

NEB expressions

a scientific update



IN THIS ISSUE

- 2 **Feature Article**
How RNA sequencing accelerates precision medicine
- 5 **NGS Library Prep Automation**
Solve the challenge of scale

SPECIAL OFFERS

- 6 **Save Your Budget**
Enjoy a 25% discount on your purchase of Q5 Polymerases
- 12 **NEB Starter Pack**
Get your free New Student Starter Pack



NEW PRODUCTS

- 7 **Easy PCR**
Experience more convenience with the new Q5 formulations
- 9 **Efficient DNA Synthesis**
Try the EnClose Cell-free dbDNA Synthesis Kit



BCR-ABL: A Case Study in Precision Medicine

By Andrew J. Barry, MS, New England Biolabs

Scientific discovery is driven by passionate scientists who push the limits of available tools to make observations and formulate and test hypotheses. These discoveries often provide a foundation for accelerating our understanding of biology in unexpected ways. In parallel, advances in technology improve the tools needed to understand biology, providing greater insight into molecular interactions, catalyzing discovery in profound ways.

In 1959, Peter Nowell and David Hungerford, cytogeneticists at the Fox Chase Cancer Center in Philadelphia, using a confocal microscope, observed that the blood cells of patients with Chronic Myeloid Leukemia (CML) carried an abnormally small chromosome 22. They named this chromosome after the city where it was discovered, and their findings were published in 1960 (1), linking the “Philadelphia Chromosome” to CML and providing the first evidence of a direct genetic link to cancer. It wasn’t until 12 years later that Dr. Janet Rowley, a physician and human geneticist at the University of Chicago, identified the specific genetic rearrangement involved in CML by pioneering a novel cytogenetics technique. She described the first ever chromosomal translocation, in which a segment of chromosome 9 had broken off and reattached to chromosome 22 (2).

Further studies of this translocation provided

insight into the mechanism behind its association with CML, showing that the translocation results in a fusion transcript, BCR-ABL, which is then translated into Bcr-Abl tyrosine kinase. It was further proven that this tyrosine kinase disrupts red blood cell function and results in the overproduction of white blood cells. These discoveries provided a target for potential therapeutic intervention and spurred efforts to discover molecules that inhibit this faulty pathway.

In the 1990s, a collaboration between oncologist Brian Druker from Oregon Health and Sciences University and Nicolas Lydon from Novartis led to the design of a small molecule, originally named STI-571, that specifically inhibited Bcr-Abl tyrosine kinase in the affected cancer cells without harming normal cells (3). 1998 marked the start of the first clinical trial of the drug, now named imatinib. The therapeutic benefit and lack of side effects were overwhelmingly positive.

In 2001, the US Food and Drug Administration (FDA) approved imatinib, marketed under the brand name Gleevec, providing a targeted therapy for patients with CML, revolutionizing the standard of care.

While the standard diagnostic tests for CML still rely on cytogenetics, FISH and RT-qPCR, more recent work comprehensively characterizes BCR-ABL using targeted RNA sequencing.

RNA-seq can detect rare or atypical fusion variants and analyze transcriptome-wide resistance mechanisms. As such, RNA-seq has become a valuable companion diagnostic. Future work includes characterizing host immune responses triggered by the therapeutic intervention, which can lead to mechanisms of resistance, and therapeutic strategies to overcome resistance.

This vignette provides a valuable, if unintended, framework for precision medicine: it traces a path from scientific observation and hypothesis testing, to elucidation of disease pathways and rational drug design aimed at restoring cellular function. The pace of therapeutic development has accelerated with technological advancements, both in the ability to observe cellular dynamics, as well as in the expanding range of therapeutic intervention approaches, including RNA silencing, genome editing, and RNA as a direct therapeutic agent.

Just as Nowell, Hungerford and Rowley used the tools of their time to study red blood cells in CML patients, RNA sequencing is a technology being applied within this framework today, enabling the ability to extract molecular information with unprecedented speed and breadth, accelerating the drug discovery process.

Bulk RNA sequencing is performed to discover transcript anomalies associated with disease,

both in the discovery of novel transcripts as well as expression profiling to understand temporal changes across the roughly 20,000 genes comprising the human transcriptome. Advances in single-cell RNA sequencing offer additional precision at the cellular level, enhancing scientists' ability to understand disease-causing pathways and inform therapeutic strategies. Detection of disease-causing transcripts can be performed rapidly and easily using either targeted gene sequencing or quantitative PCR, and the immune response can be monitored to understand resistance mechanisms. To support these RNA-based approaches, researchers rely on robust workflows for RNA purification, library preparation, and immune sequencing. As developers of research tools, NEB offers a wide range of products to support RNA-based precision medicine workflows, starting with Monarch RNA extraction kits that enable high-quality RNA purification for downstream analysis and NEBNext NGS sample preparation kits for RNA sequencing workflows.

