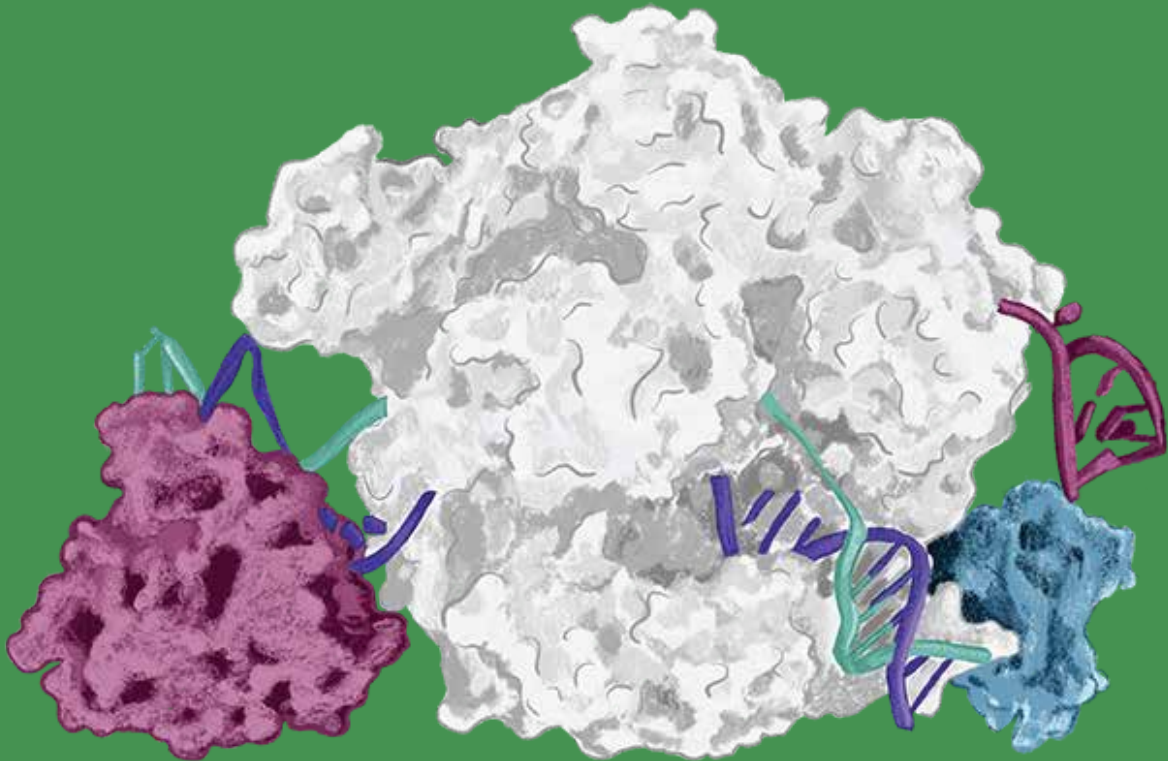


KACATUS

AccuBase™ Cytosine Base Editor

GMP-Grade



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CliniSciences Group

About AccuBase™

AccuBase™ is a cytosine base editor engineered by Base Therapeutics and manufactured for global sales by KACTUS. It creatively embeds a deaminase inside the Cas protein to prevent random binding of deaminase to non-target sites, significantly reducing off-target occurrence while still maintaining high editing efficiency. Using our protein engineering and expression platform, Structure Aided Multiplex Screening (SAMS™), KACTUS has successfully manufactured the DNA base editor. We've maximized the stability, purity, and activity of AccuBase™ by screening our AccuBase™ protein expression system, optimizing the purification process, and performing formulation development. AccuBase™ is a cytosine base editor which can convert a C•G base pair into a T•A base pair.

