

NEB expressions

a scientific update



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Redefining NGS Library Prep for The Real World: Streamlining for Speed and Savings

Photo credit: The Koues lab

How NEBNext UltraExpress helps address key challenges at a University Core Genomics Center

By Betsy Young, Ph.D., Senior Product Marketing Manager for Next Generation Sequencing, New England Biolabs

In today's rapidly evolving genomics landscape, core facilities and research groups often need to adapt to evolving demands – such as managing high sample volumes or accelerating experiments to generate sequencing data more quickly. Genomics is a field where technological advancements continuously and rapidly reshape the landscape, necessitating faster and better reagents for faster and better libraries. This is the origin story of the NEBNext UltraExpress library prep kits for DNA, FS DNA, and RNA – innovative solutions designed to meet sequencing demands with unparalleled speed, accuracy, and efficiency. These kits offer a fast workflow, single-condition setup for adaptor concentration and PCR cycle number, minimal hands-on time, and reduced consumables usage and costs. NEBNext UltraExpress is truly streamlined for speed.

Challenging to the core

At the University of Michigan's Advanced Genomics Core, the sample variety is astounding – from reptile skin from the Museum of Zoology, to surgical samples from the University Medical Center. All demand the same attention to detail and high-quality treatment to transform them into genomic insights. Dr. Olivia Koues, Director of the Advanced Genomics Core, is well acquainted with the challenges of building processes to support the diverse needs of genomic research, where adaptability is crucial. "It's never the same from day to day. It feels like there's always something new coming out, so if you don't like change, it's a problem in my facility because we are constantly evolving. We're trying to stay not just cutting edge but a leader in those fields."

Given the variety and volume of samples processed at Dr. Koues' facility, the streamlined efficiency of the NEBNext UltraExpress kits becomes even more important. Whether in a core laboratory like the Advanced Genomics Core, which serves as a shared technology resource providing guidance, expertise

and services across the organization, or in individual research labs seeking to optimize their sequencing workflows, the adaptability of the NEBNext UltraExpress kits is invaluable. Dr. Koues explains, "We're a large facility, and the samples we receive run the gamut of all the research done at the University of Michigan, which is a large institution. Everything from bulk RNA and DNA to single-cell and spatial tissue blocks and cell suspensions."

The need for speed

Time is critical in any laboratory experiment, and in the Koues lab the number and variety of samples must be quickly and meticulously prepared before sequencing. The NEBNext UltraExpress library prep kits address this challenge head-on with their short workflow times. For example, the NEBNext UltraExpress RNA library prep workflow has transformed what was once a multi-day process into a single-day protocol. This significantly enhances lab productivity, allowing more samples to be processed and sequenced in a shorter timeframe.

The workflow times for each of the NEBNext UltraExpress kits are as follows:

- NEBNext UltraExpress DNA Library Prep Kit: 1 hr. 50 min.
- NEBNext UltraExpress FS DNA Library Prep Kit: 1 hr. 45 min.
- NEBNext UltraExpress RNA Library Prep Kit: 3 hours

For Dr. Koues, the flexibility and speed of NEBNext UltraExpress initially caught her attention. "When we consider new kits and methods that we're going to adopt, we try to pick and choose based on what we think can accommodate the most samples. We're constantly trying to streamline and make things efficient because we try to get people the best data possible as quickly as possible." The projects submitted to the sequencing core may be large or small, but resources are always in demand, and every project is important. Setting expectations for data delivery across the range of projects can be challenging, but the scientists relying on the data have no time to waste.

“The time and robustness of the kit are key because we only have a couple of technicians. Those technicians are prepping all our libraries, not just the bulk RNA or the bulk DNA projects, but they’re doing the single-cell library preps, the spatial library preps – anything that feeds onto a sequencer goes through the hands of these two individuals”. Continues Dr. Koues, “Larger projects that come in can be a challenge too. Shorter workflows mean we can prep more samples and turn them around quickly. As the sequencing platforms increase in throughput, we can sequence more samples at once, and we’re able to keep that four-week turnaround time for almost all projects.” By combining rapid turnaround and reliable performance, NEBNext UltraExpress helps the University of Michigan Advanced Genomics Core to consistently meet tight deadlines while delivering excellent data quality.

A single-condition workflow

Speed alone speaks to both research and core labs engaged in high-throughput NGS, but simplicity is another feature most users can appreciate. One of the stand-out features of the

NEBNext UltraExpress kits is the single-condition workflow with providing a universal protocol that works across a wide range of input masses, sample types, and downstream applications. By removing the requirement for individually adjusted adaptor concentrations and fine-tuned PCR cycle numbers, NEBNext UltraExpress works for most samples within the kit’s stated input range:

- NEBNext UltraExpress DNA Library Prep Kit: 10 – 200 ng pre-sheared DNA
- NEBNext UltraExpress FS DNA Library Prep Kit: 10 – 200 ng intact DNA
- NEBNext UltraExpress RNA Library Prep Kit: 25 – 250 ng total RNA

Performance without Compromise

While the speed and flexibility were initial draws for Dr. Koues to test the NEBNext UltraExpress Kits, the consistent data quality ultimately made the difference, especially for challenging sample types that can sometimes require extensive work due to suboptimal performance.

This is a significant challenge at the University of Michigan Advanced Genomics Core, tasked with the acceptance of samples derived from a broad spectrum of RNA extraction methods, which can result in inconsistent quality of RNA. “We don’t control how extractions are performed externally, and not all samples come to us DNase-treated or of high quality...”

I can’t control those metrics. Kits that handle contaminants are very important to us, as well as those that can accommodate a range of inputs,” explains Dr. Koues. The Core often deals with what are termed ‘fringe’ or ‘marginal’ samples – those samples that others might reject based on not meeting acceptable input amounts and sample quality. It is here that the NEBNext UltraExpress kits have truly made a difference, enhancing outcomes for challenging samples. Dr. Koues said, “It’s really helped what we would consider lower input, low-quality samples that have been challenging. We’ve found that the kits are performing better than anything we’ve tried in the past, minimizing cleanups, re-preps, or random failures.”

