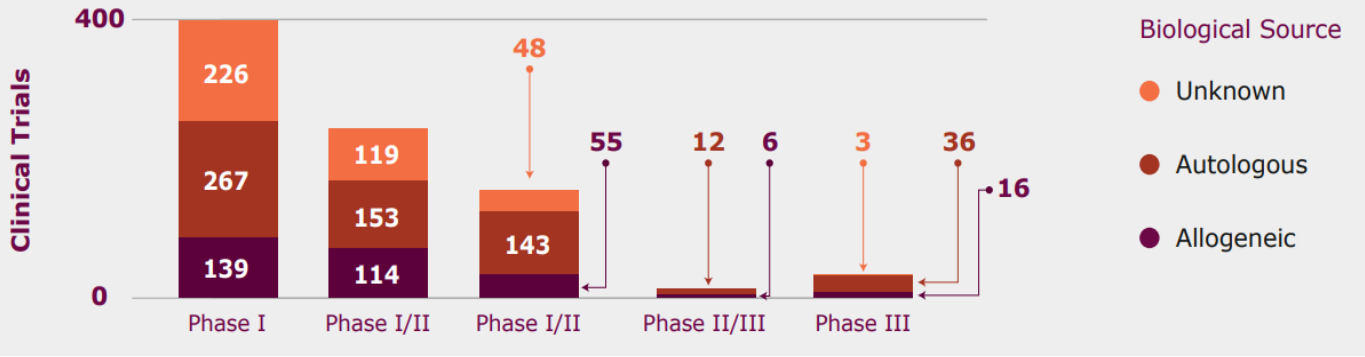


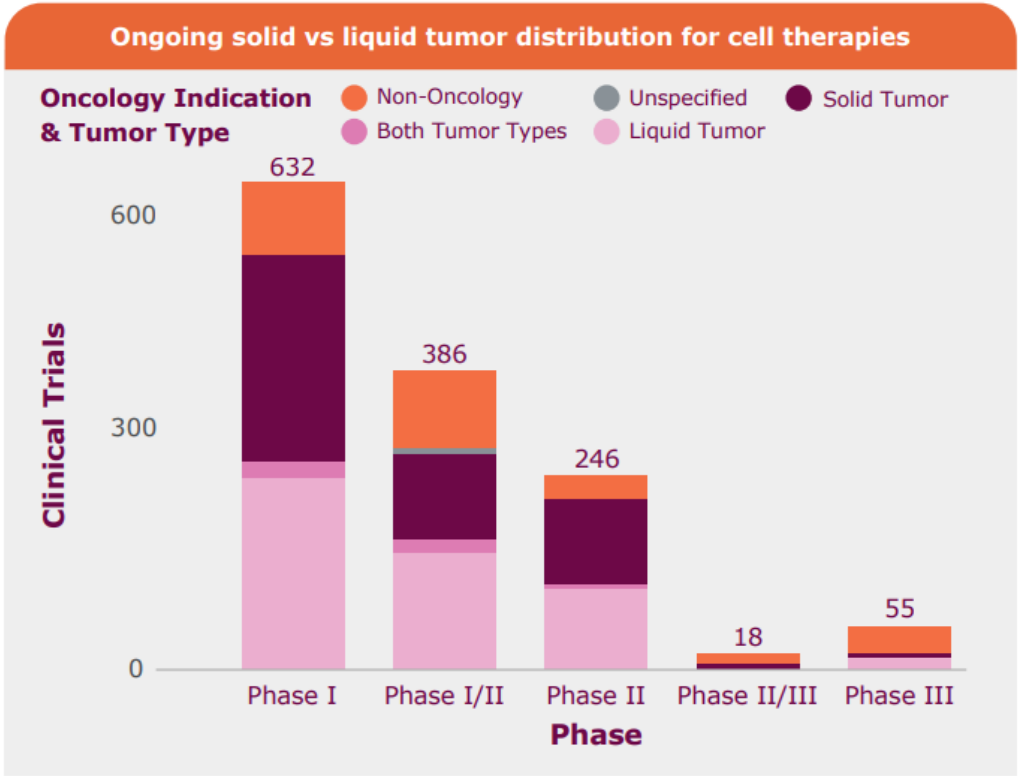
The global CAR T cell therapy market is expected to surpass 15 Billion US$ per year by 2028.0

FDA-Approved CAR T Cell Therapies

Brand Name	KYMRIAH™	YESCARTA™	TECARTUS™	BREYANZI®	ABECMA®	CARVYKTI®
Full name	tisagenleleucel	axicabtagene ciloleucel	brexucabtagene autoleucel	lisocabtagene maraleucel	idecabtagene vicleucel	ciltacabtagene autoleucel
Development name(s)	CTL019 CART-19	KTE-C19 axi-cel	KTE-X19 brexu-cel	JCAR017	bb2121 ide-cel	JNJ-68284528 cilta-cel
Target	CD19	CD19	CD19	CD19	BCMA	BCMA
Year approved	2017	2017	2020	2021	2021	2022
Indications	• ALL • DLBCL	• DLBCL • Follicular lymphoma • Primary mediastinal large BCL	Mantle cell lymphoma	• DLBCL • High-grade BCL • Primary mediastinal large BCL • Follicular lymphoma	Multiple myeloma	Relapsed or refractory multiple myeloma