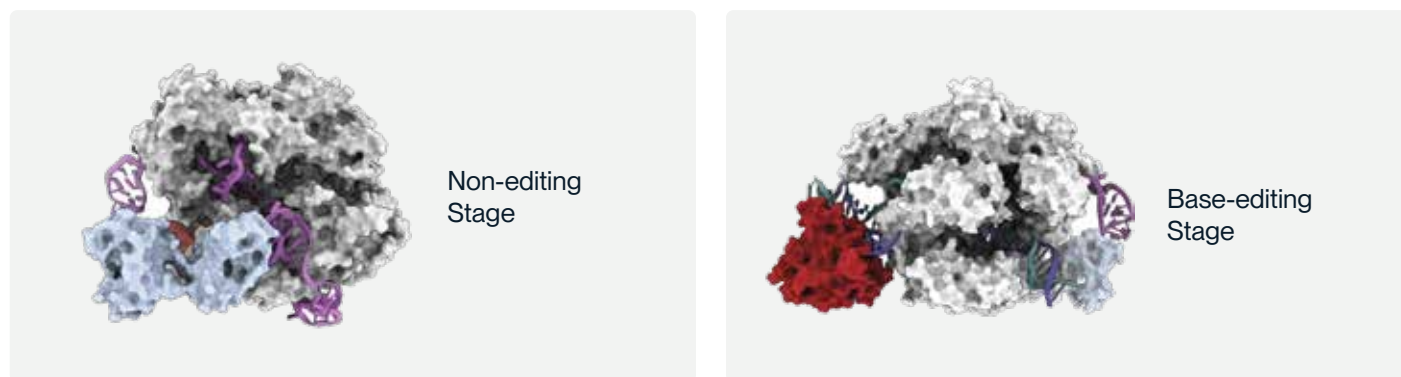


Figure 1. Structural image of AccuBase™ in non-editing state and base-editing state.

After forming a ribonucleoprotein (RNP) with sgRNA, the AccuBase™ protein remains in a non-editing state before binding to the target DNA (Figure above, left). The deaminase is encapsulated inside the Cas9n protein and does not interact with any non-target DNA, thus significantly reduces the risk of off-target effects.

When the RNP binds to the target DNA, the conformation of AccuBase™ changes, leading to the exposure of deaminase domain and effectively editing bases within the 3-12 window range of the target site (with the first position being the farthest from the PAM) (Figure above, right).

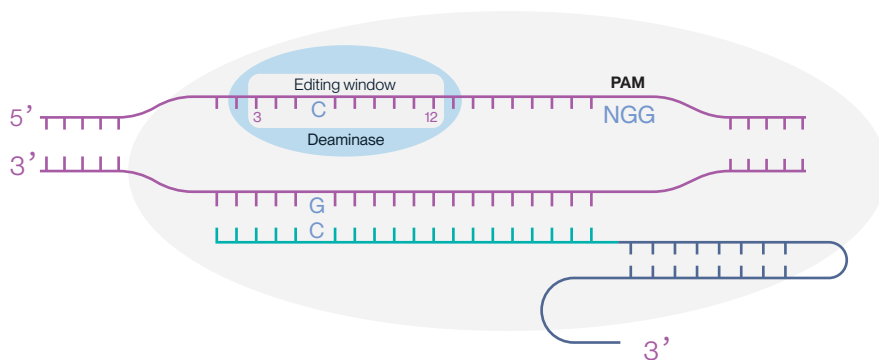
Product Specifications

Parameter	Specification
Express System	E. Coli
Concentration	10mg/ml
Molecular Weight	210.14kDa
Form	Liquid
Storage Buffer	30 mM Tris, 300 mM NaCl, 0.1 mM EDTA, 1 mM DTT, 50% Glycerol, pH8.0
Storage	Store at -80 ±10°C

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How does AccuBase™ work?



AccuBase™ is ideal for:

- Correcting a single point mutation
- Gene knockout by introducing premature stop codons or inducing exon skipping by disrupting splice acceptor (SA) sites or splice donor (SD) sites

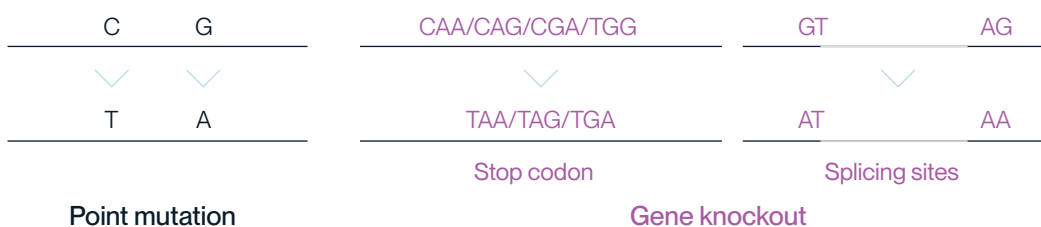


Figure 2. AccuBase™ mechanism of action.