Figure 1: NEBNext UltraExpress workflows are designed for speed

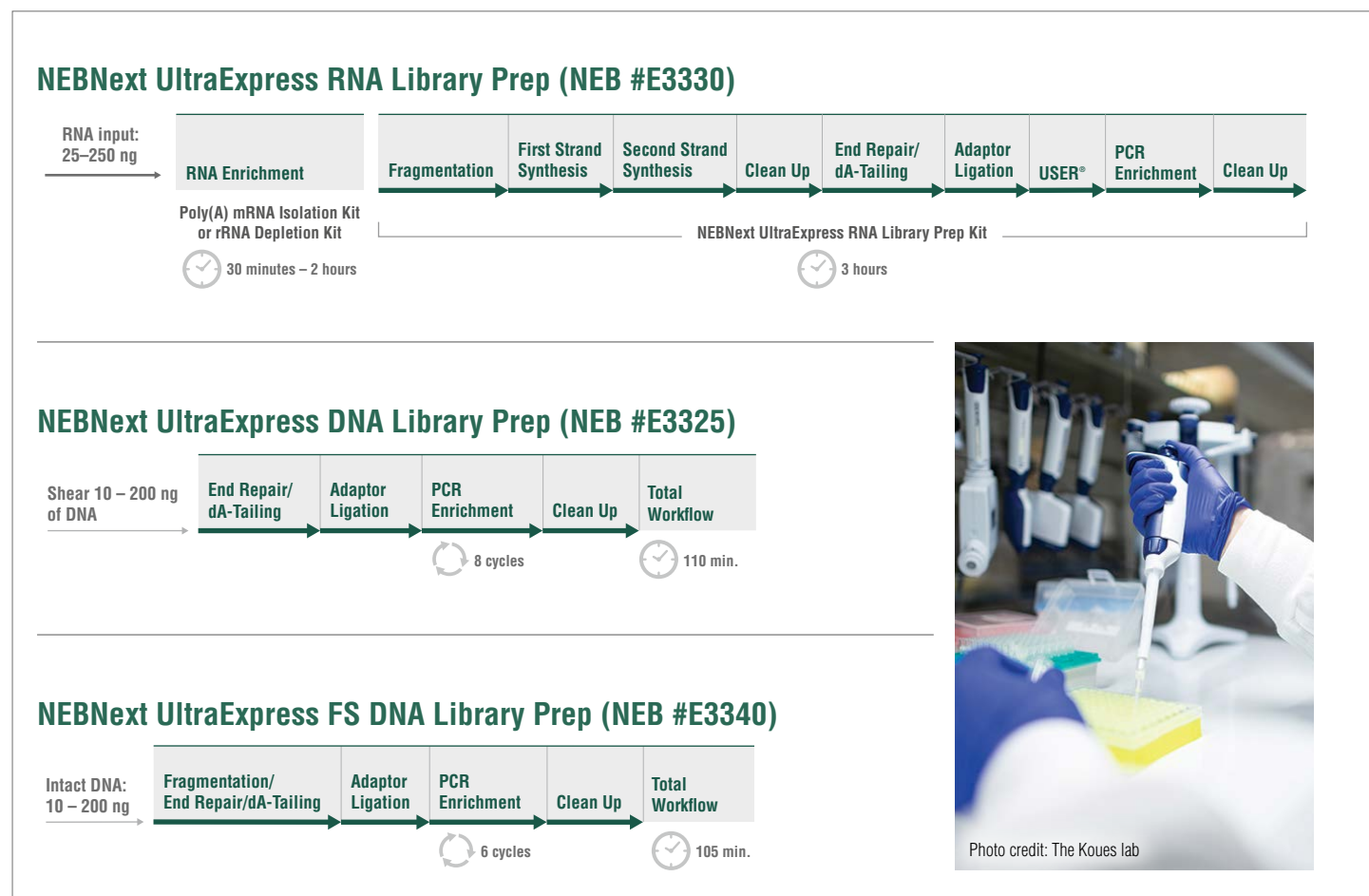


Photo credit: The Koues lab

Streamlined for Speed



Using fewer consumables

In addition to the technical advantages of the NEBNext UltraExpress kits, there is a significant reduction in plastic usage, benefiting a lab's bottom line and its ecological impact (Figure 2). These kits reduce the overall number of tips and tubes by streamlining the workflow and minimizing the number of components required. Whether you're motivated by the cost savings of needing to purchase fewer tips and tubes, or you're inspired by a more ecologically friendly library prep kit, NEBNext UltraExpress saves.

Happy Customers, Happy Lab

Implementing the NEBNext UltraExpress Kits marked a significant improvement at the University of Michigan Advanced Genomics Core. Dr. Koues reflects on the transition: "I think there was a lot of buy-in once they ran it and we didn't have some of the issues that we've been having in the past with fall-out samples or excess adaptor dimer – I can't stress

that enough, that's the bane of my lab...when you do 96 samples or more, and then QC results come back and a third of them look like junk. Then we have to clean them up, or maybe we have to fail them or re-prep them. That makes work challenging because you're a little disheartened at the end of that process, especially if it happens over and over again."

Keeping both the scientific community of the University of Michigan and the 28 core lab staff members satisfied and motivated is a priority for Dr. Koues. The UltraExpress Kits are playing an important role. "The staff are really happy with it right now and I'm not the one doing the hands-on work. I'm glad that I'm not getting a lot of complaints. People don't like change, but we've been running this since it launched. We made the switch pretty quickly because it fixed a lot of our issues."