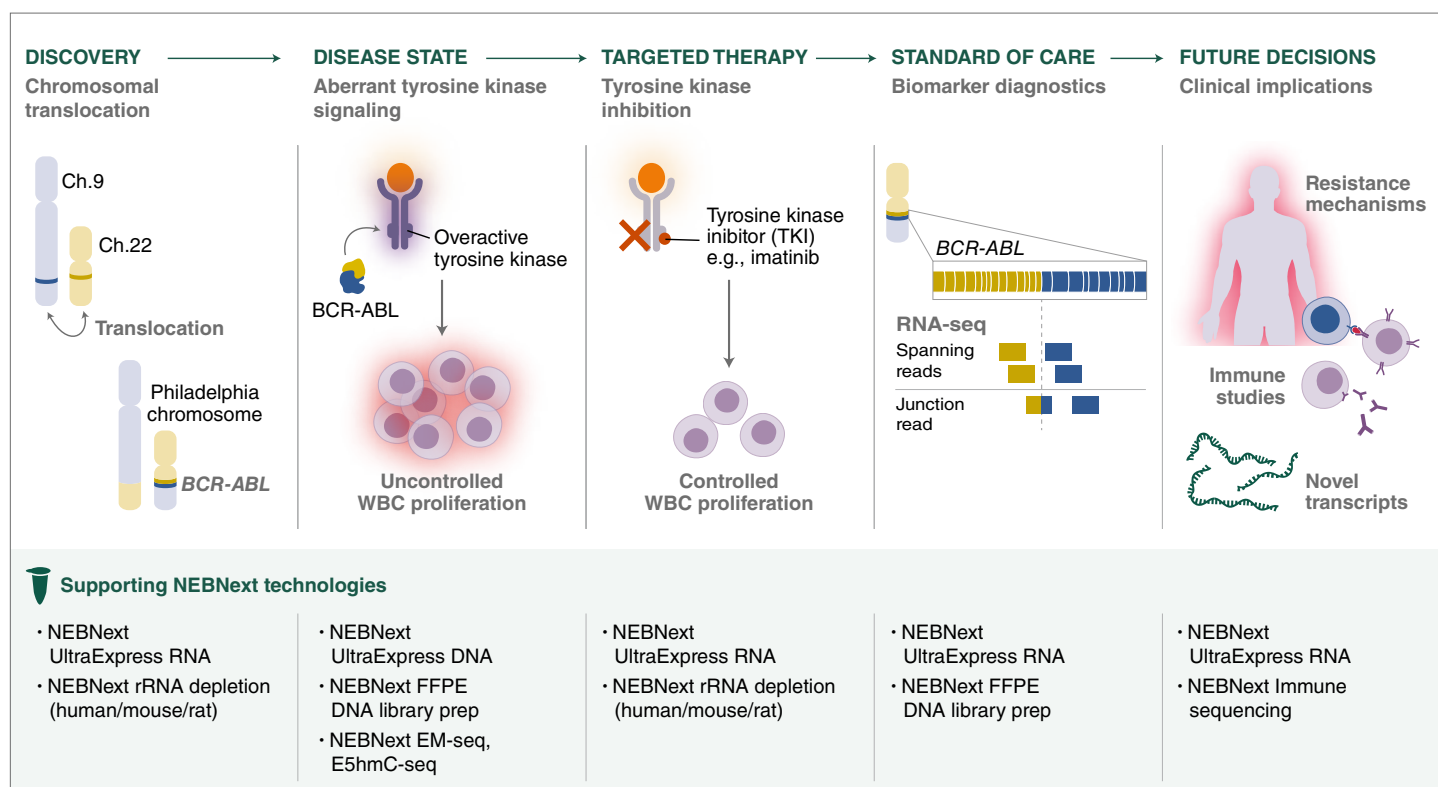
Efforts have been focused on producing streamlined faster, higher accuracy workflows to provide researchers with cutting-edge tools offering broad insight into the underpinnings of disease and hope for future therapies. The NEBNext UltraExpress RNA Library Prep Kit allows for the production of sequence-ready libraries in a single day. The NEBNext Single Cell/Low Input RNA Library Prep Kit is incorporated into single-cell workflows, using a template switching mechanism to generate libraries from as little as 2 picograms of RNA input. Immune profiling is made simple through the NEBNext Immune Sequencing Kit, providing targeted sequencing of the full immune repertoire, with available primer sets for both mouse and human in both B- and T-Cells. Most recently, the NEBNext Low-bias Small RNA Library Prep Kit was developed to provide unfettered insight into this emerging class of biomarkers, offering a 3.5-hour workflow while maintaining accurate representation of the cellular material across the range of small RNAs classes.

