



EXTENSIVE EXPERIENCE. SUPERIOR QUALITY. **INNOVATIVE SOLUTIONS.**

R&D AND MANUFACTURING SUPPORT FOR THE
BIOTECHNOLOGY AND BIOPHARMA INDUSTRY



be **INSPIRED**
drive **DISCOVERY**
stay **GENUINE**



LET NEB'S SCIENTIFIC EXPERTISE HELP **DRIVE YOUR INNOVATIONS FORWARD**

In recent years, there has been a dramatic rise in the number of biologics and companion diagnostics developed and commercialized, and these important areas of biotechnology are more reliant than ever on cutting edge molecular biology tools and techniques. For instance, companion diagnostics, based on DNA amplification, can foster a better match of effective therapies with patients; personalized medicines, utilizing next-generation sequencing, can also help tailor treatments for specific patients; and a wide range of biologics is now being developed as a result of advancements in recombinant technologies.



THE NEB DIFFERENCE

At NEB, we have **decades of experience** in practicing molecular biology, which has led to the introduction of a broad product portfolio that has the potential to touch almost every stage of today's biotechnology discovery and development processes. With this expertise in hand, we are ready and able to **collaborate with biotech companies**, large and small, to support their discoveries and help them move through clinical testing, manufacturing, and quality control, and into regulated markets around the world.

COLLABORATION

We're here to champion your efforts. We have **extensive scientific expertise** and can devote the necessary attention to developing solutions for your specific needs – along with the manufacturing capacity to **scale up quickly**. Whether you're looking for a custom version of an existing product, to find a new way around a development roadblock, or to license one of our technologies, our team is **ready to work with you**.

PRODUCT PORTFOLIO

We can provide an entire **suite of enzymes** that have the potential to **accelerate your discovery efforts**. Our expertise in enzymology has enabled us to develop unique enzymes that enable **faster, more robust workflows**. Further, enzymes can be provided both in small aliquots and in bulk, in different formats (liquid, lyophilized and glycerol-free), as well as packaged into complete kits. And if you cannot find what you need, let's see if we can come up with a solution that does!

QUALITY

Our attention to quality is **second to none**. We are fully compliant and certified to ISO 9001:2008 and ISO 13485:2003 standards, and have recently completed building a **GMP manufacturing facility** for reagents used in more regulated markets.

TECHNICAL SUPPORT

You can be sure that the people you contact for technical support are as knowledgeable as the scientists who work in our labs – because they're one and the same. When you pick up the phone or send an email, you **get right to the source of useful information** and effective solutions.

GLOBAL SUPPLY CHAIN

In addition to our headquarters in the USA, NEB has warehousing capabilities in Canada, China, UK, Germany, Japan and Singapore, which can be used to not only **access our products rapidly**, but also get them to your collaborators and customers. NEB also has a number of Freezer Program options that combine onsite access with **improved ways of managing your lab inventory and cash flow**.



THINK OF NEB AS YOUR EXPERIENCED **PARTNER** THROUGHOUT THE BIOTECHNOLOGY **DISCOVERY** PROCESS

SYNTHETIC BIOLOGY AND DNA ASSEMBLY

A more recent expansion of the biotechnology field, synthetic biology utilizes genes and proteins as parts or devices, with the goal of re-designing and/or assembling these parts in novel ways to create a new and useful functionality.

Recent advances in biofuels generation, the production of biochemicals, and understanding the minimal genome all benefit from synthetic biological approaches. Historically, conventional genome engineering in the agricultural industry has involved the insertion of new genes in plants. Synthetic biology approaches enable the insertion of entire genetic pathways to produce desirable traits, such as disease resistance or improved nutritional value.

The pharmaceutical industry has also benefitted from advances in synthetic biology. Examples include the design of minimal synthetic cells, containing a genetic circuit linking genetic regulators with an output signal, such as luminescence or fluorescence for phenotypic cell-based screening, the generation of small molecule libraries from the reorganization of synthetic biology parts, and cell-free metabolic engineering.