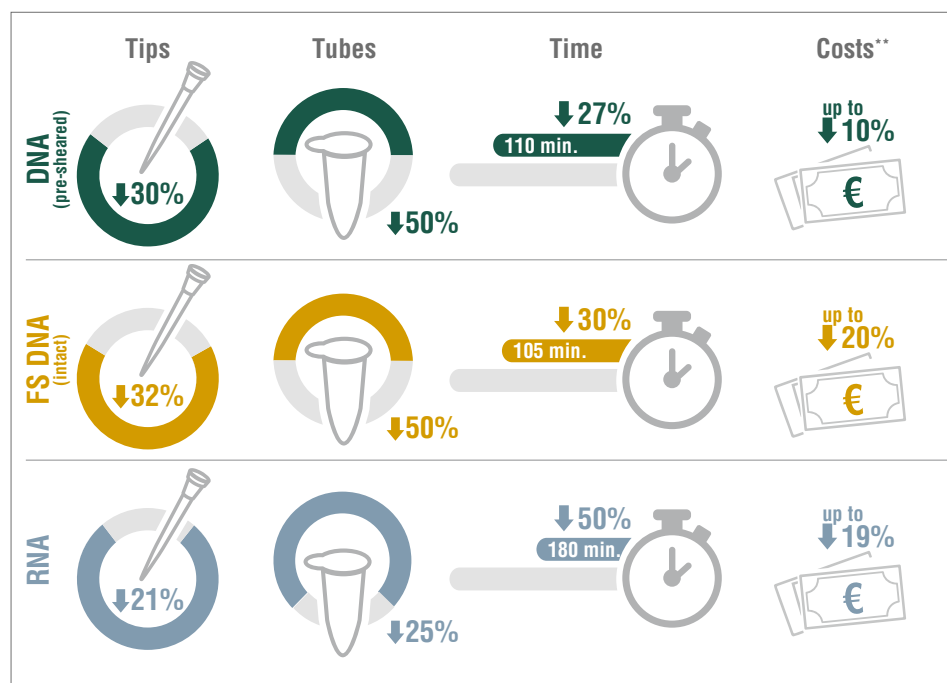
NEBNext UltraExpress library prep kits for DNA, FS DNA, and RNA represent a leap forward in speed and efficiency. As genomics

continues to evolve towards faster sequencing and data interpretation, and researchers ask more questions about the genomic underpinnings of health and disease in a range of organisms, NEB and the NEBNext UltraExpress kits ensure they have the support they need to answer them faster and with lower resource expenditure than ever before.



Photo credit:
The Koues lab

Figure 2: Savings with NEBNext UltraExpress*



* As compared to NEBNext Ultra II

** Based on recommended European list price

Top 5 reasons to choose NEBNext UltraExpress

- 1 Fast workflow
- 2 High quality libraries from a wide input range
- 3 Single protocol for all input amounts
- 4 Fewer steps, consumables, and cleanups
- 5 Automation friendly

NGS library prep? We've got you covered.

The ideal NEBNext solution for your needs

NEBNext stands for innovation and advancement in NGS sample preparation. All NEBNext products are available in a convenient kit format or as separate modules and offer flexible library prep workflows that can be easily scaled and automated. Whether for standard or special applications, with NEBNext UltraExpress and NEBNext Ultra II Kits you will find the right solution for your research needs.

NEBNext UltraExpress

The Efficiency Kits

with streamlined workflows for central applications and input amounts. Save time, consumables, and costs.



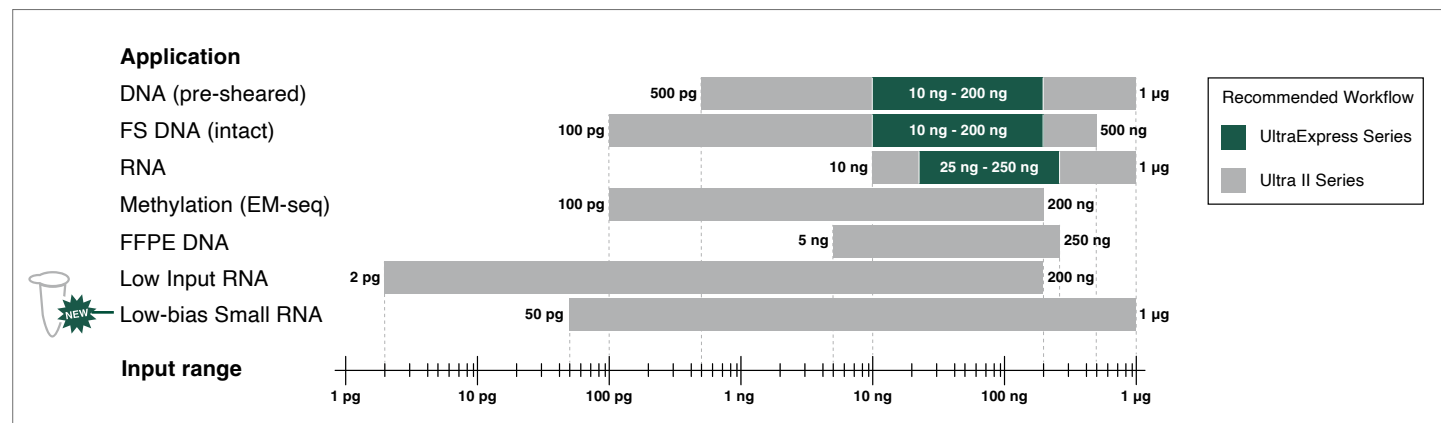
NEBNext Ultra II

The Specialist Kits

with flexible, modular workflows for special applications. Your choice for demanding samples with low or high input amounts.



Find the right NEBNext kit based on your input range



Ordering Information

PRODUCT	NEB #	SIZE
NEBNext UltraExpress Series		
NEBNext UltraExpress DNA Library Prep Kit (pre-sheared)	E3325S/L	24/96 rxns
NEBNext UltraExpress FS DNA Library Prep Kit (intact)	E3340S/L	24/96 rxns
NEBNext UltraExpress RNA Library Prep Kit	E3330S/L	24/96 rxns
NEBNext Ultra II Series		
NEBNext Ultra II DNA Library Prep Kit for Illumina	E7645S/L	24/96 rxns
NEBNext Ultra II FS DNA Library Prep Kit for Illumina	E7805S/L	24/96 rxns
NEBNext Ultra II RNA Library Prep Kit for Illumina	E7770S/L	24/96 rxns
NEBNext Enzymatic Methyl-seq v2 Kit	E8015S/L	24/96 rxns
NEBNext UltraShear FFPE DNA Library Prep Kit	E6655S/L	24/96 rxns
NEBNext Single Cell/Low Input RNA Library Prep Kit for Illumina	E6420S/L	24/96 rxns
NEBNext Low-bias Small RNA Library Prep Kit	E3420S/L	24/96 rxns



Need help with product selection? The **NEBNext Selector Tool** can help you.



Interested in giving NEBNext a try? Request a free sample from your [local distributor](#).



For samples, tools and the full NEBNext product portfolio, visit www.NEBNext.com

Kind of a big deal.