Cell Therapy Clinical Trials





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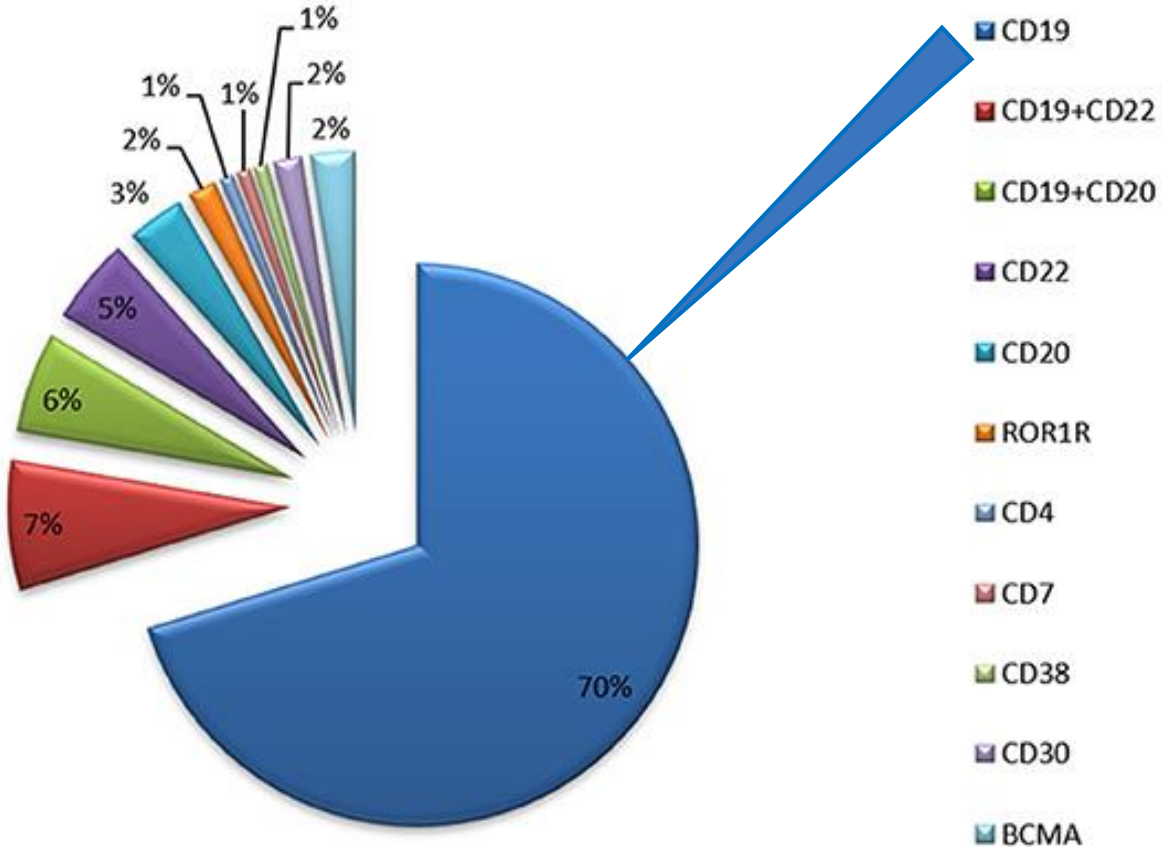
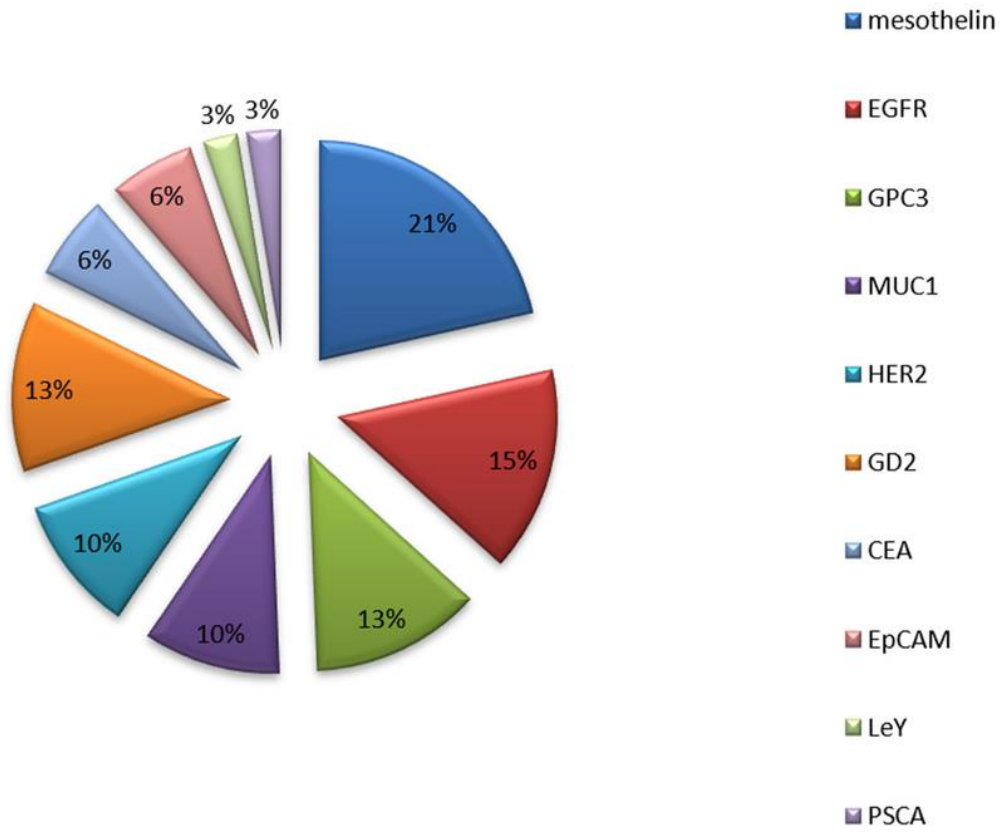
Source: https://alliancerm.org/

Cell Therapy Targets

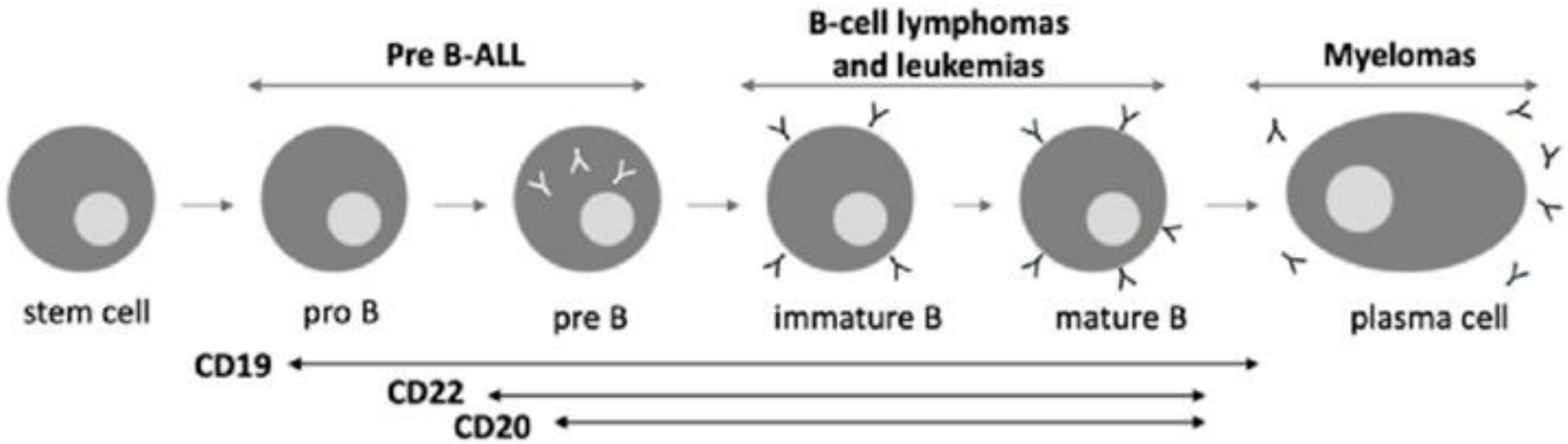
Current clinical target of CAR-T therapy in hematological malignancies



