BPS Bioscience

Distributor Update
Vol. 13 Issue 5

Welcome to our latest distributor newsletter, including product highlights and our newest marketing tools. This issue highlights our TCR-specific antigen portfolio, as well as two new kits for protein degradation.

As always, we have a lot of exciting new products to share. These products are provided in a separate excel file, in order to make uploading easier. Note that there are multiple tabs in this file, including deleted products, size or price changes, and updates to product names. Make sure you are updating all the information provided.

We are already well into the third quarter, and we want to meet with all our distributors to discuss sales and plans for the remainder of 2024. Please contact the International team to schedule a meeting.

Let us know how we can support your sales efforts—we want to hear from you! Our most successful distributors are those we hear from the most often.

Product Highlights

Marketing Tools

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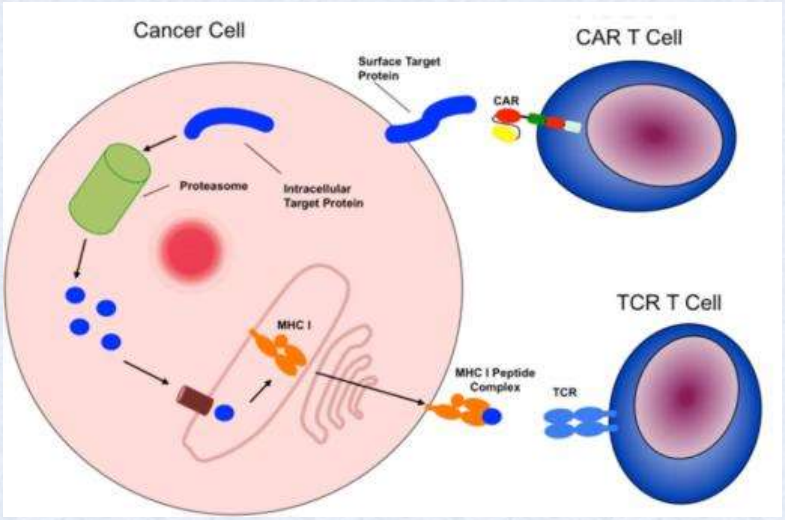
Product Spotlight!

Adoptive Cell Therapy Using Antigen-Specific TCRs

CAR-T vs. TCR-T



TCR-T (T-cell receptor-engineered T-cell therapy) and CAR-T (chimeric antigen receptor T-cell therapy) are advanced immunotherapies used in the treatment of cancers. Both approaches involve modifying a patient's T-cells to recognize and attack cancer cells, but they differ in their mechanisms and advantages.

CAR-T therapy is designed to target specific antigens present on the surface of cancer cells. This approach has been highly successful for cancers that express distinct, identifiable surface markers, such as targeting the B cell marker CD19 in B-cell malignancies. CARs are synthetic receptors that are grafted onto T-cells, and they are relatively easy to design and produce compared to TCRs; moreover, some CAR-T cells can be produced as off-the-shelf products.

TCR-T therapy, on the other hand, only targets cancer-specific antigens that are presented on major histocompatibility complex (MHC) molecules. This allows the detection of not only surface antigens, but also intracellular proteins, such as neoantigens. Additionally, TCR-T cells can be engineered to recognize a wider variety of antigens compared to CAR-T cells, including mutated proteins or viral antigens. These traits are important because they

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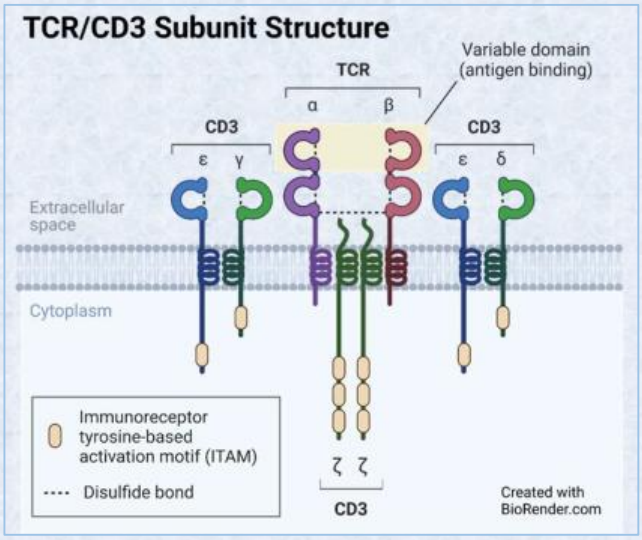
mean TCR-T therapy can potentially target antigens associated with solid tumors or specific mutations not available to CAR-T approaches.