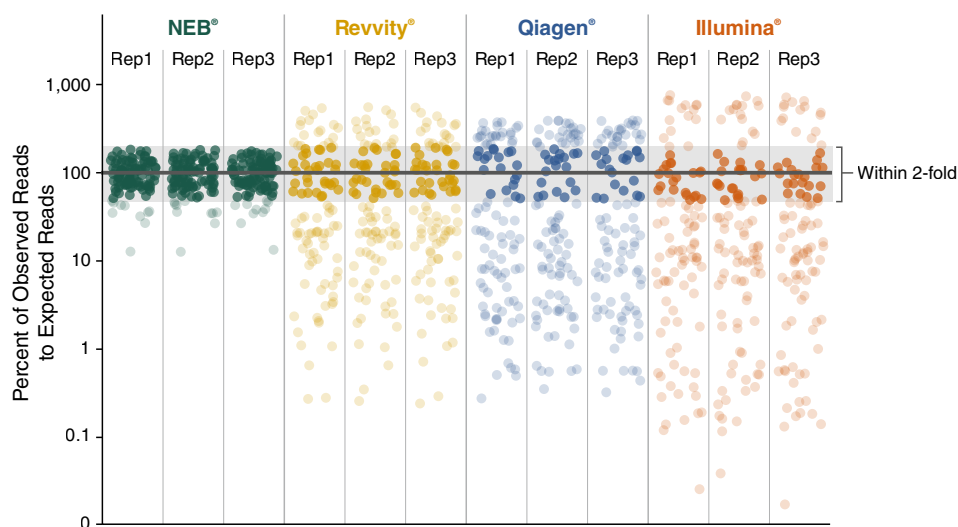
The Peacock Mantis Shrimp (Odontodactylus scyllarus) is very small but can unfurl its appendages and become quite powerful.



Successfully see more small RNAs with the NEBNext® Low-bias Small RNA Library Prep Kit

Bias in small RNA library prep can seriously impact the accuracy of your data, skewing the representation of rare RNA species. The [NEBNext Low-bias Small RNA Library Prep Kit](#) minimizes biased representation of small RNAs, more accurately reflecting the number and proportion of unique small RNAs present. NEB's next-generation kit utilizes a streamlined workflow for the capture of small RNAs (<120 nt) with a 5' phosphate and 3' hydroxyl group, and can be used to identify microRNAs (miRNAs), transfer RNAs (tRNAs) and tRNA-derived fragments, small nucleolar RNAs (snoRNAs), piwi-interacting RNAs (piRNAs), and plant miRNAs. Designed for the preparation of Illumina®-compatible small RNA sequencing libraries, this latest NEBNext kit is kind of a big deal!

NEBNext Low-bias Small RNA Library Prep Kit produces libraries with the lowest bias.



NEBNext Low-bias Small RNA libraries were made using a mix of 100 synthetic control miRNAs, including five that had 3' 2'-O-methyl ends. Libraries were prepared from 0.3 ng of the synthetic miRNA mix to compare library-generated bias between the NEBNext Low-bias Small RNA Library Prep Kit and small RNA kits from Revvity® (NEXTFLEX Small RNA Sequencing Kit V4), Qiagen® (QIAseq® miRNA Library Kit) and Illumina (TruSeq® Small RNA Library Prep). Libraries were sequenced on an Illumina NextSeq 500 (1 x 56 bases), and expected reads were calculated from total reads mapped to the synthetic controls, divided by the total number of control sequences (black line at 100%). Percent of observed reads to expected reads was calculated for each control sequence and plotted across replicates.



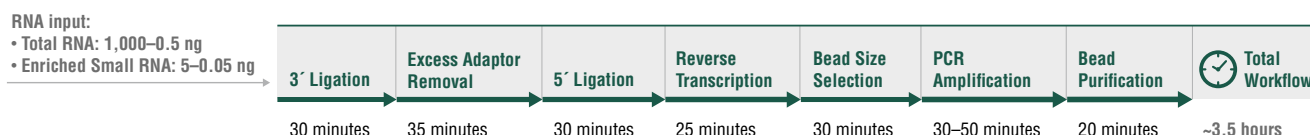
NEBNext Low-bias Small RNA Library Prep Kit



Kit Advantages:

- Analyze all RNA species present without library prep-generated bias
- Simplify and streamline your library prep workflow (~3 hrs 30 min), saving time
- Derive insights from biologically relevant input amounts
- Learn a single protocol for standard and 2'-O-methylated samples
- Expand your insights with up to 480 compatible UDI primer pairs, available separately

NEBNext Low-bias Small RNA Library Prep workflow



Start small by requesting a sample at [NEBNext.com](https://www.nebnext.com), today!



Learn more in our webinar:
Breaking Through Bias to Redefine Precision in Small RNA Library Prep



Need help with product selection?

If you need assistance navigating the ever-growing NEBNext product line, NEBNext Selector tool can help guide your product selection.

Visit nebnextselector.neb.com

Ordering Information

PRODUCT	NEB #	SIZE
NEBNext Low-bias Small RNA Library Prep Kit	E3420S/L	24/96 rxns