GMP Compliance

ISO13485 Certification

ISO13485:2016 certification is an internationally recognized standard that sets out the requirements for a quality management system that ensures companies adhere to stringent quality control measures, regulatory compliance, and risk management practices throughout the entire product lifecycle. Our company has obtained ISO13485:2016 certification to demonstrate our commitment to producing safe, reliable, and high-quality proteins and enzymes.

Approval ID: 00034327

Regulatory Documentation

AccuBase™, GMP-Grade (GMP-KD-0001) comes with customizable regulatory documentation including **Data Sheet, MSDS, COA, TSE/BSE statement, CoO**. KACTUS has a comprehensive documentation system including a digital quality management system, specification program, criteria support documents, and quality reports. Our product release process involves 15+ contaminant detection steps, 30+ quality tests, 4+ report reviews, and 4+ product release checkpoints. We can customize your documentation package based on relevant regulatory filings.

Quality Specifications for AccuBase™

AccuBase™, GMP-Grade (GMP-KD-0001) is manufactured according to cGMP guidelines in our 10,000m² manufacturing facility and undergoes the following quality release testing.

Parameter	Acceptance Criteria
pH	8.0±0.5
Concentration	9.0-11.0mg/mL
Purity (electrophoresis)	≥ 80.0%
Purity (RP-HPLC)	≥ 88.0%
Purity (SEC-HPLC)	≥ 80.0%
Residual DNase	Sample/Control ≤ 3.0
Residual RNase	Sample/Control ≤ 3.0
Residual Host Cell Protein	≤ 100.0ng/mL
Residual Host Cell DNA	≤ 200.0ng/mL
Endotoxin	≤ 10.0EU/mg
Sterility	Negative
Mycoplasma	Negative

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Why choose AccuBase™?

Near-Zero Off-Target Event Measurement

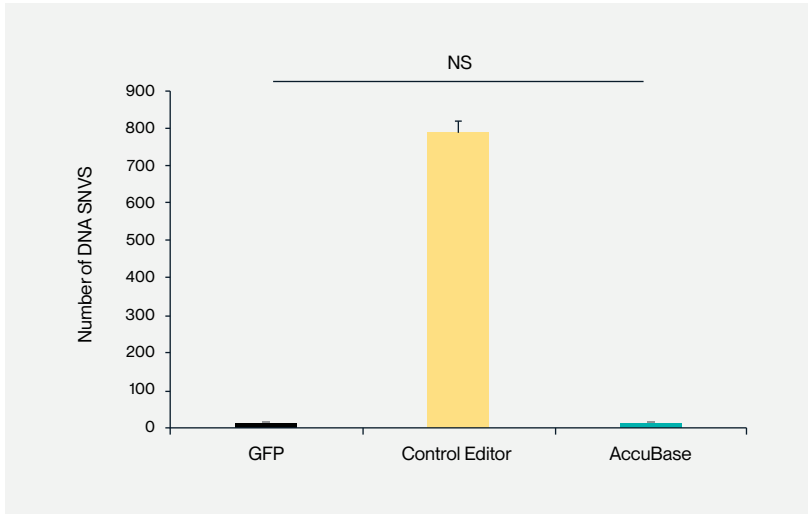


Figure 3. Measurement of off-target effects by GOT1. By leveraging the GOT1 (genome-wide off-target analysis by teo-cell embryo injection) to measure the off-target effects throughout the whole genome, it was shown that compared to the control base editor (with 700 SNVs detected), the number of SNV obtained after editing by AccuBase™ is similar to the GFP (negative control) group, suggesting a near-to-zero off-target effects of AccuBase™.

