INFOGRAPHIC

From Nobel Discovery to Next-Generation Innovation

WILEY

BD Biosciences

SECTION 1

The Nobel Discovery

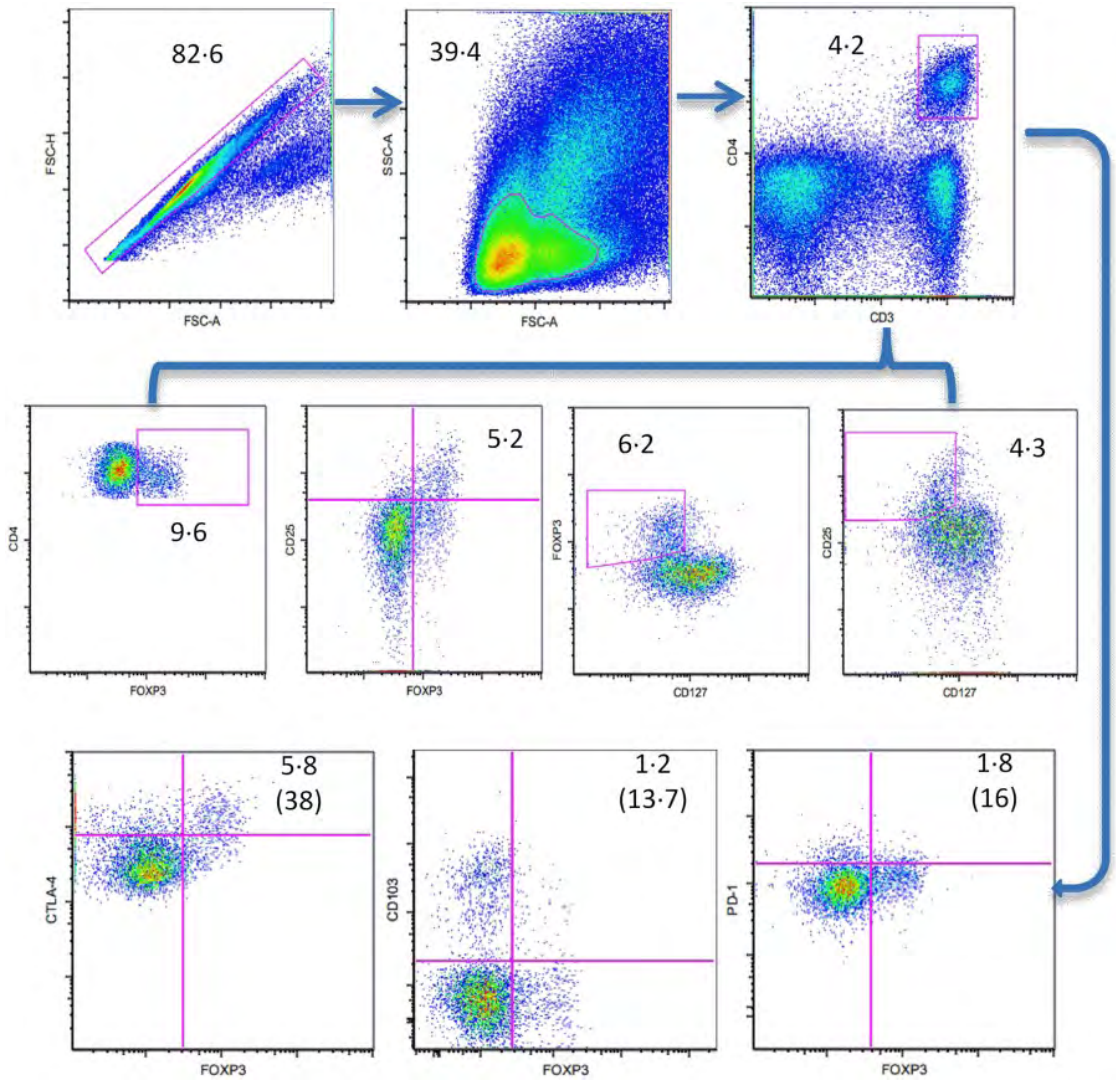
The 2025 Nobel Prize in Physiology or Medicine

The 2025 Nobel Prize in Physiology or Medicine was awarded to Mary E. Brunkow, Frederick J. Ramsdell, and Shimon Sakaguchi for their discoveries concerning peripheral immune tolerance.