www.neb.com

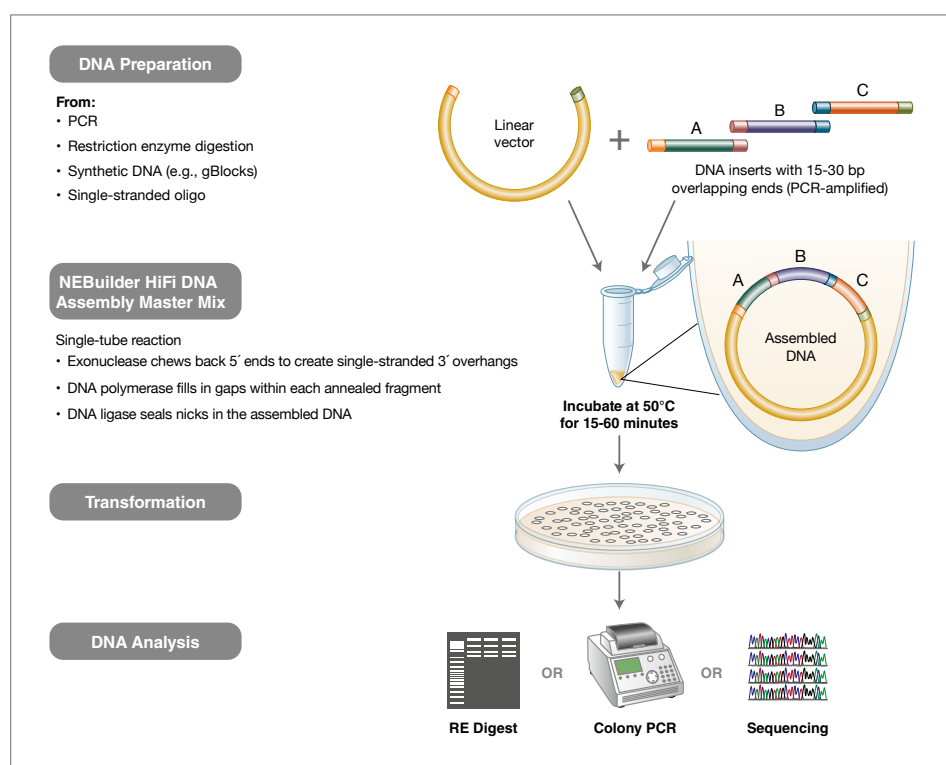


Assemble and Express with Confidence

Clone smarter with NEBuilder HiFi DNA Assembly

NEBuilder HiFi DNA Assembly enables virtually error-free joining of DNA fragments, even those with 5'- and 3'-end mismatches. Available with and without competent *E. coli*, this flexible kit enables simple and fast seamless cloning, utilizing a new proprietary high-fidelity polymerase. Find out why NEBuilder HiFi is the next generation of DNA assembly and cloning.

Overview of the NEBuilder HiFi DNA Assembly cloning method



Reasons to choose NEBuilder HiFi DNA Assembly

- 1 Save time**
Enjoy simple and fast seamless cloning in as little as 15 minutes.
- 2 Flexibility**
Use it for "standard-size" cloning and larger gene assembly products, up to 12 fragments.
- 3 Compatible with downstream applications**
Use DNA immediately for transformation or amplification.
- 4 Adaptable**
Adapts easily for multiple DNA manipulations, including mismatch and ssOligo assembly.
- 5 Site-directed mutagenesis**
Use to perform multisite mutagenesis.
- 6 Increased stability**
Store at -20°C, with improved stability over competition.

20%
DISCOUNT*

Assemble and express with confidence:
Enjoy now an exclusive 20% discount on your purchase of selected NEB products! Simply enter the promo code "Confidence25" when ordering.

*The 20% discount is applicable to the list price. It is valid until December 31, 2025, and cannot be combined with other discounts. The offer is available only in selected countries. For more details, please contact your local distributor.



Get started designing primers with the [NEBuilder Assembly Tool](#).



Generate a custom protocol with the [NEBuilder Protocol Calculator](#).

Ordering Information

PRODUCT	NEB #	SIZE
NEBuilder HiFi DNA Assembly Master Mix	E2621S/L/X	10/50/250 rxns
NEBuilder HiFi DNA Assembly Cloning Kit	E5520S	10 rxns
NEBuilder HiFi DNA Assembly Bundle for Large Fragments	E2623S	20 rxns

20%
DISCOUNT*



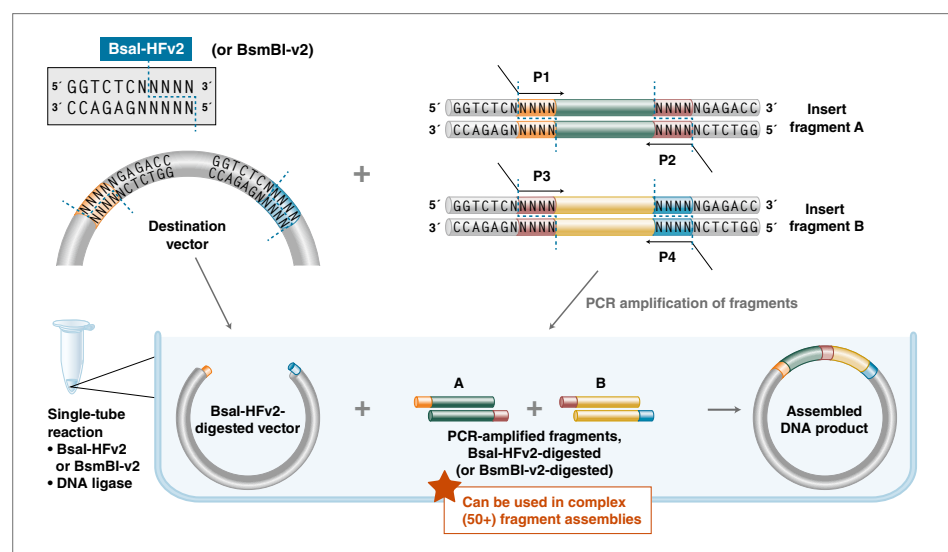
Explore the wise choice at
[NEBuilder.neb.com](https://www.neb.com)

Assemble and Express with Confidence

Assemble complex constructs without restriction site constraints

Golden Gate Assembly is a molecular DNA assembly technique that utilizes simultaneous digestion with Type II restriction enzymes (which cleave outside their non-palindromic recognition sequence) and ligation by a DNA ligase to enable the scarless, ordered assembly of multiple fragments. With constant advances in both the development of new enzymes, tools and research on maximizing enzyme functionality (e.g., ligase fidelity), NEB is the industry leader in pushing the limits of Golden Gate Assembly and related methods.

Golden Gate Assembly Workflow for complex assemblies



In its simplest form, Golden Gate Assembly requires a Type IIS recognition site, in this case, BsaI-HFv2 (GGTCTC), or BsmBI-v2 (CGTCTC) added to both ends of a dsDNA fragment. After digestion, these sites are left behind, with each fragment bearing the designed 4-base overhangs that direct the assembly.

Reasons to choose NEBridge Golden Gate Assembly

- 1 Scar-free cloning**
Seamless assembly with no residual sequences.
- 2 Multi-fragment assembly**
Assemble 2 to 50+ fragments in order, in a single reaction.
- 3 Save time**
Perform single insert cloning in just 5 minutes.
- 4 Robust performance**
High efficiency even with GC-rich or repetitive regions.
- 5 Broad size range**
Works with fragments from <100 bp to >15 kb.
- 6 Library preparation**
Generate libraries with high efficiencies.