References:

1. Nowell, P.C. and Hungerford, D.A. (1960). "A minute chromosome in human chronic granulocytic leukemia". *Journal of the National Cancer Institute*.
2. ROWLEY, J. A "New Consistent Chromosomal Abnormality in Chronic Myelogenous Leukaemia identified by Quinacrine Fluorescence and Giemsa Staining." *Nature* 243, 290–293 (1973). <https://doi.org/10.1038/243290a0>
3. Druker, BJ, Tamura, S, Buchdunger, E, et al. "Effects of a selective inhibitor of the Abl tyrosine kinase on growth of Bcr-Abl positive cells." *Nat Med* 1996;2:561-566



To learn more about the products mentioned in this article,
continue to page 4.



Key features of the NEB products mentioned in this article:

Product Name	NEB #	Features
Monarch Spin RNA Isolation Kit (Mini)	T2110	- Isolates up to 100 µg of high-quality total RNA - Handles diverse samples (cells, fibrous/lipid-rich tissues, bacteria, yeast, plants, insects) - Removes genomic DNA contamination - Retains small RNAs (<200 nt) in the total RNA pool
NEBNext UltraExpress RNA Library Prep Kit	E3330	- Generates directional RNA-seq libraries in ~3 hours - Reduces steps and cleanups (streamlined workflow) - Uses one protocol across input amounts - Supports 25–250 ng total RNA and automation
NEBNext rRNA Depletion Kit v2 (Human/Mouse/Rat)	E7400	- Cleaner RNA-seq data with efficient removal of cytoplasmic and mitochondrial rRNA - Flexible and robust performance across inputs (10 ng–1 µg) and RNA quality - Fast, low-touch workflow completed in ~2 hours
NEBNext UltraExpress DNA Library Prep Kit	E3325	- Faster library prep with a streamlined <2-hour workflow and fewer steps - Consistent, high-quality libraries from 10–200 ng pre-sheared DNA using a single protocol - Automation-ready and efficient with fewer cleanups and consumables
NEBNext FFPE DNA Library Prep Kit	E6650	- High-quality data from FFPE DNA with repair reagents and optimized library prep - Increased library yields and sensitivity with improved sequencing metrics and somatic variant calling - Automation-friendly workflow across a 5–250 ng input range
NEBNext Enzymatic Methyl-seq v2 Kit	E8015	- Superior sensitivity of 5mC and 5hmC detection with even GC coverage - Detects more CpGs with fewer sequencing reads using high-performance library preparation - Flexible 0.1–200 ng input range with larger insert sizes and separate index primers
NEBNext Enzymatic 5hmC-seq Kit	E3350	- High-sensitivity detection of 5hmC with even GC coverage - High-efficiency library preparation across a 0.1–200 ng input range - Compatible EM-seq and E5hmC-seq data for combined analysis
NEBNext Single Cell/Low Input RNA Library Prep Kit for Illumina	E6420	- Delivers high-yield, high-quality libraries from single cells or 2 pg–200 ng RNA - Improves detection of low-abundance transcripts - Provides uniform transcript coverage across inputs and sample types - Minimizes handling steps and hands-on time
NEBNext Immune Sequencing Kit	E6320 (Human) E6330 (Mouse)	- Enrich for and sequence both B&T cell receptors - Enables deeper receptor repertoire analysis - Uses UMIs for accurate transcript quantification
NEBNext Low-bias Small RNA Library Prep Kit	E3420	- Minimizes bias (low-bias performance) - Supports broad, biologically relevant inputs (0.5–1,000 ng total RNA; 0.05–5 ng enriched small RNA) - Completes in a single-day workflow - Multiplexes up to 480 LV Unique Dual Index primer pairs (available separately)



For further product information and the full NEBNext product portfolio, visit www.NEBNext.com

Save the date!

After the great success of the first edition we're looking forward to reconnect at the **2nd NGS Innovation Summit** in 2027!

- Network with leading minds of the European NGS community
- Experience the cutting-edge scientific program
- Connect with NEB's technical experts and partner companies



September 09–10, 2027
Heidelberg, Germany

“The summit was an exhilarating blend of scientific innovation and social interaction, arguably making it one of the most engaging events I’ve ever participated in.”