Current clinical target of CAR-T therapy in solid tumor



CD19 is a Therapeutic Target



- CD19 is a cell surface protein restricted to B cells and follicular dendritic cells
- Not expressed in bone marrow stem cells
- Clinically effective immunotherapy target
- CAR T cells can eradicate B cell malignancies and potentially autoimmune diseases

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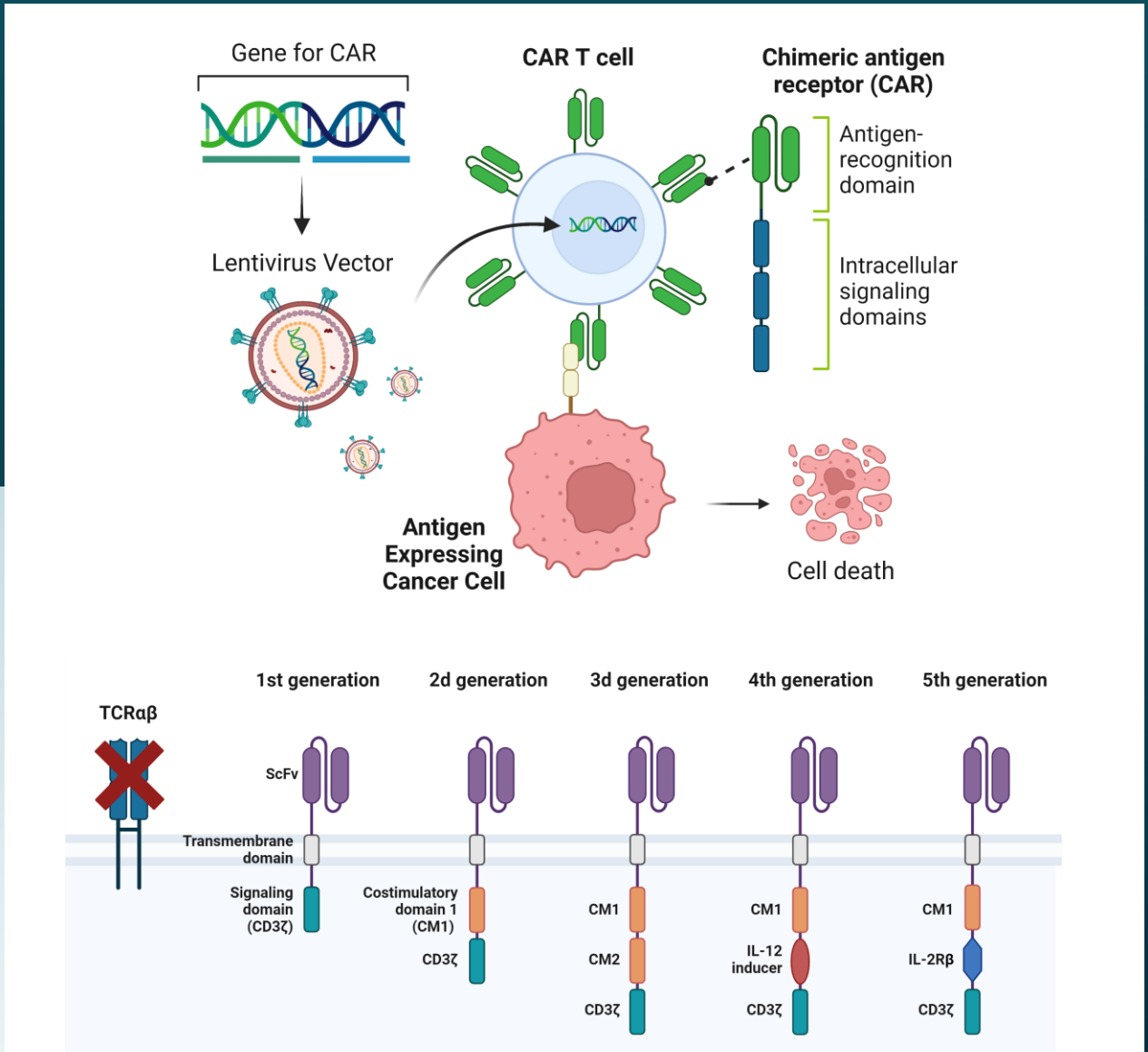
Chimeric Antigen Receptors (CAR)

- Construct containing an extracellular antigen-recognition domain, a transmembrane domain, and intracellular signaling domains
- Encoding plasmid usually transferred *ex vivo* using viral vectors
- Field in evolution – CAR are engineered to address cell exhaustion, toxicity, etc



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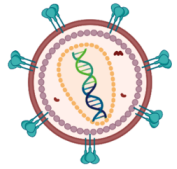
Workflow / Tools for Evaluation and Validation

The therapeutic agent is a population of immune cells, with specific set of challenges for developers

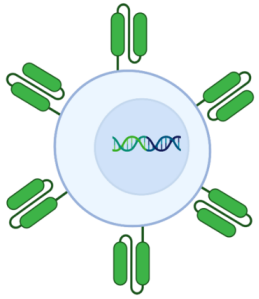
- New technologies
- Living cells: Difficult to obtain, manipulate and expand
- Clinical efficacy limited by cell exhaustion, rejection, side effects (cytokine storms)
- Complex characterization and functional validation
- Evolving regulatory landscape