Type IIS Restriction Enzymes for Golden Gate Assembly

PRODUCT	NEB #
BbsI	R0539
BbsI-HF	R3539
BsaI-HFv2	R3733

PRODUCT	NEB #
BsmBI-v2	R0739
BspQI	R0712
BtgZI	R0703

PRODUCT	NEB #
Esp3I	R0734
PaqCI	R0745
SapI	R0569



For designing primers, try the [NEBridge Golden Gate Assembly Tool](#).



For the design of high-fidelity Golden Gate assemblies, use the [NEBridge Ligase Fidelity Tool](#).

Ordering Information

PRODUCT	NEB #	SIZE
NEBridge Golden Gate Assembly Kit (BsmBI-v2)	E1602S/L	20/100 rxns
NEBridge Golden Gate Assembly Kit (BsaI-HFv2)	E1601S/L	20/100 rxns
NEBridge Ligase Master Mix	M1100S/L	50/250 rxns



Get started at GoldenGate.neb.com

Assemble and Express with Confidence

Cell-free protein expression in just hours

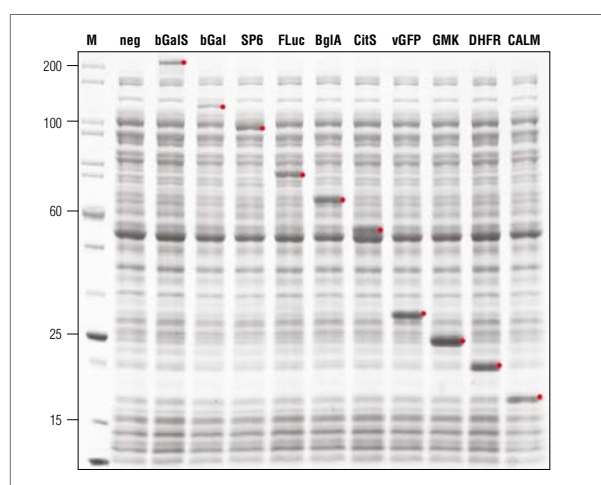
The NEBExpress Cell-free *E. coli* Protein Synthesis System is a coupled transcription/translation system designed to synthesize proteins encoded by a DNA or mRNA template under the control of a T7 RNA Polymerase promoter. The kit includes a high-activity *E. coli* extract, reaction buffer, and optimized T7 RNA Polymerase – just add your template and go.

ADVANTAGES

- Synthesize high yields of protein (typically 0.5 mg/ml)
- Protein can be synthesized and visualized in approximately 2–4 hours
- Includes components for coupled transcription/ translation
- Synthesize proteins from 17 to 230 kDa
- Templates can be plasmid DNA, linear DNA, or mRNA
- No RNase contamination
- Flexible reaction conditions

Use it for:

- Rapid protein generation for analysis
- High-throughput screening
- Epitope mapping and folding studies
- Expression of toxic proteins

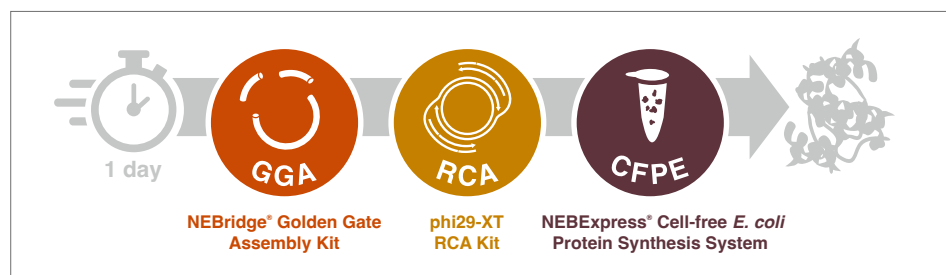


The NEBExpress Cell-free *E. coli* Protein Synthesis System can be used to express a wide range of proteins.

50 μ l reactions containing 250 ng template DNA were incubated at 37°C for 3 hours. The red dot indicates the protein of interest. M = Unstained Protein Standard, Broad Range (NEB #P7717), "neg" = negative control, no DNA

From DNA assembly to protein expression in a single day

Combining NEB tools for a rapid 1-day workflow:



Golden Gate Assembly (GGA):

Uses Type IIS restriction enzymes for high efficiency, modular DNA assembly.

Rolling Circle Amplification (RCA):

Amplifies circular DNA templates generating high product yield in a short reaction time.

Cell-Free Protein Expression (CFPE):

Enables rapid protein synthesis without live cells.



Read the application note
[Accelerating DNA Construction to Protein Expression](#)

*The 20% discount is applicable to the list price. It is valid until December 31, 2025, and cannot be combined with other discounts. The offer is available only in selected countries. For more details, please contact your local distributor.

Ordering Information

PRODUCT	NEB #	SIZE
phi29-XT RCA Kit	E1603S/L	100/500 rxns
NEBExpress Cell-free <i>E. coli</i> Protein Synthesis System	E5360S/L	10/100 rxns
PURExpress <i>In Vitro</i> Protein Synthesis Kit	E6800S/L	10/100 rxns



Migrate to Monarch

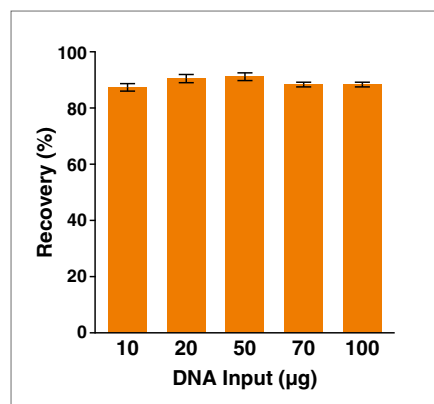
Purification of high-quality DNA and RNA in a sustainable kit design

Recover pure, intact DNA and RNA in minutes with our fast, user-friendly protocols and optimized buffer systems, and focus your time on the experiments that will drive your research forward. The Monarch nucleic acid purification portfolio can serve your needs, whether you are isolating nucleic acids from biological samples, cleaning up DNA and RNA from enzymatic reactions, extracting DNA fragments from gels, or purifying plasmids. Monarch kits are all designed with sustainability in mind; kits and spin column components are made with significantly less plastic than leading suppliers, and are packaged with responsibly-sourced, recyclable packaging.