Wencke Walter, Head of Innovation,
Munich Leukemia Laboratory

Solve the challenge of scale for NGS Library Prep

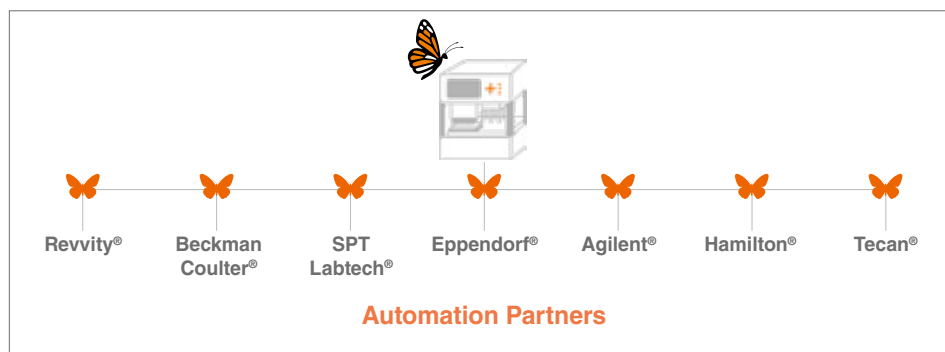
Liquid-handling automation platforms are becoming ever-more essential for scalable, reproducible library preparation in next generation sequencing (NGS) workflows. The range of automation platforms continues to grow, so knowing where to look for support automating your library prep workflow can save both time and money. NEBNext library prep kits and reagents are designed with automation compatibility in mind, ensuring that your library quality doesn't suffer as your throughput grows.

NEBNext workflows are designed with automation in mind

- Reagent fill volume overages accommodate liquid handling platforms
- Save time and reduce consumables waste with fewer bead clean-up steps
- Modular kit components for workflow flexibility
- Simple addition-only workflows eliminate lossy transfers
- Expert field application support for reagents and instrumentation

NEBNext automation on a wide range of liquid-handling platforms

Through close collaboration with automation partners and a global network of Field Application Specialists, NEB supports the development, optimisation, and deployment of robust, automated protocols.



Talk to us

Our dedicated Automation Field Application Specialists can help you to realize the biggest gains in throughput and reproducibility by providing platform-specific technical guidance and honest, expert-level feedback on your automation challenges.



For automation consultation, please reach us at

NEBNextAutomation@neb.com



For automated solutions for NEBNext reagents, visit

www.neb.com/automation

NEBNext automation case study

Designed for simplicity and efficiency, the NEBNext kits enable development of low bias, high-sensitivity NGS protocols with minimal plastic waste. In combination with SPT Labtech's firefly+ platform at the European Molecular Biology Laboratory (EMBL) core facility GeneCore, a robust protocol for fully walkaway automation is created, enabling more streamlined, end-to-end workflows and supporting labs to scale automation more easily.



Learn more in the webinar

Rethinking mRNA Workflows: From Manual Processes to Automated Precision

available on demand.

The finest in fidelity



Benefit from the quality of Q5 DNA Polymerase

Q5 High-Fidelity DNA Polymerase sets the standard for both fidelity and robust performance. With fidelity >280 times higher than *Taq* DNA Polymerase, Q5 results in ultra-low error rates. Q5 is a designed polymerase, improving speed, fidelity, and reliability of performance.

25%
DISCOUNT*

High-Fidelity PCR with NEB:

Enjoy now an exclusive 25% discount on your purchase of Q5 Polymerases! Simply enter the promo code “Q52026” when ordering.

*The 25% discount is applicable to the list price of Q5 products listed in this issue. It is valid until December 31, 2026, and cannot be combined with other discounts. The offer is available only in selected countries. For more details, please contact your local distributor.



Extremely low error rates

At ~280X higher than *Taq*, Q5 offers unparalleled fidelity for your most important samples.



Robust amplification with minimal optimization

High specificity and yield are absolute requirements for today's molecular biology techniques.

↑AT
↑GC

Superior coverage, regardless of GC content

Q5 displays superior performance for a wide range of high-GC or high-AT templates.



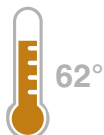
Shorter PCR protocols

Incorporating the SSo7d processivity-enhancing domain enables shorter extension times, as low as 5 seconds per kb.



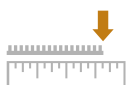
RT setup

Aptamer-based hot start requires no initial denaturation step and enables room temperature setup.



Universal annealing temperature

Compatible with a universal annealing temperature protocol.



Amplification of long templates

Reliably amplify simple templates up to 30 kb and complex templates up to 20 kb.