Avoids creation of INDELS and chromosomal translocation

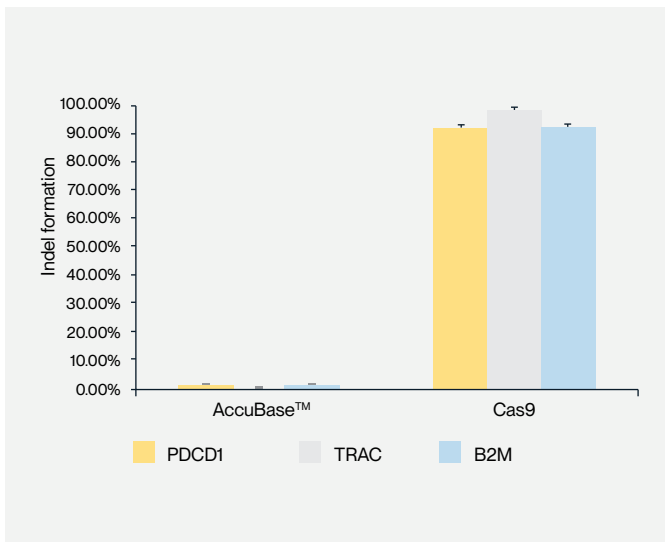


Figure 4. Compared with Cas9 protein, AccuBase™ does not produce DNA horizontal insertions and deletions (INDELS).

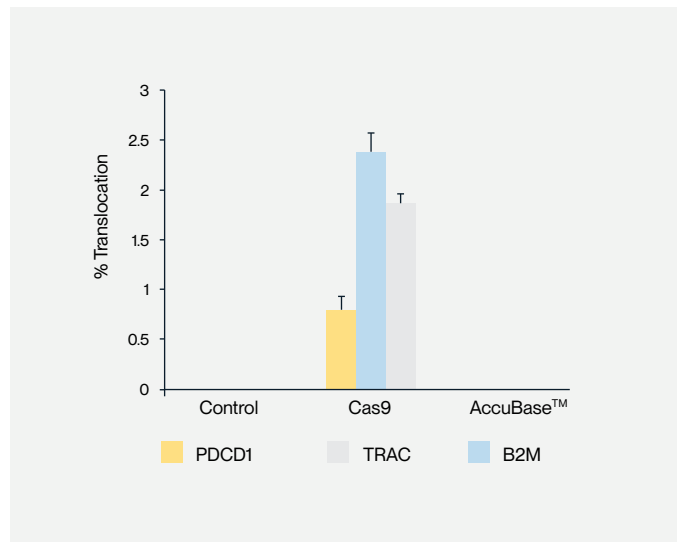
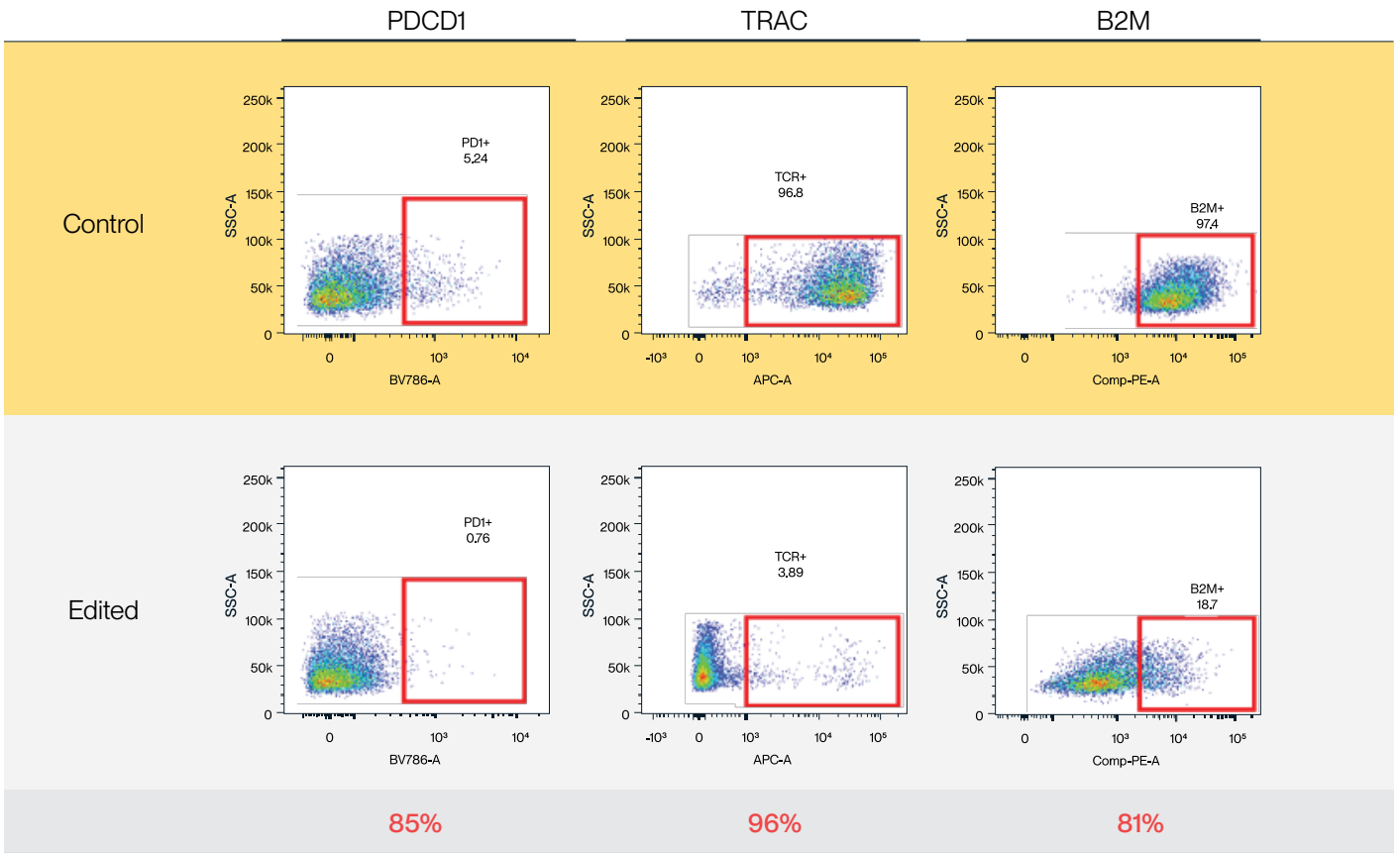