CAR-T	TCR-T
Recognizes their target antigen via the scFv binding domain of CARR	Relies on interactions with peptide-major histocompatibility complex (pMHC)
Recognizes and targets cell surface antigens	Can target both cell surface antigens and intracellular antigens
Great therapy outcomes in treatment of blood cancers but little effect on solid tumors	Displays encouraging curative outcomes in the therapy of solid tumors

T Cell Receptor Engineering (TCR)

TCR therapy is a more versatile method that can target more types of cancer; however, it also tends to have more off-target effects since the antigen recognition process is not as selective as with CARs. Therefore, researchers have focused on optimizing the TCR to recognize specific cancer antigens and minimize cross reactivity and off-target effects.



This process involves identifying tumor-associated antigens that have limited expression on normal tissues, such as PRAME, MART-1 or MAGE, and then identifying the exact peptide sequence that binds the MHC molecule. The TCR itself is engineered to improve its stability, specificity, and binding affinity for the specific cancer antigen-MHC complex. Then the engineered TCR is introduced into T-cells and expanded for clinical testing and therapeutic use.

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TCR Product Offering: BPS offers a unique portfolio of tools to enhance TCR research, including TCR knockout reporter cell lines, lentiviral vectors to introduce the engineered TCR genes into the T cells, T cell isolation kits, tumor antigen-specific peptides that can be used for "loading" MHCs or stimulating antigen-specific CD8⁺ T cells, and much more. In particular, ready-to-use antigen-specific TCR-expressing reporter cells are available for the design and optimization of co-culture bioassays, or to use as positive controls in bioassays.

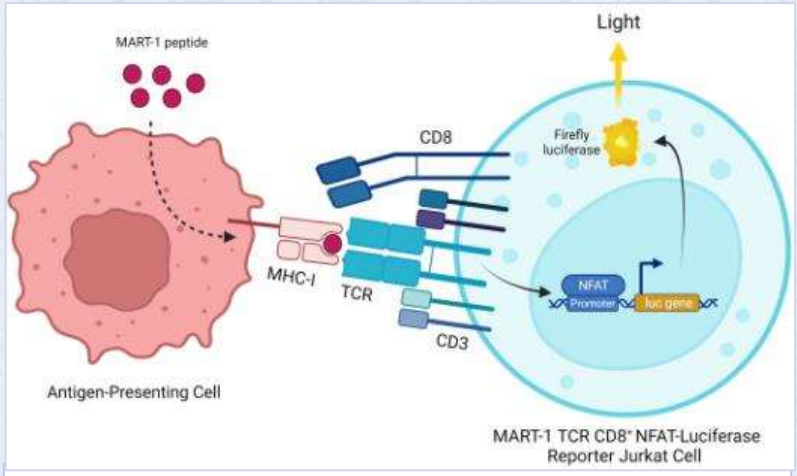

Illustration of a functional co-culture assay used to validate the MART-1 TCR (DMF4) CD8⁺ NFAT-Luciferase Reporter cell line (#78772).

Many of the commonly studied cancer targets below are expressed primarily in testes but are absent from other normal tissues, making them valuable targets for adoptive T-cell transfer and cancer vaccines. Click each antigen to see the full list of lentivirus, peptides, and cell lines available from BPS for that target.

MAGE (Melanoma Antigen): MAGE antigens are expressed in a wide range of tumors, including melanoma, lung cancer, and breast cancer.

PRAME (Preferentially Expressed Antigen in Melanoma) is expressed in a variety of cancers, including melanoma, leukemia, and solid tissues.

NY-ESO-1 (New York Esophageal Squamous Cell Carcinoma 1): NY-ESO-1 is another cancer/testis antigen expressed in several types of tumors, including melanoma, sarcoma, lung cancer, and ovarian cancer.

MART-1 (Melanoma Antigen Recognized by T-cells 1) is overexpressed in melanoma cells and can also be found in certain types of sarcomas.