What Are Regulatory T Cells (Tregs)?

Regulatory T cells are specialized immune cells that prevent the immune system from attacking the body's own tissues. Making up 5-10% of CD4+ T cells, Tregs are essential for preventing autoimmune diseases.

The laureates' discoveries launched the field of peripheral tolerance, spurring development of medical treatments across cancer immunotherapy, autoimmune diseases, organ transplantation, and cellular therapies.



Human Treg characterization with key markers CD4, CD25, and Foxp3. **Source:** https://doi.org/10.1111/cei.12804.

SECTION 2

The Science Behind Tregs

How Tregs maintain immune balance:

Secrete anti-inflammatory molecules (IL-10, TGF-β)

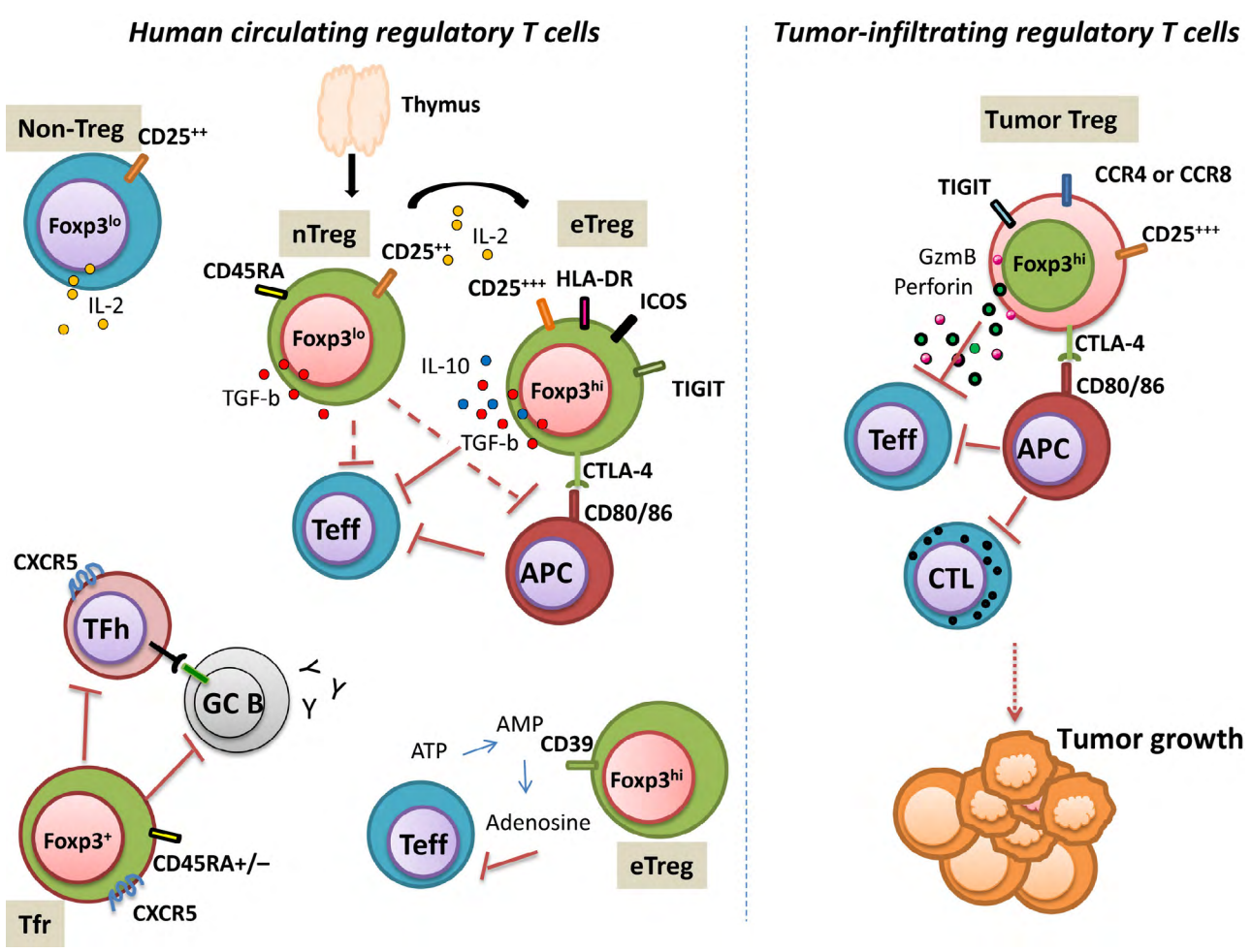
Block activation signals to other immune cells