Often these projects rely on the ordered assembly of multiple DNA sequences to create large, artificial DNA structures. To this end, methods have evolved to simplify this process. Tools such as **NEBuilder® HiFi DNA Assembly (NEB# E2621, E5520, E2623)** and **NEB Golden Gate Assembly Mix (NEB# E1600S)** can be used to rapidly create many functional DNA structures, from a simple joining of two metabolic genes, all the way up to the creation of an artificial genome.

 NEB provides a wide range of products to support synthetic biology, DNA assembly and other cloning techniques. Find out how these products can speed up your workflows for both simple and complex reaction design at **CloneWithNEB.com**.

FEATURED PRODUCT: NEBuilder® HiFi DNA Assembly

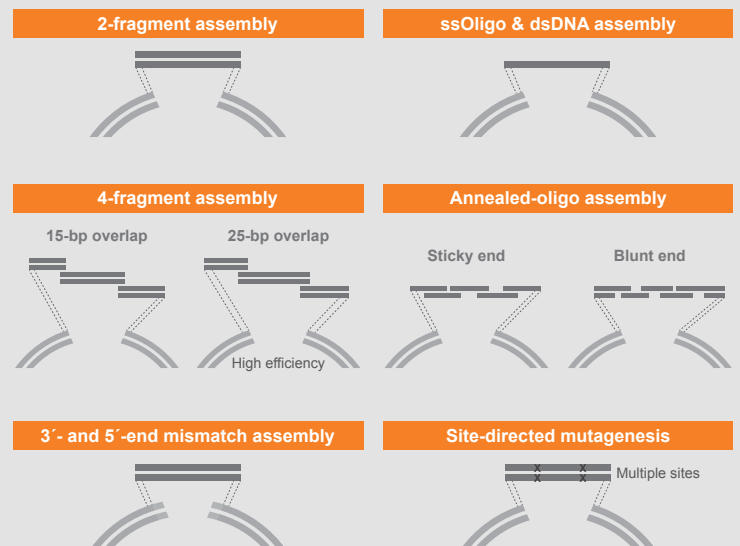
NEB #E2621S/L/X

- Enjoy simple and fast seamless cloning in as little as 15 minutes
- Use one system for both "standard-size" cloning and larger gene assembly products, up to 12 fragments
- DNA can be used immediately for transformation or as template for PCR or RCA
- Adapts easily for multiple DNA manipulations, including site-directed mutagenesis
- Design primers using our free online tool at **NEBuilder.neb.com**
- No licensing fee requirements from NEB for NEBuilder products



Visit **NEBuilderHiFi.com** for more details.

Not your average DNA assembly reagent



NEBuilder HiFi DNA Assembly can be used for a variety of DNA assembly methods.



GENOME EDITING (CRISPR/CAS9)

Perhaps no other tool in genomic engineering has received more attention of late than CRISPR-based methods. Programmable nucleases enable the generation of permanent mutations by generating site-specific double stranded breaks. Knock-outs and knock-ins can be rapidly introduced in cell lines and model organisms.

The validation of small molecule targets by knocking out gene function or rescuing drug sensitivity by modifying drug resistant alleles is now a standard method for target validation. By combining next generation sequencing for the discovery of compound-resistant mutations and CRISPR-based methods for target validation, drug-target pairs can be identified and validated in model systems, such as mammalian cells, as well as model organisms.

NEB provides reagents to support a broad variety of CRISPR/Cas9 genome editing approaches. From the introduction of Cas9 and single guide RNA (sgRNA) into plasmids, to direct introduction of Cas9 ribonucleoprotein (RNP), and the detection of edits using next generation sequencing or enzymatic mutation detection, NEB provides reagents that simplify and shorten genome editing workflows.