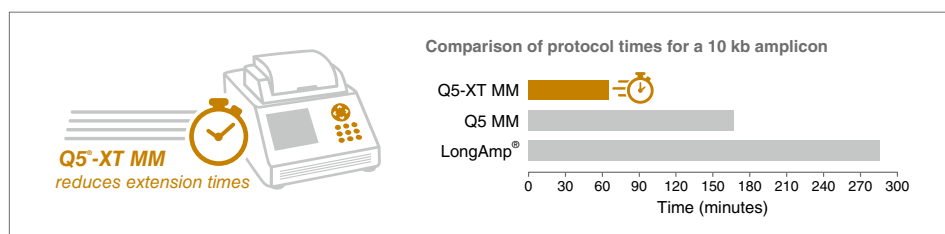


Experience more convenience with Q5



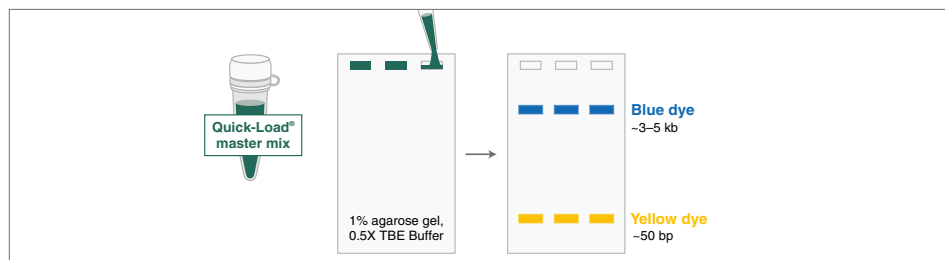
Q5-XT Hot Start High-Fidelity 2X Master Mix

When DNA targets are long or complex, or when speed is a priority, Q5-XT Hot Start High-Fidelity 2X Master Mix is your optimal choice. The new Q5 formulation offers fast cycling conditions as low as 5 seconds per kb and a reliable amplification of diverse targets up to 30 kb while maintaining the performance you expect of Q5.



Q5 Quick-Load High-Fidelity 2X Master Mixes

The Q5 Quick-Load Master Mixes combine exceptional fidelity with the convenience of direct gel loading. The built-in Quick-Load dyes eliminate the need for loading buffer while delivering the same high-performance amplification as standard Q5 formulations. Blue and yellow tracking dyes enable easy reaction setup and clear monitoring of DNA fragments during electrophoresis.



Ordering Information

PRODUCT	NEB #	SIZE
Q5-XT Hot Start High-Fidelity 2X Master Mix	M2499S/L	100/500 rxns
Q5 Quick-Load High-Fidelity 2X Master Mix	M0578L	500 rxns
Q5 Quick-Load Hot Start High-Fidelity 2X Master Mix	M0580L	500 rxns
Q5 High-Fidelity 2X Master Mix	M0492S/L	100/500 rxns
Q5 Hot Start High-Fidelity 2X Master Mix	M0494S/L/X	100/500/500 rxns
Q5 High-Fidelity DNA Polymerase	M0491S/L	100/500 units
Q5 Hot Start High-Fidelity DNA Polymerase	M0493S/L	100/500 units
Q5 High-Fidelity PCR Kit	E0555S/L	50/200 rxns
Q5 Blood Direct 2X Master Mix	M0500S/L	100/500 rxns
Q5U Hot Start High-Fidelity DNA Polymerase	M0515S/L	100/500 units
NEBNext Ultra II Q5 Master Mix	M0544S/L/X	50/250/500 rxns
NEBNext Q5U Master Mix	M0597S/L	50/250 rxns



Universal annealing temperature with Q5

Q5 is compatible with a universal annealing temperature protocol of 62°C (or 60°C for Q5 Master Mixes).

RECOMMENDED 3-STEP CYCLING PROTOCOL		
STEP	TEMPERATURE	TIME
Initial Denaturation	98°C	30 seconds
25-35 cycles	98°C	5-10 seconds
	62°C or 60°C	20 seconds
Final Extension	72°C	20-30 seconds/kb*
	72°C	2 minutes
Hold	4-10°C	

*The extension time can be set to accommodate the longest amplicon in the workflow.

The new application note showcases the use of a common annealing temperature across many PCR assays, and for which critical applications it's worth optimizing.



Scan the QR code to read the application note:
Universal Annealing Temperature in PCR and its Impact on Amplification Results



Interested in giving Q5 a try? Request a free sample from your local distributor.