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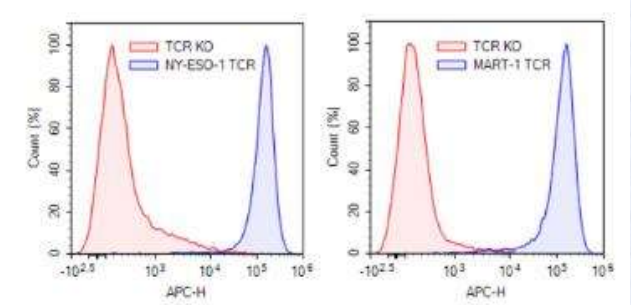
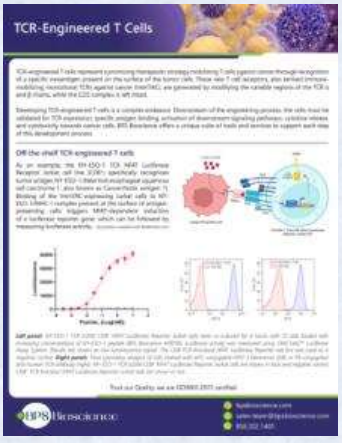


Expression of transgenic TCR in Jurkat cells transduced with TCR lentiviruses

Some of the most popular BPS products are the **TCR knockout** reporter cell lines, which allow researchers to reintroduce specific TCR variants to compare how different TCRs influence signaling cascades. BPS also offers knockouts for B2M (β2-microglobulin), a component of the MHC class 1 molecules required for antigen presentation and stabilization of the MHC complex. The TCR/β2M knockout cell lines are particularly useful to evaluate CAR-T cells, since the lack of endogenous TCRs and MHC class I molecules provides a clean background to study the specific interactions and efficacy of CAR-T cells without interference from native TCRs.

CD8+ TCR Knockout NFAT-Luciferase Reporter Jurkat Cell Line	#78757
CD4+ TCR Knockout NFAT-Luciferase Reporter Jurkat Cell Line	#82319
TCR Knockout NFAT-Luciferase Reporter Jurkat Cell Line	#78556
TCR/B2M Knockout NFAT Luciferase Reporter Jurkat Cell Line	#78557
TCR Knockout Jurkat Cell Line	#78539
TCR/B2M Knockout Jurkat Cell Line	#78552
B2M Knockout NFAT Luciferase Reporter Jurkat Cell Line	#78363

Resources: Learn more about using antigen-specific TCRs for adoptive cell therapy on our website landing page. We also offer a helpful flyer on TCR-engineered T cells (click image or go to Dropbox for the different print size files).



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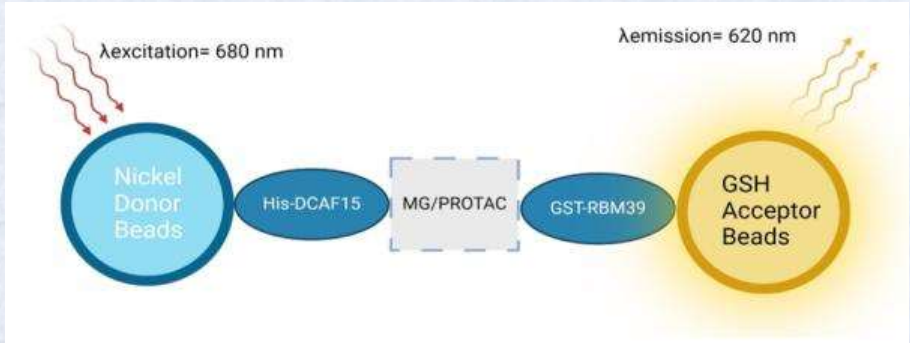
Highlight: Molecular Glues

Molecular glues are a class of small molecules that facilitate or stabilize interactions between proteins or other biomolecules that would not typically interact. They are called "glues" because they essentially "stick" 2 different proteins together, bringing them in close proximity to enable a specific biological pathway. Molecular glues have been increasingly recognized for their potential in drug discovery, particularly in targeting previously "undruggable" proteins.

Most commonly, molecular glues are used to target and modulate the activity of E3 ubiquitin ligases, which are involved in tagging proteins for degradation. By facilitating the interaction between specific E3 ligases and target proteins, PROTACs and other molecular glue compounds can alter cellular processes, making them promising therapeutic treatments for cancer, immune disorders, and neurodegenerative diseases.