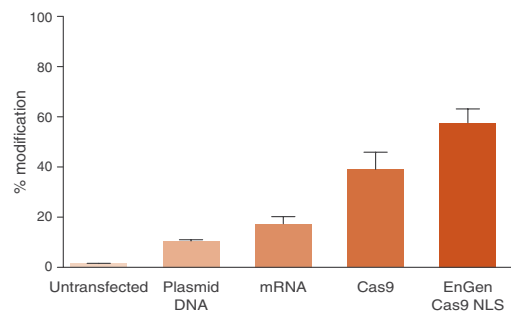
For more details on how NEB can help improve your genome editing efficiencies, visit www.neb.com/GenomeEditing.

FEATURED PRODUCT: EnGen® Cas9 NLS

NEB #M0646T/M

- Ideal for direct introduction of Cas9/sgRNA complexes
- Dual NLS for improved transport to the nucleus
- Compatible with the EnGen sgRNA Synthesis Kit, *S. pyogenes* (NEB #E3322S) and the EnGen Mutation Detection Kit (NEB #E3321S)

Increased genome editing efficiency using Cas9 RNP delivery



Cas9 and sgRNA targeting a human gene were delivered to HEK293 cells by transfection. Transfected plasmid DNA contained expression cassettes for 2x NLS (N- and C-terminal) Cas9 and sgRNA. Plasmid DNA was delivered using TransIT-X2 (Mirus). Transfected mRNA was modified with pseudouridine and 5-methylcytosine and encoded 2x NLS (N- and C-terminal) Cas9. sgRNA was co-transfected with the mRNA using TransIT-mRNA. Cas9 RNPs were delivered in reverse transfections using Lipofectamine RNAiMAX (Life Technologies) using 10 nanomolar final concentration of ribonucleoprotein (RNP). Cas9 has no NLS in the protein sequence. EnGen Cas9 has N- and C-terminal NLSs. The efficiency of editing was determined using T7 Endonuclease I assay and is expressed as % modification.



Visit www.neb.com/M0646 for more details.



NEXT GENERATION SEQUENCING

Next generation sequencing (NGS) has proven a valuable technology across a broad range of activities involved in the development and application of novel therapies. Library preparation is a critical part of the NGS workflow; successful sequencing requires the generation of high quality libraries of sufficient yield and quality. Further, with sample numbers and types increasing, high performance is required from ever-decreasing input quantities and from samples of lower quality.

With over 40 years of expertise in enzyme research and manufacturing, **NEB is a world leader in the development of innovative technologies supporting sample prep for next generation sequencing.** With over 50 application-specific products available, the NEBNext® product portfolio supports a broad range of sequencing based technologies, including whole genome sequencing, transcriptome and single-cell sequencing (RNA-seq) and target enrichment.



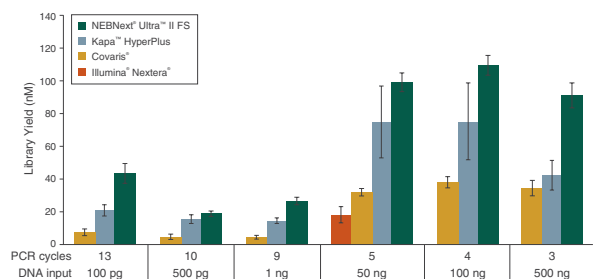
Find out how NEBNext kits can help streamline your workflows and generate high quality libraries, even with limited amounts of DNA or RNA, at **NEBNext.com**.

FEATURED PRODUCT: NEBNext® Ultra™ II FS DNA Library Prep Kit for Illumina®

NEB #E7805/L

- Perform fragmentation, end repair and dA-tailing in a single enzyme mix
- Experience reliable fragmentation with a single protocol, regardless of DNA input amount or GC content
- Prepare high yields of high quality libraries from a wide range of input amounts: 100 pg – 0.5 µg

NEBNext Ultra II FS DNA produces the highest yields, from a range of input amounts



Libraries were prepared from Human NA19240 genomic DNA. For NEBNext Ultra II FS, a 20-min. fragmentation time was used. For Kapa HyperPlus libraries, input DNA was cleaned up with 3X beads prior to library construction, as recommended, and a 20-min. fragmentation time was used. Illumina recommends 50 ng input for Nextera, and not an input range; therefore, only 50 ng was used in this experiment. "Covaris" libraries were prepared by shearing in 1X TE Buffer to an insert size of ~200 bp using a Covaris instrument, followed by library construction using the NEBNext Ultra II DNA Library Prep Kit (NEB #E7645). Error bars indicate standard deviation for an average of 3–6 replicates performed by 2 independent users.