New member of the Monarch family Monarch Spin High-Capacity DNA Cleanup Kit (100 µg)

Introducing a high-capacity version of our DNA Cleanup Kit for purification and concentration of up to 100 µg of DNA from various sample types, featuring precision-engineered spin columns.



Monarch Spin High-Capacity DNA Cleanup Kit (100 µg) offers a wide range of DNA input amounts.

DNA purifications were performed using the Monarch Spin High-Capacity DNA Cleanup Kit (100 µg) with varying amounts of DNA. To assess average DNA recovery, DNA input (1 kb DNA Ladder, NEB #N3232) ranging from 10 to 100 µg was used and eluted in 100 µl of Monarch Buffer EY, in triplicate. DNA concentrations for both input and eluted samples were measured using a Trinean DropSense 16. Percent recovery calculations were based on the measured DNA concentrations and the elution volume.

ADVANTAGES

- Elute in just 50 µl for highly concentrated DNA
- Compatible with microcentrifuges and vacuum manifolds helping to prevent buffer retention and salt carryover
- No pH monitoring required
- Modified protocol provided for oligonucleotide, genomic DNA, or RCA products
- Significantly less plastic in columns and kit compared to leading suppliers



For more information, visit
www.NEBMonarch.com



Interested in giving Monarch a try?
Request a free sample from your
[local distributor.](#)

Explore the Monarch portfolio and order the kits for your applications

PRODUCT	HIGHLIGHT FEATURE	NEB #	SIZE
Monarch Spin Plasmid Miniprep Kit	Easily purify plasmids with convenient colored buffer system	T1110S/L	50/250 preps
Monarch Spin DNA Gel Extraction Kit	Extract excellent DNA yields and elute in as little as 5 µl	T1120S/L	50/250 preps
Monarch Spin PCR & DNA Cleanup Kit (5 µg)	Purify DNA in 5 minutes and elute in as little as 5 µl	T1130S/L	50/250 preps
Monarch Spin High-Capacity DNA Cleanup Kit (100 µg)	Purify and concentrate up to 100 µg DNA	T1135V/S/L	10/50/200 preps
Monarch Spin gDNA Extraction Kit	Purify high-quality, genomic DNA from several sample types	T3010S/L	50/150 preps
Monarch HMW DNA Extraction Kit for Cells & Blood	Achieve DNA from cells & blood in the Megabase size range	T3050S/L	5/50 preps
Monarch HMW DNA Extraction Kit for Tissue	Achieve DNA from tissue samples in the Megabase size range	T3060S/L	5/50 preps
Monarch Mag Viral DNA/RNA Extraction Kit	Isolate viral nucleic acids using a magnetic bead-based protocol	T4010S/L/X	100/600/3×600 preps
Monarch Spin RNA Cleanup Kit (10, 50, 500 µg)	Efficiently purify and concentrate RNA after enzymatic reactions	T2030S/L , T2040S/L , T2050S/L	10/100 preps, 10/100 preps, 10/100 preps
Monarch Spin RNA Isolation Kit (Mini)	Purify RNA from multiple sample types and elute in as little as 10 µl	T2110S	50 preps

Brewing a better understanding of the Microbial World

By Joanne Gibson, Ph.D.,
New England Biolabs



2024 Passion in
Science Awards recipient
Anne Madden.
The Microbe Institute,
Yarmouth, ME, USA

Dr. Anne A. Madden, a pioneering microbiologist and the founder of The Microbe Institute (microbeinstitute.org) is transforming our understanding of the microbial world. Sparked by a simple yet profound question during her Ph.D. research – "What good is a wasp?" – Madden's explorations have led to groundbreaking discoveries, including the innovative Wasp Beer Project. By exploring unconventional sources for beneficial microbes, she challenges scientific assumptions and passionately advocates for democratizing microbial research. Her work questions the notion that valuable scientific discoveries can only come from expected sources and underscores the potential of microbes as allies in innovation and sustainability. Her vision for The Microbe Institute is akin to creating a "NASA for microbes", aiming to involve the public in microbial discovery to find the transformative technology of tomorrow while helping anyone – regardless of their background – find inspiration in the microbial cosmos.

The First Wasp Yeast Beer

Brewing beer relies on yeast – an organism responsible for fermenting sugars into alcohol and producing flavors. Although thousands of yeast species exist, commercial beer production has long relied on just a few: predominantly ale yeasts (*Saccharomyces cerevisiae*) and lager yeasts (*Saccharomyces pastorianus*). These domesticated strains have been honed for centuries to create flavorful, consistent beer. However, the craft brewing industry craves new flavors.

The story of Wasp Beer, in some ways, began when Dr. Madden was studying the microbiome of paper wasps and became involved in an outreach project collaborating with brewing scientist John Sheppard and applied ecologist Rob Dunn at North Carolina State University. Contrary to the common view of wasps as pests, they uncovered that these insects harbor wild yeast strains capable of unique fermentative properties for the brewing world. Typically, wild yeasts are poor performers in brewing due to their inability to ferment maltose or tolerate high alcohol concentrations, and because they produce undesirable flavors. However, when Dr. Madden isolated *Lachancea thermotolerans*, she found it efficiently metabolized maltose and tolerated higher alcohol levels, ultimately producing a beer with delightful tart notes, with hints of honey and tropical fruit. It became a game-changing yeast for the brewing industry.

The debut of this wasp yeast beer at the World Beer Festival in Raleigh, NC in 2014 marked a significant innovation in brewing. The yeast's ability to impart a clean sourness to the beer without the need for additional souring agents simplified production processes and reduced risks of contamination. It cut down on sour beer brewing time and costs – advantages quickly recognized and

appreciated by amateur and professional brewers. This breakthrough demonstrated how rethinking assumptions about microbial habitats can lead to significant technological advancements.

What began as a short-term outreach project soon evolved into a full-fledged scientific breakthrough. Within months, Dr. Madden and her team worked with commercial brewers to bring lactic acid yeast beers to market and were on the path to what would eventually lead to a patent on the yeast. Media outlets took notice, and the project received widespread coverage on PBS NewsHour, National Geographic, and Dr. Madden was invited to give TED and TEDx Talks.