1 Engineer CAR Gene

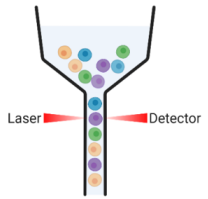
2 Create Viral Vector



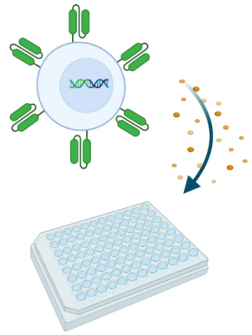
3 Create CAR-T cell via Transduction



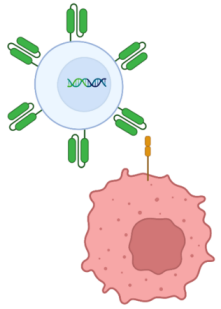
4 Target Binding Verification via Flow Cytometry



5 Cell Activation Assays



6 Cell Killing Assays



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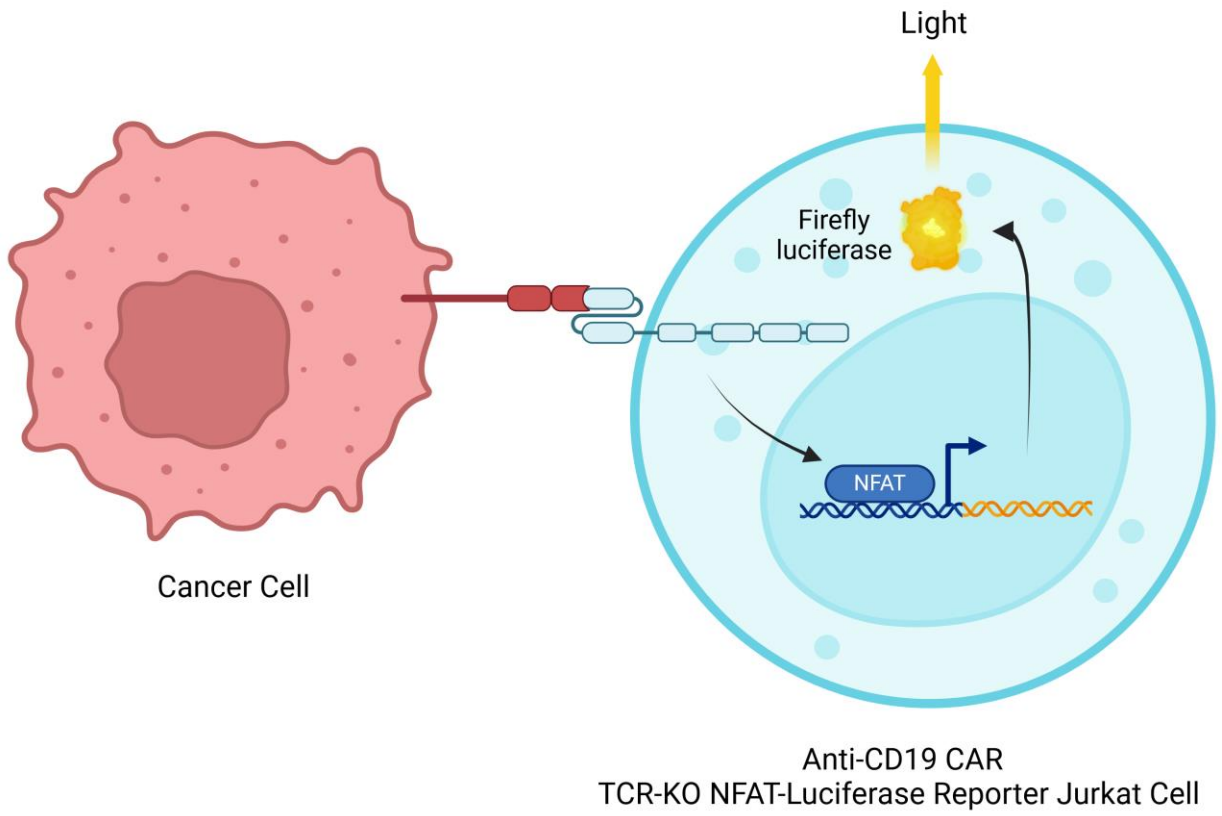
- Quick PCR™ Plus Assembly Kit
- Lentiviruses
- AAVs
- Cell Lines
- Primary Cells
- Cell Media
- Activating Antibodies
- Recombinant Proteins
- Antibodies
- Cytokine Assay Kits
- CAR Luciferase Reporter Cells
- ONE-Step™ Luciferase Assay System
- Cancer Cell Lines
- Antigen Overexpression Cell Lines
- Luciferase Reporter Target Cells

TCR-knockout Reporter T Cells

Objective: Express and evaluate various CAR constructs of interest

Products: TCR-KO cell lines responding to CAR activation with luciferase expression

Application: Use to assess CAR activation in T cells



78556 TCR Knockout NFAT-Luciferase Reporter Jurkat Cell Line
78557 TCR/B2M Knockout NFAT Luciferase Reporter Jurkat Cell Line