Visit www.neb.com/E7805 for more details.

NOVEL SOLUTIONS TO ADVANCE YOUR TECHNOLOGIES FASTER

TARGET ENRICHMENT

Genomic information has been widely applied to the development of novel biomarkers associated with a wide variety of human diseases. Techniques including whole genome sequencing, whole exome sequencing and RNA sequencing are now routinely applied to identifying genetic variation across patient cohorts demonstrating common phenotypes in the presentation of disease. These data are used for the identification of therapeutic targets, as well as the elucidation of disease pathways and mechanisms of therapeutic resistance. Downstream in these pipelines, genomic data is increasingly being applied to pharmacogenomics studies aimed at understanding the efficacy of therapies on stratified patient populations.

Inclusion of genomic profiling in clinical trials has become commonplace, both prospectively and retrospectively. For prospective studies, targeted gene panels are being applied across trial participants, with the goal of matching therapeutic response outcomes with patient genotypes. Retrospectively, broad genomic profiling of patients with either a positive or negative therapeutic response are being used to identify specific variants with the potential to serve as biomarkers to predict therapeutic efficacy.

Finally, targeted gene panels focusing on specific biomarkers with proven predictive value are being developed as companion diagnostics. These assays, which are included as part of a therapy's FDA approval process, are now commonly used to determine therapeutic applicability for a specific patient.

NEBNext Direct[®] employs a **unique technology that enables highly specific target enrichment of genomic regions** of interest. This innovative approach balances the speed and precision of multiplexed PCR-based approaches with the content scalability typical of hybridization-based methods. This flexibility allows a single workflow for assays ranging from single gene tests to comprehensive panels including several hundred genes.



Regardless of sample type or assay content, NEBNext Direct allows you to enrich your targets with precision. Learn more at NEBNextDirect.com.

FEATURED PRODUCT: NEBNext Direct[®] Custom Ready Panels

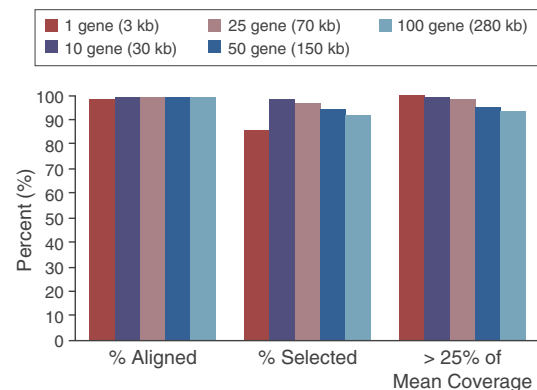
NEB #E6631S/L/X

- Choose from a single gene to hundreds of genes
- Experience unmatched specificity and coverage uniformity
- Eliminate synthesis and optimization steps for faster turnaround
- Improve sensitivity with our Unique Molecule Index (UMI)
- Generate results in one day with our automation-friendly workflow



Visit NEBNextDirect.com for more details.

NEBNext Direct Custom Ready Panels demonstrate optimum performance across a wide range of panel sizes



Key target enrichment metrics demonstrate consistent performance across a range of panel sizes. 100 ng of DNA was tested against panels of 1, 10, 25, 50 and 100 genes, and sequenced using Illumina paired-end 150 bp sequencing. Larger panels included all genes present in smaller panels.

For research use only; not intended for diagnostic use.