Consume growth factors needed by inflammatory cells

Why This Matters

Mutations in the FOXP3 gene cause IPEX syndrome, where infants develop severe multi-organ autoimmunity. Without functional Tregs, the immune system attacks the pancreas, intestines, and skin. IPEX demonstrates that Tregs are essential for survival.

Treg dysfunction links to type 1 diabetes, multiple sclerosis, and inflammatory bowel disease. In cancer, Tregs can be problematic—tumors recruit them to suppress anti-tumor immunity.



Heterogeneity in human Treg cell phenotype and function. **Source:** https://doi.org/10.1002/cti2.1005.

SECTION 3

The Discovery Journey

1995

Identifying Regulatory T Cells

Shimon Sakaguchi discovered that removing CD4+CD25+ T cells from healthy mice triggered widespread autoimmunity. He had found cells whose job was to suppress immune responses—"regulatory T cells."

2001

The Master Gene

Mary Brunkow and Frederick Ramsdell discovered that mutations in the Foxp3 gene caused IPEX syndrome. Foxp3 was the master regulator determining whether a T cell becomes regulatory or not.

2003

Connecting the Discoveries

Sakaguchi proved that Foxp3 was specifically expressed in CD4+CD25+ regulatory T cells. The CD4+CD25+Foxp3+ signature became the global standard for identifying Tregs.

These discoveries have enabled multiple clinical trials.

SECTION 4

Transforming Medicine

Treg-Based Cellular Therapies

Isolating and expanding patient Tregs for reinfusion. Clinical trials underway for type 1 diabetes, graft-versus-host disease, and organ transplantation.

Cancer Immunotherapy

Developing strategies to reduce Treg activity in tumors while preserving protective functions elsewhere. Checkpoint inhibitors work partly by overcoming Treg suppression.

CAR-Treg Engineering

Engineering Tregs with chimeric antigen receptors to target specific tissues, offering unprecedented precision in suppressing unwanted immunity.

Low-Dose IL-2 Therapy

Ultra-low doses of IL-2 preferentially expand Tregs, showing promise for chronic graft-versus-host disease and lupus.

Autoimmune Disease Treatment

Restoring Treg function through adoptive cell therapy and small molecules that enhance Treg stability.

SECTION 5

How Flow Cytometry Enabled Discovery

Flow cytometry analyzes thousands of cells per second, measuring multiple markers simultaneously to identify specific populations.

1990s
3-4 color analysis enabled Sakaguchi's CD4+CD25+ discovery

2000s
Intracellular staining allowed Foxp3 detection, confirming Treg identity

TODAY
40-50+ parameter spectral analysis reveals Treg heterogeneity with unprecedented detail

Four Essential Capabilities:

	Capability	Function
1	Multi-Parameter Analysis	Detect CD4 and CD25 simultaneously
2	Intracellular Detection	Analyze Foxp3 inside cells
3	Cell Sorting	Isolate pure Treg populations
4	Quantification	Track Treg frequency in disease

Complementary Technologies:

- Single-cell genomics
- Mass cytometry
- Tissue imaging
- TCR sequencing

SECTION 6

The Role of BD Biosciences Technology

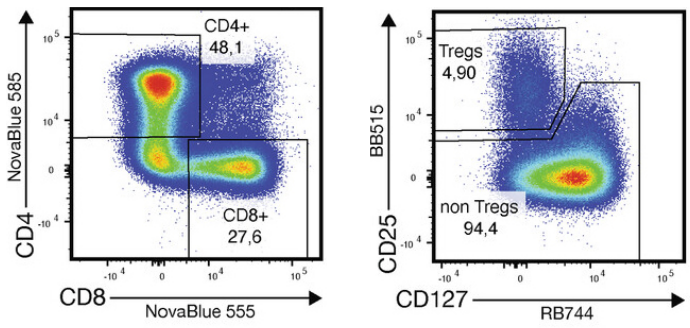
Commercializing Flow Cytometry

In 1974, BD Biosciences introduced the first commercial FACS instrument, making fluorescence-activated cell sorting accessible to laboratories worldwide—including those where the Nobel laureates worked. The conventional multi-color platforms that emerged enabled Sakaguchi to characterize CD4+CD25+Foxp3+ Tregs.

Modern Spectral Flow Cytometry

Today's spectral platforms analyze 40-78 parameters simultaneously—more than 10 times the capability that enabled the original discoveries. BD Biosciences spectral instruments exemplify this evolution.

Gated on CD14⁻ CD19⁻ CD20⁻ CD3⁺ TCRγδ⁻



Visualization of CD4+ and CD8+ T cells, as well as CD4+ regulatory T cells (Tregs) acquired on a BD FACSDiscover™ S8 Cell Sorter.
Adapted from: https://doi.org/10.1002/cyto.a.24841.

Contemporary spectral flow cytometers offer researchers unprecedented capability to study Treg biology. The BD FACSDiscover™ Platform exemplifies this technology class, featuring up to 40 parameters and advanced spectral unmixing capabilities that enable comprehensive Treg phenotyping.

Platform Example	Technical Capabilities	Research Applications
Spectral Cell Analyzers (e.g., BD FACSDiscover™ A8 Cell Analyser)	• Combined spectral detection and cellular imaging • 78 fluorescence detectors and 8 scatter and imaging detectors • Dual-mode operation with high-speed (35,000 events/sec) or imaging (12,500 events/sec) acquisition, plus integrated Autoloader for walkaway automation	• Resolve rare Treg subsets with 40+ parameter analysis • Visualize Foxp3 subcellular localization • Distinguish tissue-resident from circulating Tregs • Image-based doublet discrimination
Spectral Cell Sorters (e.g., BD FACSDiscover™ S8 Cell Sorter)	• First spectral sorter with sort-capable imaging • Six independent imaging-enabled detectors • 78 fluorescent detectors across five lasers	• Sort pure Treg populations for downstream analysis • Isolate cells based on morphology + phenotype simultaneously • Visual confirmation of Foxp3+ cells during sorting • Enable genomics and functional validation studies
Advanced Fluorochromes (e.g., BD Horizon RealBlue™/RealYellow™)	• Laser-specific dyes with reduced spectral overlap • AI-guided design for optimized resolution • Multiple emission variants available	• Improved detection of dim markers like CD25 on Tregs • Enhanced Foxp3 resolution • Simplified high-parameter panel design • Compatible with conventional and spectral platforms
CAR Detection Tools (e.g., BD® CAR Detection Reagents)	• Specialized reagents for engineered T cells • Compatible with cell therapy workflows	• Monitor CAR-Treg therapeutic products • Track engineered cells during manufacturing • Quality control for cellular therapies

SECTION 7

Deeper Insights with Spectral Technology

Spectral flow cytometry has transformed Treg research by enabling multidimensional single-cell analysis.

Comprehensive Phenotyping	Analyze 40+ markers simultaneously: surface receptors (CD25, CTLA-4, GITR), transcription factors (Foxp3, Helios), functional molecules (CD39, CD73), and tissue-homing markers (CD62L, CCR7)
Experimental Flexibility	Design complex panels without traditional filter restrictions, enabling experiments impossible with conventional systems
Data Quality	Advanced unmixing algorithms and autofluorescence correction improve detection of dim markers
Imaging Parameters	Real-time imaging parameters enable the measurement and visualization of cell morphology, intracellular protein localization, and cell quality control

These capabilities address longstanding challenges in Treg research:

Heterogeneity: Distinguishing functional Treg subsets within complex populations

Functional states: Simultaneously assessing activation, suppressive capacity, and tissue-homing potential

Rare populations: Detecting tissue-resident Tregs at <0.1% frequency

Quality control: Visual confirmation prevents artifacts from cell aggregates or debris

Then vs. Now:

4-color analysis, basic CD4+CD25+Foxp3 characterization

1990s-2000s

40-78 parameter spectral analysis with real-time imaging and AI-assisted workflows

TODAY

SECTION 8

Enabling Next-Generation Treg Research

Modern flow cytometry platforms—including those from BD Biosciences and other manufacturers—support researchers pursuing the therapeutic frontiers described in Section 4. Here's how advanced cytometry specifically addresses current research challenges:

Characterizing Treg Subsets

Scientific challenge:

Tregs are not uniform—they include naive, effector, memory, and tissue-resident populations with distinct functions.

How technology helps:

Multi-parameter analysis (40+ markers) resolves these subsets simultaneously. For example, researchers can now distinguish naive (CD45RA+Foxp3lo), effector (CD45RA-Foxp3hi), and tissue-resident (CD69+CD103+) Tregs in a single experiment—work that previously required multiple separate assays.

Advancing Cancer Immunotherapy

Scientific challenge:

Understanding Treg infiltration in tumors requires detecting rare populations (<1% of tumor cells) while characterizing their functional state.

How technology helps:

High-sensitivity detection resolves low-frequency tumor-infiltrating Tregs. Imaging capabilities distinguish Tregs in contact with tumor cells from those in surrounding stroma. Specialized reagents track engineered CAR-Tregs in preclinical models.

Developing Cellular Therapies

Scientific challenge:

Manufacturing Treg-based therapeutics demands ultra-pure populations—contaminating conventional T cells can cause adverse effects.

How technology helps:

Image-enabled sorting confirms cell morphology during isolation, achieving >98% purity. High-parameter panels monitor phenotypic stability during ex vivo expansion. Specialized detection reagents validate CAR expression in engineered products.

Understanding Transplant Tolerance

Scientific challenge:

Identifying biomarkers that predict graft acceptance requires comprehensive phenotyping of rare Treg populations before and after transplantation.

How technology helps:

Quantitative analysis tracks subtle changes in Treg frequency (±0.5%). Imaging in tissue samples reveals spatial organization of Tregs relative to graft vasculature. High-dimensional profiling identifies tolerance signatures combining multiple markers.

Integrating Multi-Omics

Scientific challenge:

Phenotype alone doesn't reveal what Tregs are actually doing—transcriptional and proteomic data provide complementary insights.

How technology helps:

Flow cytometry isolates specific Treg subsets for downstream single-cell RNA sequencing, proteomics, or epigenetic analysis. Platforms can integrate directly with multiomics workflows, enabling correlation of surface phenotype with molecular function.

SECTION 9

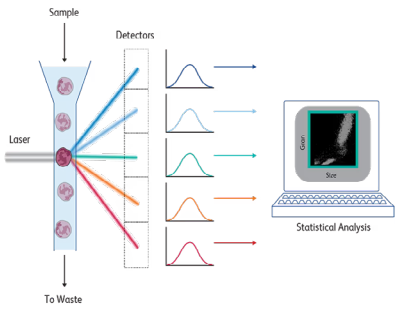
Resources to Advance Your Research

Further Reading & Resources

- **Splice variants of human FOXP3 are functional inhibitors of human CD4+ T-cell activation**
- **Dynamics of peripheral tolerance and immune regulation mediated by Treg**
- **Human FoxP3+CD4+ regulatory T cells:** Their knowns and unknowns
- **Targeting Treg cells in cancer immunotherapy**
- **OMIP-102: 50-color phenotyping of the human immune system**
- **Mastering Spectral Flow Cytometry:** Foundational Concepts and Techniques

SECTION 10

Advancing Immunology Research



The technologies described in this document represent decades of innovation in flow cytometry—from the first commercial FACS instruments that enabled Treg discovery to today's spectral platforms revealing unprecedented cellular detail.

To learn more about flow cytometry platforms and how they support immunology research, visit:

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