Researchers are exploring various strategies to design and develop new molecular glues with high specificity and efficacy. BPS has developed two new assay kits to optimize drug development:

#82251 Molecular Glue/PROTAC® Optimization Kit for RBM39-DCAF15
#82588 Molecular Glue/PROTAC® Optimization Kit for CDK/Cyclin K-DDB1 Complex

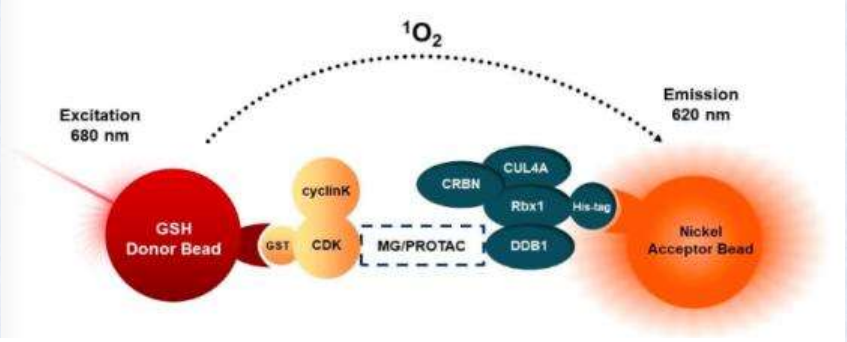


The Molecular Glue/PROTAC® is incubated with DCAF15 complex and RBM39, bringing them in close proximity. DCAF15 contains a His-tag, which is recognized by the donor beads. RBM39 contains a GST tag that binds to the GSH- AlphaLISA™ acceptor beads. Upon excitation, a singlet oxygen is generated that excites the acceptor bead, which emits light proportional to the level of interaction between RBM39 and DCAF15.

The two kits feature RBM39 and CDK12/ Cyclin K. RBM39 regulates RNA splicing, translation, and RNA degradation. Dysregulation of RBM39 affects RNA splicing and gene expression, and is linked to tumorigenesis. Aryl sulfonamides such as E7820 can act as

molecular glue between RBM39 and DCAF15-associated E3 ubiquitin ligase complex, leading to ubiquitination and selective degradation of the RBM39.

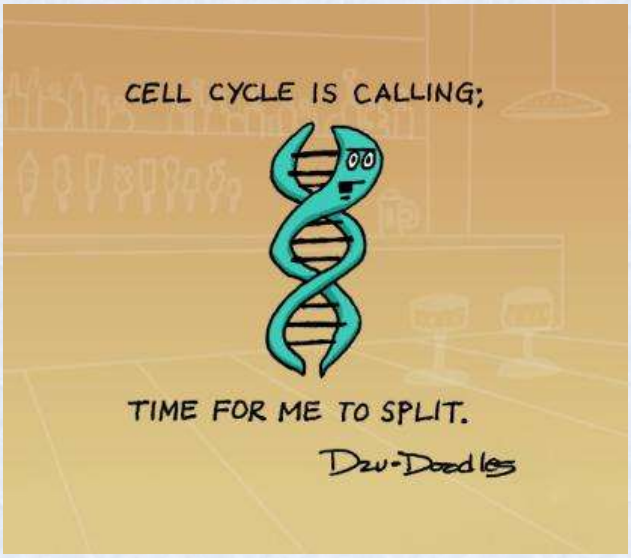
Similarly, CDK12/ Cyclin K is involved in transcriptional regulation, DNA damage repair, and genomic stability. The molecular glue (CR8) forms a complex between the CDK12/ cyclin K and the DDB1 portion of the CUL4 complex (an E3 ubiquitin ligase), leading to ubiquitination and degradation of CDK12/ Cyclin K.

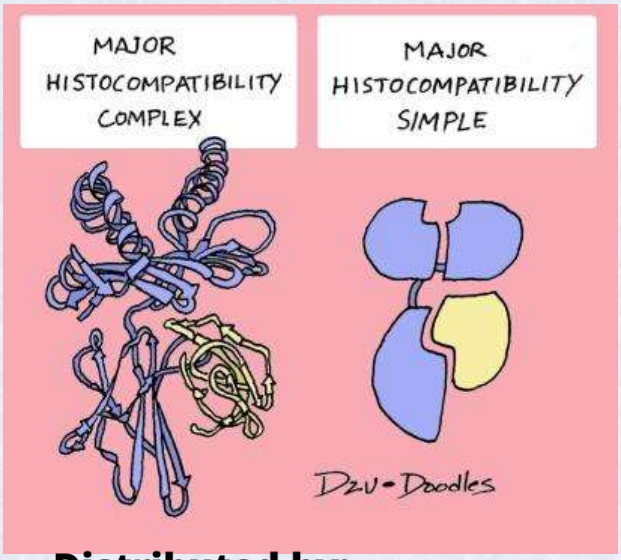


The Molecular Glue/PROTAC® brings the DDB1 containing complex and CDK/Cyclin K into close proximity. The DDB1/Cereblon complex contains a His-tag, which is recognized by the Nickel- AlphaLISA™ acceptor bead. CDK12/Cyclin K contains a GST-tag that binds to the donor bead. Upon excitation, a singlet oxygen is generated that excites the acceptor bead, which emits light proportionally to the level of protein interaction.