Learn more about Q5 at
www.Q5PCR.com

Congratulations to the winners of the **2026 Passion in Science Awards®**

At New England Biolabs, we believe science has the power to build a greener, more compassionate world. The Passion in Science Awards recognize members of the scientific community whose work extends beyond the laboratory — advancing discovery while positively impacting society, education, sustainability, and creativity.

Out of numerous submissions, **11 winning projects** were awarded across **four categories** that are aligned with NEB's values:

AWARD WINNERS



Arts & Creativity

Highlighting innovative intersections between science, art, and creative expression.

Saurja DasGupta (USA); A Pilgrimage to Life's Beginning
Jules Ho (USA); Charismatic Critter Club
Anne-Frances Miller (USA); Plant Pigment Chemistry and Textile Art
Haolun Tian (Canada); Algal Blooms: Aerial Brushstrokes



Scientific Mentorship & Advocacy

Recognizing scientists who educate, mentor, and promote engagement within the scientific community.

Richard O'Rorke (New Zealand); DNADRV - The DNA Biodiversity Drive
Alexandra Szabo (Germany); Podcast PhD: The Experience
Hemanshi Galaiya (Australia); Young Stripes STEM Education



Humanitarian Duty

Celebrating scientists applying science to improve human health and well-being worldwide.

Kehinde Abereojie (UK); Sexual Health Education Program
Rojelio Mejia (USA); Breaking the Poverty and Parasite Cycle



Environmental Stewardship

Honoring efforts to protect natural resources and promote sustainability in or beyond the lab.

Homere Alves Monteiro (USA); Fight Deforestation with Ants' Museomics
Chukwudi Ikegwu (USA); Innovating Amphibian Conservation

We invite all winners to be our guests at a celebration ceremony in October 2026 at our headquarters in Ipswich, MA, USA. In addition, the winners receive a \$1,000 scholarship for their work or a charitable donation to the charity of their choice.



Learn more about the award winners and their projects at
www.neb.com/PassionInScience

Your choice for efficient DNA synthesis



EnClose™ Cell-free dbDNA™ Synthesis Kit

The EnClose Cell-free dbDNA Synthesis Kit (NEB #E9301) enables enzymatic generation of closed-ended linear dsDNA containing a sequence of interest. By combining phi29-XT DNA Polymerase for rolling circle amplification with TelN Proteolomerase for deconcatenation and end closure, it provides a streamlined one-day workflow. The kit produces high yields (>10 µg) of cell-free dbDNA for your downstream applications.

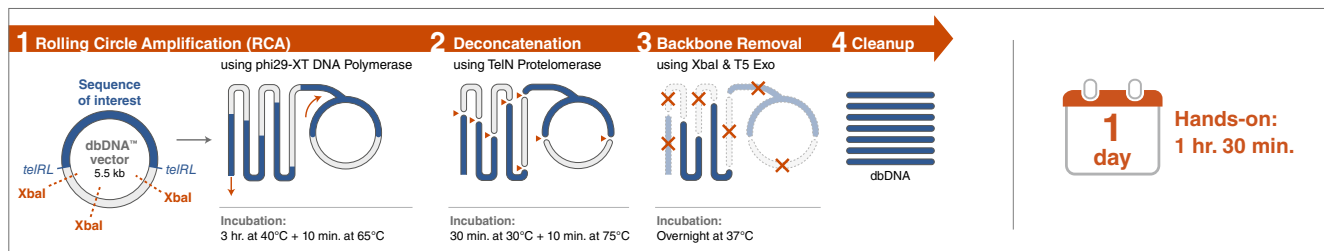


Enhanced stability

dbDNA is a linear, double-stranded DNA with covalently-closed ends.



Streamline manufacturing



Simplify regulatory complexity

- No endotoxins
- No bacterial sequences
- No antibiotic markers



Ideal for downstream applications

- IVT template generation
- CRISPR HDR template
- DNA synthesis
- AAV/LV payload
- Transient transfection
- DNA/RNA therapeutics



Scalability

Rapid scale-up from R&D to production with a simple and robust enzymatic workflow.