Figure 5. Compared with Cas9 protein, AccuBase™ does not cause chromosomal translocation.

High Base Editing Activity

Activated Primary T Cells



FACS efficacy %

$$\text{Facs efficacy \%} = (\text{positive control} - \text{KO group}) / \text{positive control} * 100\%$$

Figure 6. AccuBase™ RNP was electroporated into activated primary T cells. According to flow cytometry, AccuBase™ can efficiently knock out PD1, B2M, and TRAC proteins on the membrane of activated primary T cells at the protein level. For PD1 and B2M, the knockout efficiency exceeded 80%, while the knockout efficiency of TRAC reached 96%.

Unactivated Primary T Cells

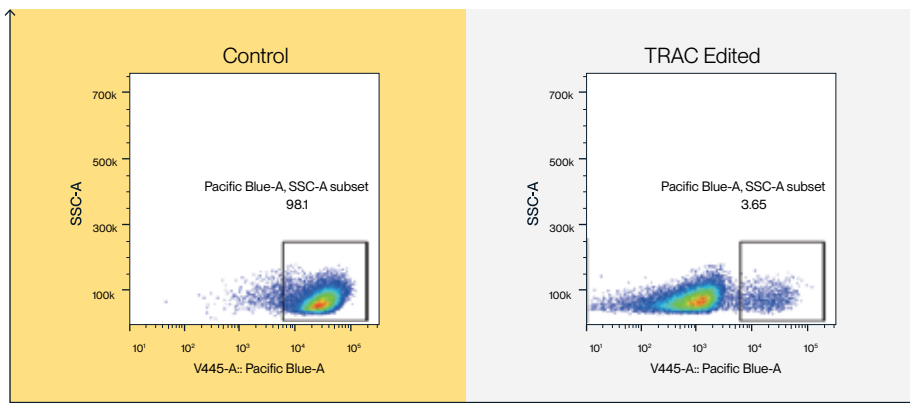


Figure 7. AccuBase™ RNP was electroporated into unactivated primary T cells. According to flow cytometry, AccuBase™ can efficiently knock out the TRAC protein of unactivated primary T cells at the protein level, with a knockout efficiency of up to 96%.