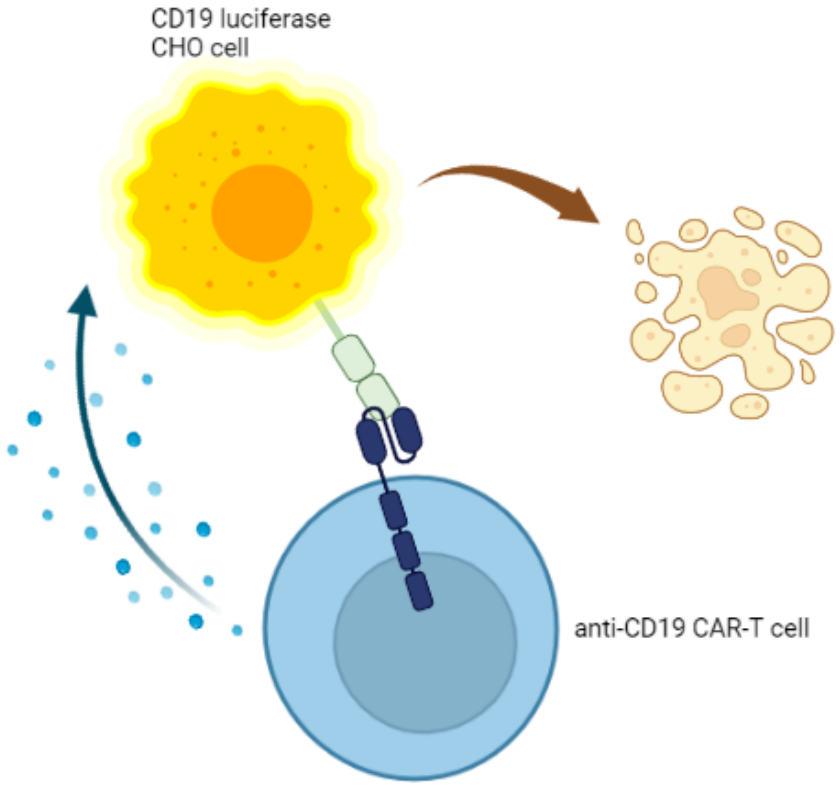
Recipient TCR-knockout T Cells

Objective: Express and evaluate various CAR constructs of interest

Products: TCR-KO cell lines to use with luciferase target cells

Application: Measure cytotoxicity against target cells (CAR T cell biological effect)

78539 TCR Knockout Jurkat Cell Line
78552 TCR/B2M Knockout Jurkat Cell Line



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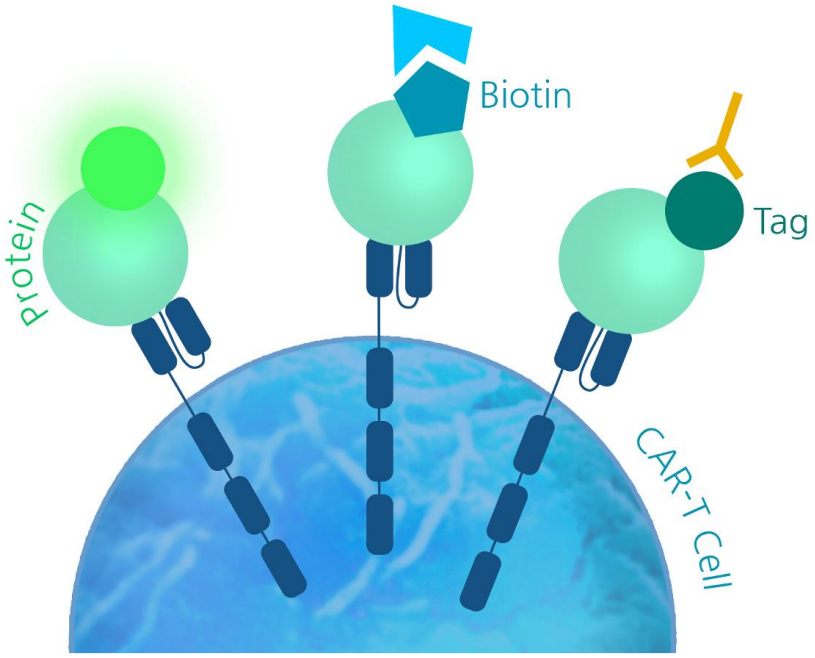
Evaluation of CAR Expression

Objective: Detect anti-CD19 CAR construct and measure expression levels

Product: Target protein (example CD19) with tag, may be biotinylated or conjugated with a fluorophore.

Application: Use for flow cytometry analysis of CAR expression and for cell sorting (FACS).



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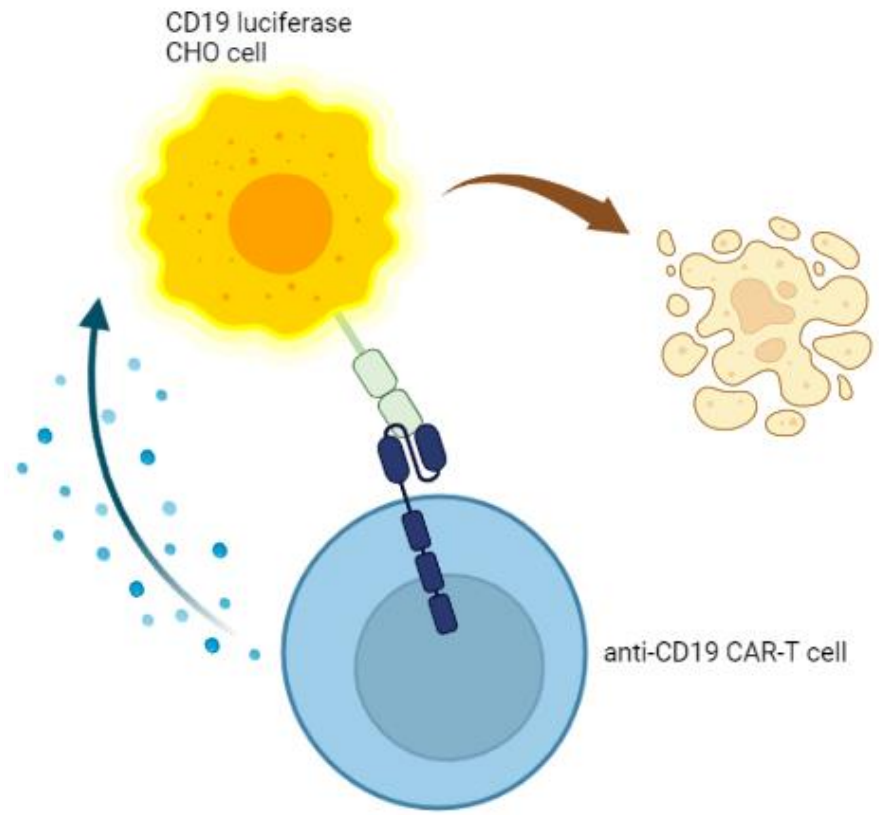
Luciferase Target Cells



- **Purpose:** Measure the killing of CD19-positive cells by CAR T cell (effector function)
- **Principle:** Luciferase activity correlates with number of live target cells; no interference from immune cells
- **Application:** Co-culture assay for functional validation of the CAR T cells
- **Companion assays:** Assay kits to measure cytokine expression induced by binding of immune cell to CD19-positive target cell (interferon, Il-2, IL-10, and more)