Learn more about the benefits of dbDNA in our latest eBook:

Cell-free enzymatic solutions for DNA manufacturing: enhancing next-generation therapeutics with dbDNA synthesis



Ordering Information

PRODUCT	NEB #	SIZE
EnClose Cell-free dbDNA Synthesis Kit	E9301S	20 rxns
COMPANION PRODUCTS	NEB #	SIZE
Monarch Spin PCR & DNA Cleanup Kit (5µg)	T1130S/L	50 preps/ 250 preps
Monarch Spin High-Capacity DNA Cleanup Kit (100 µg)	T1135V/S/L	10 preps/50 preps/ 200 preps
Monarch Mag PCR & DNA Cleanup Kit	T4130V/S/L	10 preps/ 100 preps/400 preps



For more information, visit
www.neb.com/E9301

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Listen up! The message is spreading



Drive your RNA research forward

The versatility of RNA makes it a powerful tool in transforming how we understand, diagnose, and treat disease. Over the past several years, advances in RNA research have catalyzed breakthroughs in therapeutics, personalized medicine, molecular diagnostics, infectious disease research, and agricultural biology. Therefore, advanced tools for manipulation and analysis of mRNA are more important than ever. For many years, NEB has invested in the development of products to support RNA research, all of which are vetted by our own scientists in their work. Whether you are in an academic or industrial setting, we have the products, tools, services, and support that will help drive your research forward.



mRNA Therapeutics and Personalized Medicine

mRNA therapeutics have emerged as a versatile platform, enabling vaccine development, protein replacement therapies, and immunotherapies. NEB offers products for the full mRNA synthesis workflow, which are also available GMP-grade*.



RNA-based Diagnostics and Surveillance

RNA-based diagnostics enable rapid, sensitive, and specific detection of pathogens and biomarkers. NEB products for RT-qPCR, RNA-seq, and isothermal amplification deliver sensitive detection and streamlined workflows.



RNA in Agricultural Biology

RNA is emerging as a transformative technology for agricultural applications, including crop protection and precision breeding. NEB's solutions for AgBio researchers include reagents for RT-qPCR, NGS library prep, and nucleic acid purification.



RNA in Basic Research

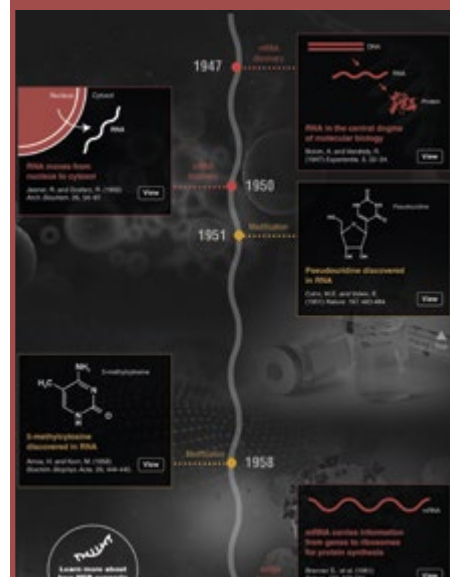
RNA research in academia focuses on understanding the role of RNA in diverse biological processes, and can be foundational for translational applications. NEB's basic research program focused on RNA biology utilizes many of our reagents and has contributed to advances in this area.

Discoveries towards mRNA therapeutics

We've put together a selection of publications and resources that span over seven decades of discoveries.



Explore the timeline and resources!



Request a free sample from your local distributor.



Find more details on products available and access helpful RNA-related resources at **NEBna.com**

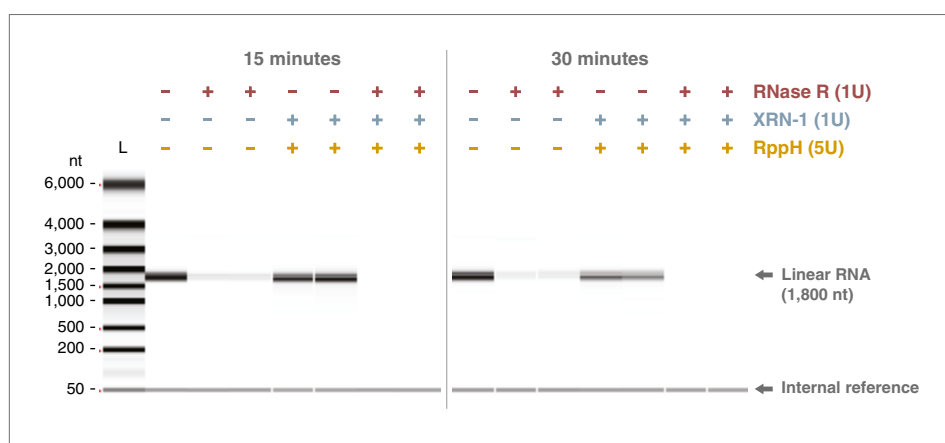
*"GMP-grade" is a branding term NEB uses to describe products manufactured or finished at NEB's Rowley facility. The Rowley facility was designed to manufacture products under more rigorous infrastructure and process controls to achieve more stringent product specifications and customer requirements. 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.