Lachancea thermotolerans is now globally available to the brewing market through one of the world's largest yeast providers, under AB Biotek's Pinnacle Crisp Sour label. Brewers worldwide have adopted this yeast to create award-winning sour beers, as well as new styles of cider and sake. While the original wasp yeast was the first primary souring yeast discovered, this method is now an industry standard for making sour beer.

The Broader Mission to Democratize Microbial Discovery

While Wasp Beer is one of Dr. Madden's most well-known projects, it's just a small part of her larger mission. In 2020, she founded The Microbe Institute, a nonprofit organization dedicated to engaging the public in microbial science through participatory art, education, and science projects. The initiatives are designed to bridge the gap between science and community and integrate microbial research into everyday life.

One notable project involved partnering with colleagues at North Carolina State University to enable students to grow and analyze their own

sourdough starters, learning about microbial ecology in the process, and submitting data to scientists at the same time (microbeinstitute.org/wild-sourdough-project). Another initiative included working with a broader network of nonprofits, artisans, storytellers, and scientists to focus on identifying naturally occurring pigment that can be used as sustainable textile dyes – a project that collaborated with Moroccan weavers to replace synthetic dyes with microbial and plant alternatives, thereby reducing environmental impact while supporting local economies. This project not only applies microbial science to traditional crafts but also demonstrates the practical benefits of microbial research in global sustainability efforts (microbeinstitute.org/morocco-natural-dyes).

Despite their critical role in everything from brewing to medicine, microbes are often misunderstood by the public. Dr. Madden is determined to change that through her talks, art collaborations, and citizen science programs. She encourages people to see microbes not as threats but as vital partners in improving our world.

By exploring the microbial world – whether it's in a wasp nest or a sourdough starter – we can unlock new possibilities for food, medicine, and sustainable living. Through The Microbe Institute, Dr. Madden continues to inspire a new generation to explore and appreciate the vast potential of the microbial world. Her work reveals that the greatest innovations often come from unexpected places and that, by embracing the unknown and questioning the accepted, science can advance in truly remarkable ways, uncovering new solutions and revealing vast opportunities for innovation and sustainability.



Advancing Research with our Enzymes for Innovation Initiative

In a recent episode of our podcast Lessons from Lab & Life, host Lydia Morrison spoke with Nathan Tanner, Associate Director of Research, about the groundbreaking work in our Enzymes for Innovation program. Below is an excerpt from their discussion.

Lydia Morrison: *Could you start by giving us an overview of the Enzymes for Innovation program at New England Biolabs?*

Nathan Tanner: Enzymes for Innovation, or EFIs, as we call them, really stem from us being scientists at NEB. We work in the lab with new enzymes every day, and our CSO, Rich Roberts, really wanted to formalize the collaboration between our research labs and the outside world. The goal is to get the innovative tools we discover into the hands of people who can develop new technologies with them. So, as we study them in the lab, we find ones we think are really interesting and commercialize them, offering them as NEB products. Our normal products are geared around a specific application, like PCR, or new library prep methods. But the EFIs are really unique. They perform activities that no other enzymes on the market do. We're excited to see what researchers and developers will do with them. We want to enable researchers and developers to innovate with these enzymes and explore their potential applications.

Lydia Morrison: *Why is it important for the scientific community to be aware of the Enzymes for Innovation program?*

Nathan Tanner: No one has commercialized an enzyme that does what the EFIs do. Sometimes we can imagine their use; other times, it's not as clear. They're unique. We like to think we're talented scientists at NEB, but we're only a small piece of the biology and biotech world. There are people out there with incredible ideas that can't do the things they want because the enzyme that would help them doesn't exist. But if they check the EFI page, they can see all these cool new activities and potentially develop new technologies.

Lydia Morrison: *How does NEB identify and develop these unique enzymes with functionality that we don't fully understand?*

Nathan Tanner: So, they all come from a research lab that specializes in that type of activity or enzyme. The lab identifies an enzyme that does something interesting, and then, importantly, we ensure these are NEB-quality products. They need to be expressible, purifiable, and stable – just like all our products.

Lydia Morrison: *Can you explain what TelN is and its significance in the Enzymes for Innovation context?*

Nathan Tanner: TelN started as an EFI and now has been promoted up the chain to a full NEB product, and is offered as GMP-grade* product. It's a protelomerase; it cuts double-stranded DNA at a really long recognition site. Instead of producing blunt double-stranded ends, the ends are covalently attached to each other. It turns out it's really useful for making protected DNA molecules for therapeutic applications – because they're protected, nothing can act on the ends. TelN has found a lot of utility for producing therapeutic DNAs, and that's why we have promoted it to our GMP-grade manufacturing, because that's the quality of product that people need for those applications. It was our first graduate from the program due to its success.



Scan code to access the [full podcast](#) for more insights into how these cutting-edge enzymes are transforming research.



To view full list of enzymes available, visit:

www.neb.com/EnzymesForInnovation

Recent EFI Graduates

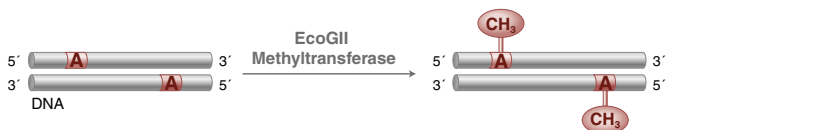
TelN Protelomerase (NEB #M0651)

Creates closed-ended DNA, facilitates hairpin DNA cleavage, and supports *in vitro* DNA template generation. Now available in GMP-grade* formulation.



EcoGII Methyltransferase (NEB #M0603)

Enables m6A methylation to mark open chromatin (e.g. RASAM**), advancing epigenetics research.



Thermostable FEN1 (NEB #M0645)

Removes single-stranded 5' DNA flaps, creating ligatable ends for DNA repair workflows.



* "GMP-grade" is a branding term NEB uses to describe products manufactured or finished at NEB's Rowley facility. The Rowley facility was designed to manufacture products under more rigorous infrastructure and process controls to achieve more stringent product specifications and customer requirements. Products manufactured at NEB's Rowley facility are manufactured in compliance with ISO 9001 and ISO 13485 quality management system standards. However, at this time, NEB does not manufacture or sell products known as Active Pharmaceutical Ingredients (APIs), nor does NEB manufacture its products in compliance with all of the Current Good Manufacturing Practice regulations.

** Ostrowski, M.S., 2023 BioRxiv, doi.org/10.1101/2023.10.09.56158

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