Created with BioRender.com

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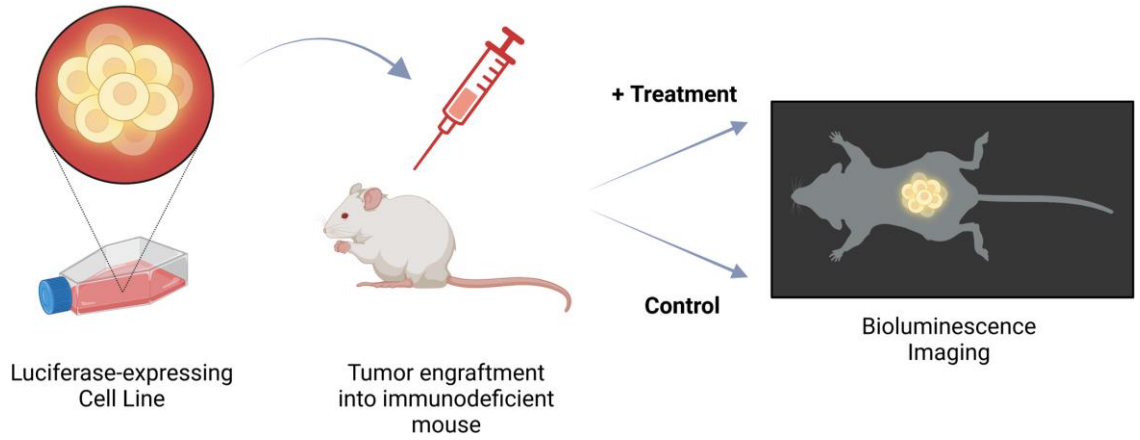
Cell Line-Derived Xenograft (CDX) Models

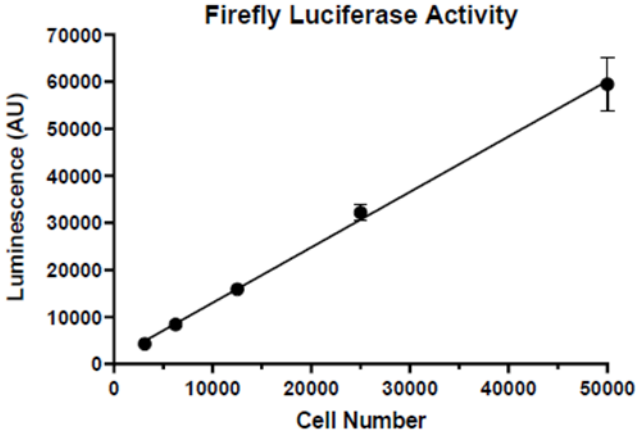


Bioluminescent cells can be used as target cells in co-culture assays or in animals as xenograft cancer models

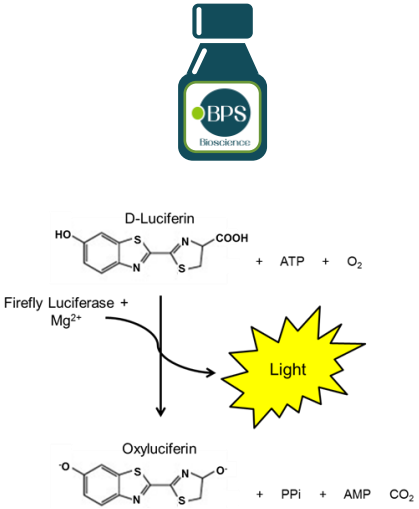
- Verified mycoplasma-free and low endotoxin
- Uniform expression of luciferase for consistent readouts
- Affordable

Well established, well characterized human tumor B cells expressing CD19

- NALM6
- Raji

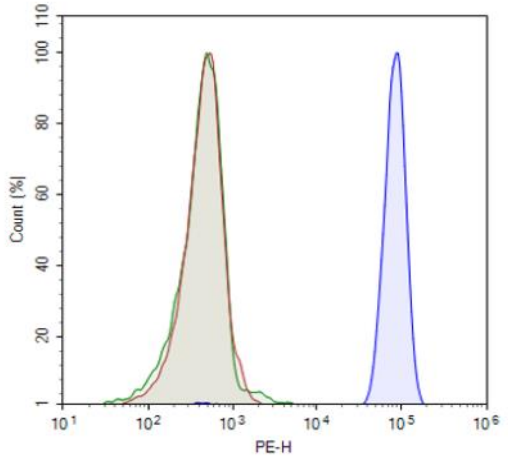


In Vivo-Luc™ Imaging Solution (#78803)

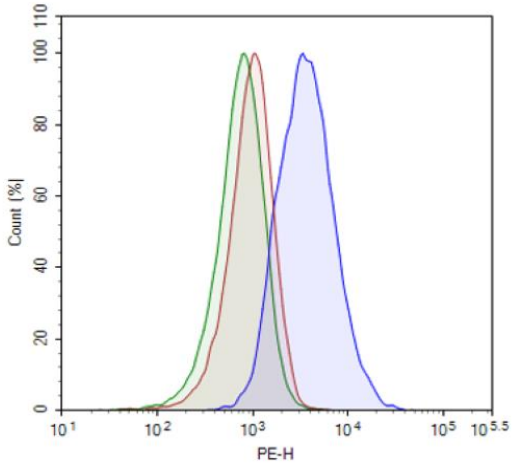


CD19 Knockout Cells

- **Purpose:** Evaluate off-target effects *in vitro* or *in vivo* (if using luciferase CDX)
- **Principle:** CD19 was genetically removed from CD19-expressing cells using CRISPR/Cas9 engineering
- **Application:** Use as negative control in co-culture assay in parallel with parental CD19-positive cell line



CD19 expression in luciferase CD19-knockout NALM6 cell line (#82168)



CD19 expression in luciferase CD19/CD20 double knockout Raji cell line (#82623)

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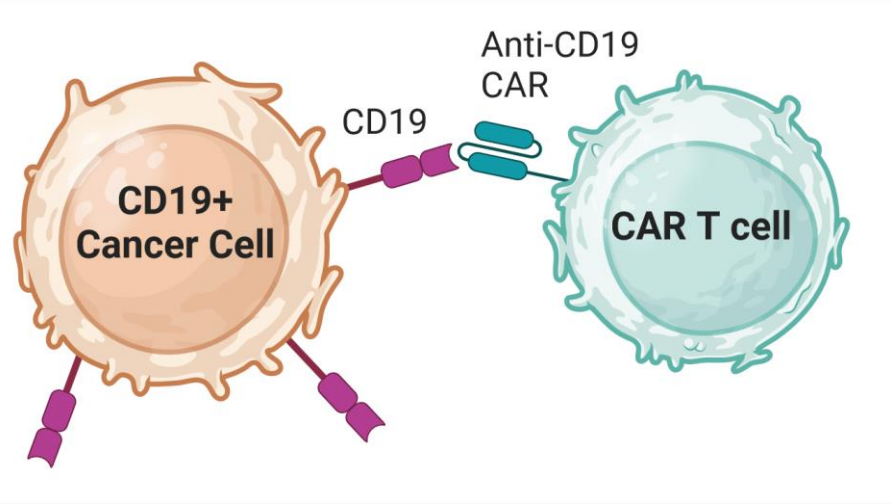
Cell Line Rental