UNIQUE SOLUTIONS TO STREAMLINE YOUR WORKFLOWS AND MAXIMIZE YIELDS

IN VITRO TRANSCRIPTION

mRNA-based medicine holds great promise for applications in infectious disease vaccination, cancer vaccination, as well as other disease treatments. Delivery of mRNA is thought to present less risk than DNA-based therapies, and has additional benefits in speed of production and personalization, versus protein delivery. Functional mRNA requires the presence of a m7G cap and poly(A) tail for recognition by the host cellular translation system. In addition, other structures may be desirable, such as the presence of modified bases or Cap-1 structures.

NEB provides a variety of tools for the *in vitro* transcription (IVT) of RNA and mRNA. Reagents can be purchased separately or as optimized kits. These reagents support applications ranging from benchtop research to large scale RNA production and purification for clinical applications.



NEB offers a selection of HiScribe RNA synthesis kits for the generation of high yields of high quality RNA that can be used in a wide variety of applications. Find out how NEB can streamline your RNA workflows at NEBrna.com.

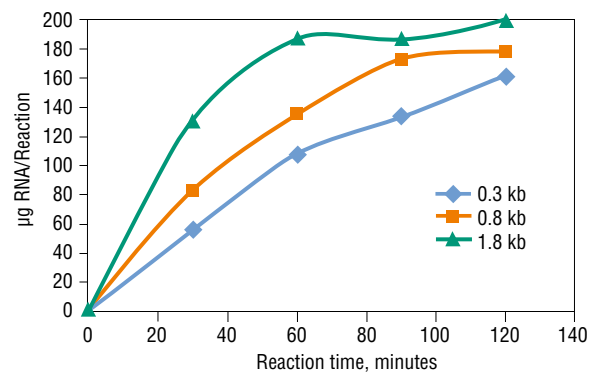
FEATURED PRODUCT:

HiScribe™ T7 High Yield RNA Synthesis Kit

NEB #E2040S

- Up to 180 µg of RNA per reaction from 1 µg of control template
- Enables full substitution of NTPs for labeling and incorporation of modified bases
- Template removal and RNA purification reagents included
- Linearized control template included for verification of RNA synthesis

Robust RNA Synthesis from a variety of template sizes using the HiScribe T7 High Yield RNA Synthesis Kit



Time course of standard RNA synthesis from three DNA templates of different sizes using HiScribe T7 High Yield RNA Synthesis Kit. Reactions were assembled according to the protocol and incubated at 37°C for the indicated time. Transcripts were purified over spin columns and quantified on a NanoDrop™ Spectrophotometer to calculate reaction yield.



Visit www.neb.com/E2040 for more details.



PROTEIN EXPRESSION & PURIFICATION

Recombinant production of proteins is one of the most powerful techniques used in biotechnology. The ability to produce an abundance of a desired protein can enable a wide range of possibilities, including its use in industrial processes or to diagnose or treat disease.

At first glance, recombinant protein expression looks quite simple. However, it can be very challenging, because so many factors influence the process. For example, each protein folds in its own unique manner; some proteins require post-translational modifications, and some proteins have activities that are detrimental to their host. Thus, no single solution exists for the successful production of all recombinant proteins.

Focused on prokaryotic systems, **NEB was one of the first companies to recognize the promise of recombinant technologies, and has since developed a wide array of protein expression solutions**, including many for proteins that are difficult to express. Each NEB technology offers different advantages, which enable you to choose the strategy that best suits your protein expression and purification needs.



Visit www.neb.com/
ProteinExpression

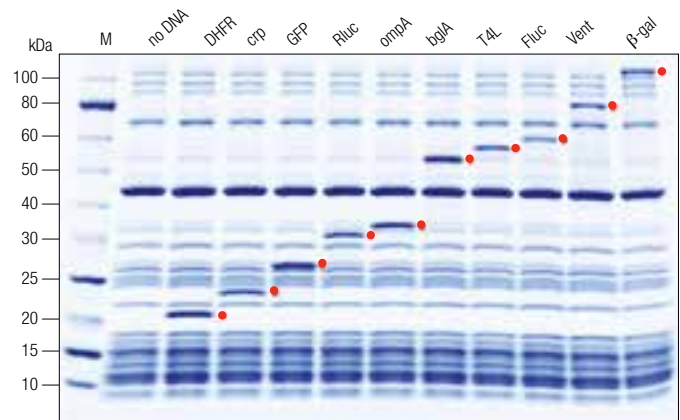
to view NEB's full portfolio of products.