Frequently Asked Questions

Product Specifications

Is AccuBase™ manufactured according to GMP guidelines?

Our GMP-Grade AccuBase™ (#GMP-KD-0001) is always manufactured according to cGMP guidelines. We also offer a research-grade version of AccuBase™ (#KD-0001) that does not undergo GMP quality control testing.

What regulatory documentation is available for GMP-Grade AccuBase™?

AccuBase™, GMP-Grade (#GMP-KD-0001) comes with customizable regulatory documentation including Data Sheet, MSDS, COA, TSE/BSE statement, and CoO. Batch production records, batch inspection records, etc, can also be provided. Please contact us so we can learn more about your specific regulatory filings.

What are the advantages of AccuBase™ over other gene editing enzymes?

Compared to Cas9 and other Cas family gene editing enzymes, AccuBase™ does not cause DNA double-strand breaks, does not require donor DNA, and is not dependent on the cell cycle for precise gene repair. It also does not produce INDELS and thus poses no risk of chromosomal translocations.

Compared to other CBEs (Cytosine Base Editors), its unique structural design allows editing only at the target site, with no random off-target activity, while maintaining high editing efficiency.

How does AccuBase™ have near-zero off-target characteristics?

AccuBase™ is an engineered DNA cytosine base editing protein, creatively embedding a deaminase within the Cas protein. When AccuBase™ protein forms an RNP with sgRNA, it remains in a non-editing state until it binds with the target DNA. The deaminase, encased inside the Cas9n protein, does not act on any non-target DNA, significantly reducing off-target risk. When AccuBase™ RNP binds to the target DNA, a conformational change in AccuBase™ exposes the deaminase domain, allowing C-to-T editing within the 3-12 window range (with the first position being far from PAM).

What is the difference between research-grade and GMP-grade AccuBase™?

- **Production Environment.** GMP-grade AccuBase™ is produced in our GMP manufacturing facilities, whereas research-grade is produced in non-GMP facilities.
- **Quality Control Testing.** GMP-grade AccuBase™ includes tests for appearance, concentration, purity (2100), purity (SEC-HPLC), purity (RP-HPLC), endotoxin, DNA enzyme residue, RNA enzyme residue, host protein residue, host DNA residue, sterility, and mycoplasma. Research-grade includes concentration, identification (Bis-Tris PAGE), purity (SEC-HPLC), and endotoxin.
- **Regulatory Documentation.** GMP-grade AccuBase™ includes complete method validation, process validation reports, COA, COO, non-animal source statements, stability studies, etc., supporting client project applications. Research-grade includes instruction manuals and COA, not supporting client project applications.
- Both research-grade and GMP-grade have the same bacterial strain origin, same materials used in production, same production process, and consistent protein activity.

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Frequently Asked Questions

Product Usage

What are the applications of AccuBase™?

- **Gene Knockout:** Through mutating start codons, introducing stop codons, and altering splice sites.
- **Gene Repair:** Repairing pathogenic sites.
- Suitable for cells that can be electroporated or directly injected, including adherent cells, suspension cells, embryonic cells (fish, mice, etc.), and plant embryos (gene gun method).

Can AccuBase™ Achieve Multi-Gene Knockout?

AccuBase™ can not only achieve single-gene knockout but also simultaneously knock out 2, 3, or more genes.

How do I design sgRNA for AccuBase™?

The single guide RNA (sgRNA) scaffold for AccuBase™ is the same as that used for spCas9. Designing sgRNA for gene knockout with AccuBase™ involves considering editing within the 3-12 position window. A simple approach is to first search for triplet codons CAA (Gln), CAG (Gln), CGA (Arg), or TGG (Trp), and then look for suitable PAMs (NGG) nearby.

Are there patent licensing issues with AccuBase™?

AccuBase™, designed and developed by Base Biotechnology, holds full independent intellectual property rights and foundational technology patents. Potential partners/clients interested in using AccuBase™ in their projects need to discuss patent licensing matters with Base Biotechnology. The company adopts an open, flexible, and sincere approach in negotiations.