- *Try Before You Buy*
- Option to rent more than 150 different cell lines
- Rent for up to 3 months for 50% of the cell line price
- After the rental period ends, the cell line can be purchased

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Custom Services

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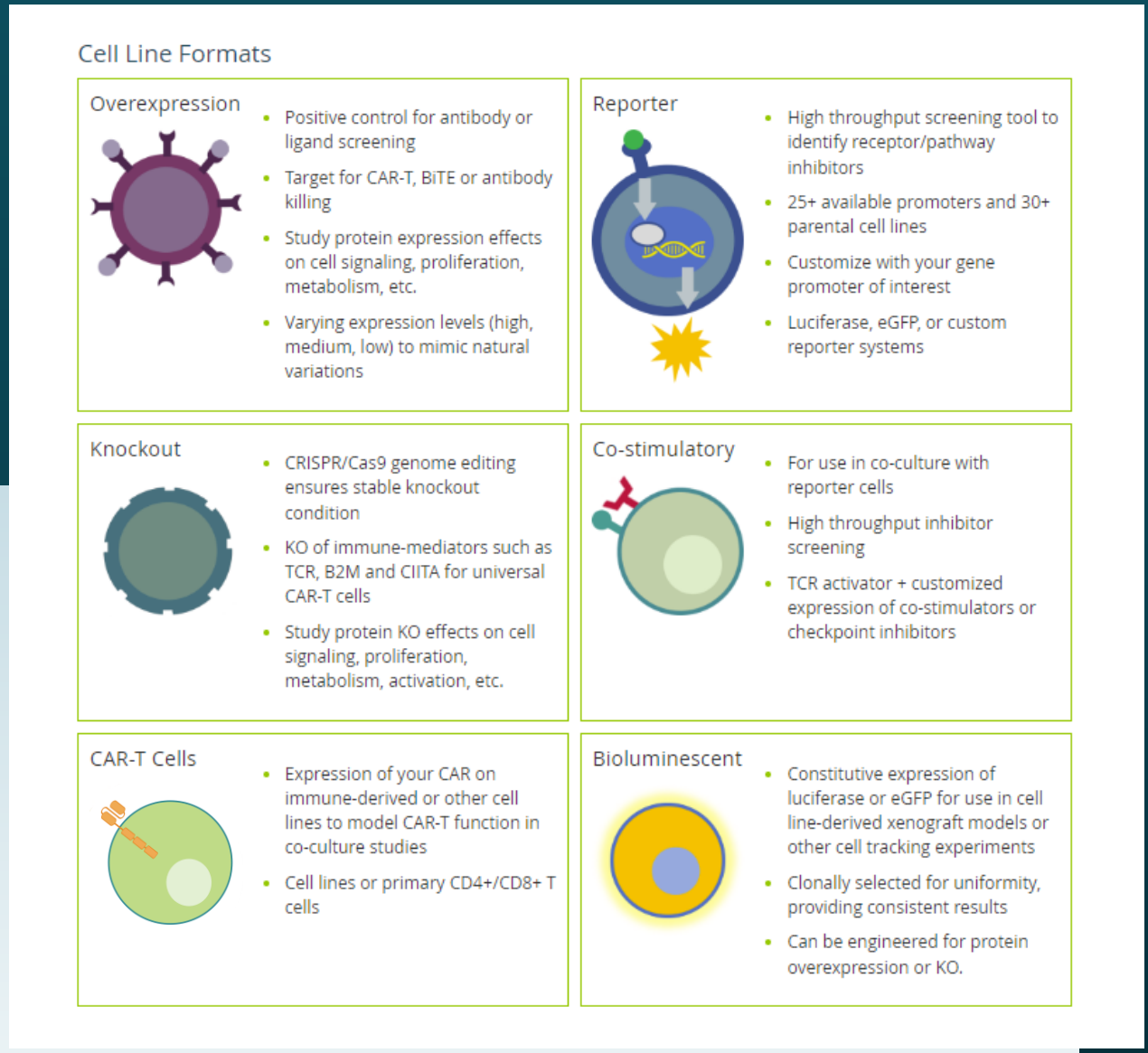
Custom Cell Lines

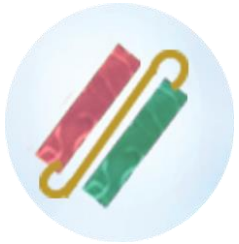
- Over 20 parental cells to chose from
- Reporter gene of choice: fluorescent proteins GFP, RFP, mCherry, Luciferase
- Projects tailored to the customer's goals



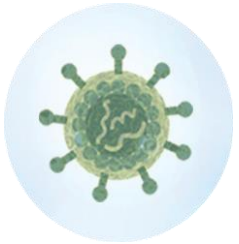
Custom CAR or TCR Services

A Milestone-Measured Process from Concept to Cells

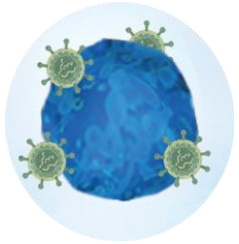
1. Researcher provides Ab sequence against antigen



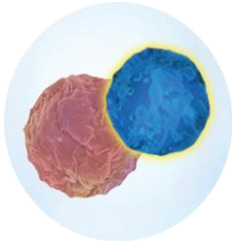
2. Engineering and validation of ScFv for specificity and affinity



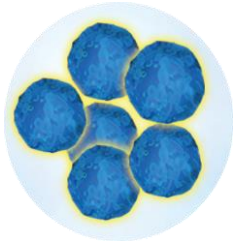
3. CAR Lentivirus production and initial validation