Development of novel Molecular Glues and PROTACS involved in the recruitment of RBM39 or CDK12 provides a framework for future efforts to manipulate protein interactions and induce E3 ligases to degrade other proteins of interest. For more information, view our technical note, Targeted Protein Degradation Approaches and Applications.

Dzung's Doodles





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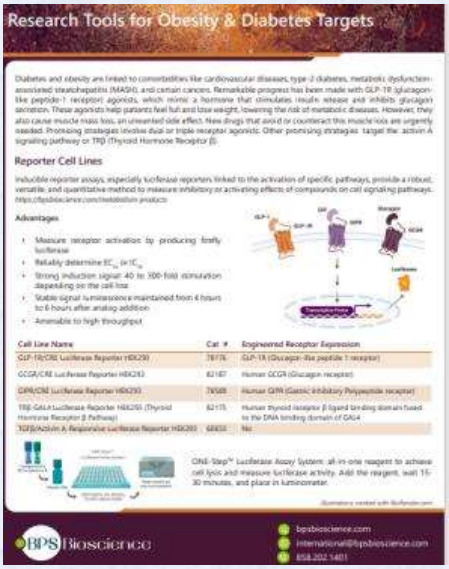
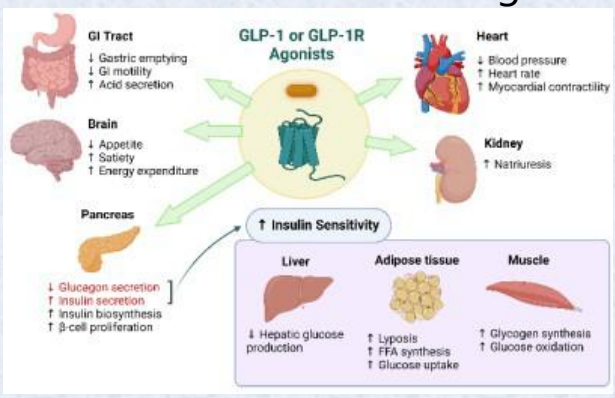
New Flyer: Research Tools for Obesity and Diabetic Targets.

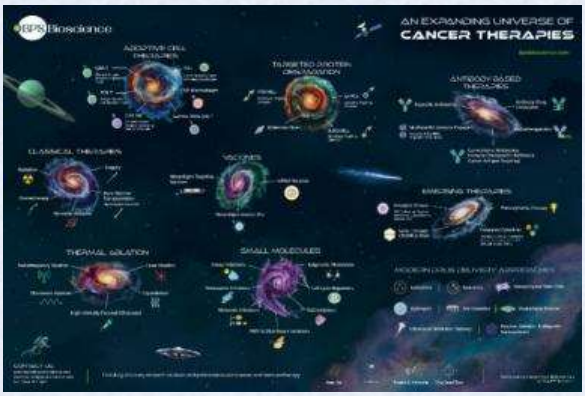


Studying glucose metabolism, diabetes, and obesity is crucial for developing effective treatments and preventative strategies to combat these interconnected health conditions and improve overall public health. Our newest flyer highlights tools for obesity and diabetes research, including our GLP-1R, GIPR, and GCGR cell lines, plus our Activin A-responsive and Thyroid Hormone Receptor β reporter cell lines and Activin A inhibitor screening kit. You can also learn more about GLP-1R and Diabetes on our new website landing page.



Download the flyer from Dropbox, or visit Literature to see our full list of available brochures, flyers, and handouts.

Don't forget to request copies of our poster, **"The Expanding Universe of Cancer Therapies".** Your customers will love hanging this artistic overview on their walls. Contact the International team so we can coordinate shipping you some posters to share with your customers!



Note: we also plan to offer a colorful 2025 calendar in the next couple of months -- stay tuned!

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