How do I use AccuBase™?

For detailed operation instructions, refer to the datasheet on kactusbio.com. For specific scientific support, contact

Ordering

How do I order AccuBase™?

You can order AccuBase™ directly online via credit card or PO.

What sizes are available?

Research-grade AccuBase™ is available in 200UG / 500UG / 1MG. GMP-Grade AccuBase™ is available in 1MG. Bulk sizes are available.

What is the relationship between KACTUS and Base Therapeutics?

Base Therapeutics has engineered AccuBase™ in-house. KACTUS has optimized the recombinant expression, purification, and large-scale manufacturing process of AccuBase™, as well as solidified the GMP compliance.

Where does AccuBase™ ship from?

AccuBase™ ships from our U.S. office located at 60 Hickory Drive, Waltham MA 02451.

What is the lead time for AccuBase™?

AccuBase™, both the research-grade and GMP-grade, is an off-the-shelf product. The lead time is up to two weeks. However, some smaller sizes may ship out next day.

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AccuBase™ ELISA Kit

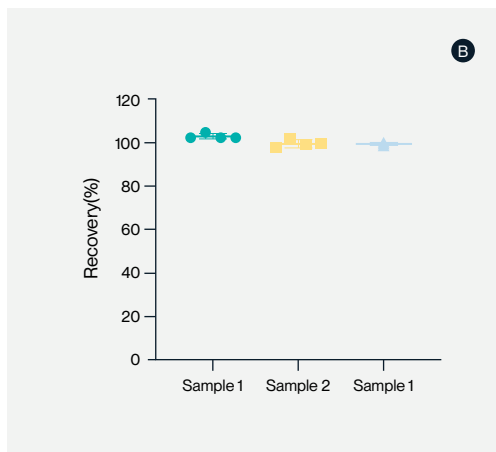
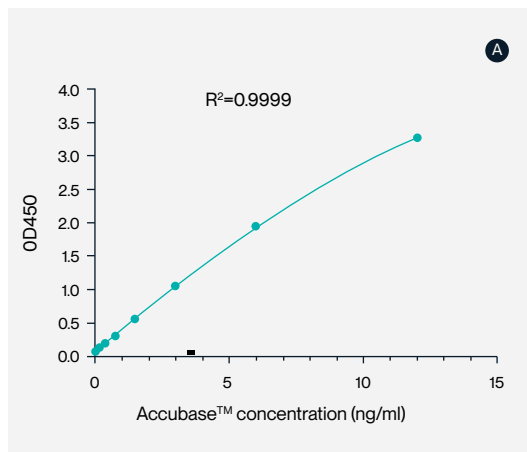


Figure 8. (A) Example 8-point standard curve for AccuBase™ ELISA. The quantitative range of this ELISA kit is 187.5 pg/mL - 12 ng/mL. (B) The recovery rate of the kit was analyzed by testing three AccuBase™ samples with known concentrations in dilution buffer using the same AccuBase™ ELISA kit. Results show that in dilution buffer, the recovery rate of various AccuBase™ sample concentrations is between 80% and 120%, indicating that this reagent kit has high accuracy.

Ordering Information

Catalog #	Product Name	Grade	Available Sizes
KD-0001	AccuBase™, BS-EP1, RUO	Research-Grade	200µg / 500µg / 1mg
GMP-KD-0001	AccuBase™, BS-EP1, GMP	GMP-Grade	1mg
RD-K-014	BS-EP1 (AccuBase) ELISA Kit	Research-Grade	96 Tests

Note: AccuBase™ is the trade name of BS-EP1.

About KACTUS

KACTUS excels in crafting and producing an array of superior-grade, highly active recombinant proteins and enzymes, catering to diverse sectors like antibody drug discovery, immunotherapy, gene therapy, and mRNA therapeutics. Our expansive catalog, boasting over 2500 recombinant proteins, encompasses a wide spectrum of targets, species, tags, and labels, each thoughtfully chosen to address the specific, unmet needs of scientists engaged in drug development. The hallmark of our product selection process is a rigorous emphasis on exceptional quality and a steadfast commitment to ensuring reliable supply, thereby upholding the highest standards of excellence and client satisfaction.

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