4. T cell preparation and transduction



5. Functional validation of CAR-T cells

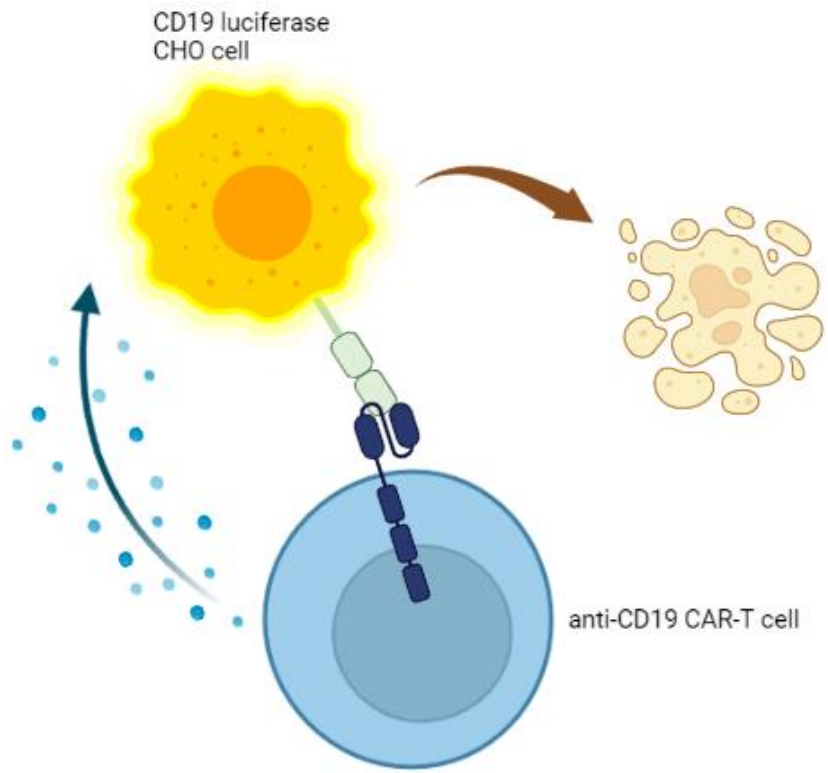


6. CAR-T cell expansion and optimization

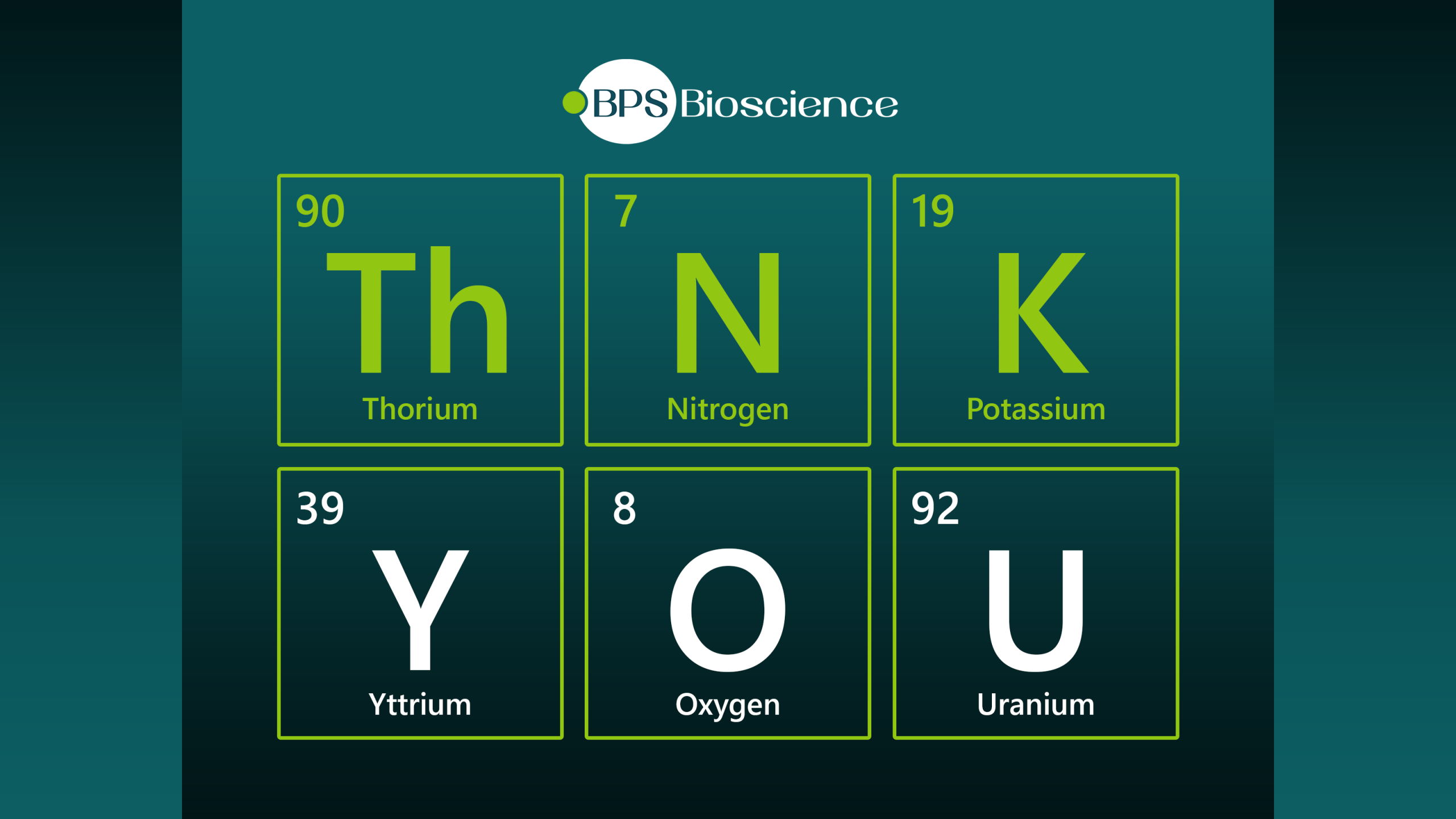
BPS Bioscience

Co-culture Assay Services for Effector Cells

- We measure the cytotoxic function of effector cells (CAR-T cells) using a cell line expressing the target of interest and a reporter gene
- Killing of the target cell is measured by decrease in reporter activity



BPS Bioscience


BPS Bioscience
90
Th
Thorium
7
N
Nitrogen
19
K
Potassium
39
Y
Yttrium
8
O
Oxygen
92
U
Uranium

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