Go Full Circle

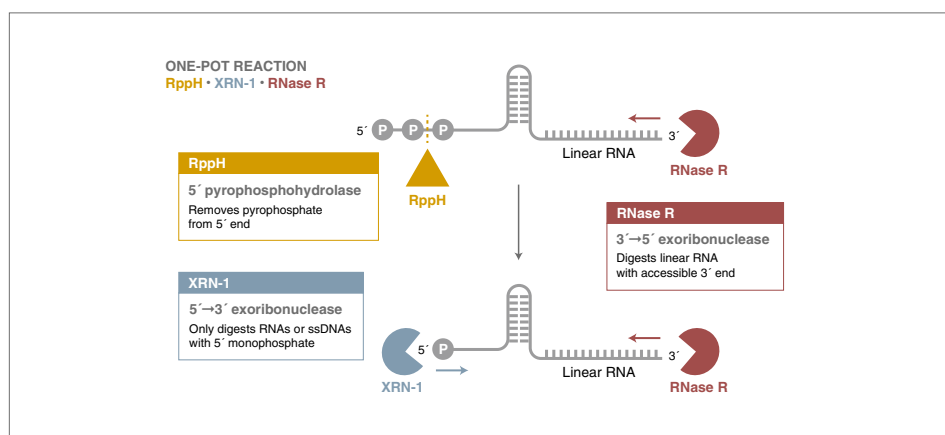
Enzymatic solutions for circular RNA enrichment

Circular RNA has emerged as a promising modality for RNA therapeutics with substantially enhanced durability relative to linear mRNA. Circular RNA research and therapeutic development demand robust, selective tools for linear RNA removal and circular RNA enrichment. This overview highlights three complementary enzymes (RNase R, XRN-1, and RppH) that support workflows from enrichment through more complete linear RNA depletion, including stubborn RNase R-resistant linear RNAs.

One-pot solution for RNase R-resistant linear RNA removal



Digesting linear RNAs from both the 5' and 3' ends with XRN-1 and RNase R, respectively, is an effective method for depletion of linear RNA transcripts. 1 unit RNase R, 1 unit XRN-1, and 5 units RppH were added to 1 µg of an RNA sample containing RNase R-resistant linear RNA. This reaction ran for 15 or 30 minutes at 37°C in 1X RNase R Reaction Buffer.



RNase R (NEB #M0100)

Core enzyme for circular RNA enrichment

RNase R is a highly processive 3' → 5' exoribonuclease that digests linear RNA with an accessible 3' end while leaving circular (and lariat) RNA intact.

Important note on enzyme:RNA ratio

Maintaining a 1:1 ratio (µg RNA : units RNase R) helps minimize star activity and unintended digestion; excessive RNase R can lead to loss of both linear and circular RNA.

XRN-1 (NEB #M0338)

Digests linear RNA from the opposite end

XRN-1 is a 5' → 3' exoribonuclease. In workflows where some linear RNAs resist RNase R (due to structure or inaccessible ends), XRN-1 adds complementary digestion from the 5' end.

Key requirement: XRN-1 digests RNAs (or ssDNA) with a 5' monophosphate.

RppH (NEB #M0356)

Unlocks XRN-1 digestion by converting 5' ends

RppH is an RNA 5' pyrophosphohydrolase. It removes pyrophosphate from the 5' end of triphosphorylated RNA, converting it to monophosphorylated RNA – the preferred substrate for XRN-1.

Ordering Information

PRODUCT	NEB #	SIZE
RNase R	M0100S	400 units
XRN-1	M0338S/L	20/100 units
RNA 5' Pyrophosphohydrolase (RppH)	M0356S	200 units



Scan the QR code to review **two methods to digest RNase R-resistant linear RNAs.**

NEW TO MOLECULAR BIOLOGY?

Start your career off on the right path. Get your free NEB Starter Pack!#

The free NEB New Student Starter Pack is available to all research students, PhD students, PostDocs, and everyone who is starting their career in molecular biology.

The NEB Starter Pack contains:

- NEB Catalog & Technical Reference (optional)
- Poster and Sticker
- Technical Guides and Brochures
- NEB Pencil, Sharpie, Notepad & Post-Its
- NEB Pull Key Ring

A welcome gift for your first order of
New England Biolabs products!



20% Discount#

+ Access to many free NEB product samples



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or contact your local distributor!

Offer available through to December 31, 2026, or while stocks last. Limited to one pack/person. Content may vary from those shown. The 20% discount voucher/offer is void where prohibited by regional or institutional laws or regulations. Please ask your local distributor for details and availability. For full terms and conditions under GDPR, please visit www.neb.com/starterpack.

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