FEATURED PRODUCT: PURExpress® *In Vitro* Protein Synthesis Kit

NEB #E6800S/L

- Express a wide range of proteins free of modifications and degradation
- Save valuable time with results available in just a few hours
- Use with plasmid DNA, linear DNA or mRNA
- One-step reaction requiring the mixing of only two tubes

Protein expression using the PURExpress *In Vitro* Protein Synthesis Kit



Reactions were carried out according to manual recommendations. Red dot indicates protein of interest. Marker M is the Protein Ladder (NEB #P7703).



For more details, visit www.neb.com/PURExpress.



GLYCOPROTEOMICS

Over the past 20 years, the list of enzymes available for glycan analysis has steadily grown, and many of these enzymes have transitioned from academic research into workflows that both characterize glycans on biotherapeutics and support glycan-based clinical tests. As a result of this, and the growing importance and understanding of protein glycosylation in disease, new demands are being placed on the quality of reagents used for glycan analysis.

NEB is committed to continually improving the quality of its glycosidases with the aim of supporting their routine use in biopharma and clinical diagnostic applications. Many of these reagents are recombinant, and all undergo several quality control assays, enabling us to provide products with lower unit cost, higher purity, and reduced lot-to-lot variation.



Visit NEBglycosidase.com to learn more, view the full list of products available, and to download our white paper, “Redesigning glycosidase manufacturing quality for pharmaceutical and clinical applications.”

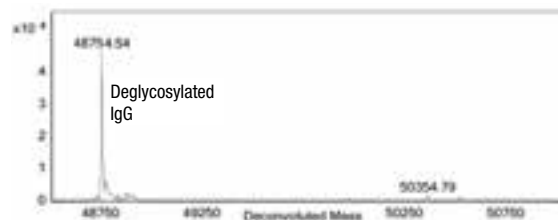
FEATURED PRODUCT: Rapid™ PNGase F

NEB #P0710S

- Speed up deglycosylation with one-step reaction setup
- Release all *N*-glycans without bias
- Achieve sensitive and reproducible results with short reaction times
- Move directly to downstream analysis

Rapid PNGase F results in complete deglycosylation with a short incubation

Rapid PNGase F (5 min. at 50°C)



*A monoclonal murine antibody was incubated for 5 min. with Rapid PNGase F, demonstrating that a short incubation is sufficient to deglycosylate every *N*-glycan site without bias.*



Visit www.neb.com/PNGaseF for more details.

APPLY NEB'S SCIENTIFIC AND MANUFACTURING EXPERIENCE TO HELP **DRIVE YOUR INNOVATION**

ARE YOU READY TO PARTNER WITH NEB?
LET'S GET THE CONVERSATION STARTED!

- Visit www.neb.com/DriveYourInnovation to learn more and request a discussion or visit from your NEB representative
- Learn more about custom or bulk opportunities at www.neb.com/NEBsolutions
- Starting a new laboratory or company? Contact your local NEB representative to see how we can help you!
For international customers, visit www.neb.com/internationalorders to locate your local NEB point of contact.

Choose NEB as your custom product and solution provider.

- EXPERTISE** | Over 40 years of experience in enzyme technologies
- RESPONSIVENESS** | Dedicated team of scientists and business professionals
- FLEXIBILITY** | Capacity to accommodate your formulation, scale-up and kitting needs
- QUALITY** | Proven track record of unsurpassed product quality; ISO 13485-certified

Contact us at NEBsolutions@neb.com or visit www.neb.com/NEBsolutions to learn more.



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