



# Onyx™

## Digital Genome Engineering Platform

Perform large-scale, massively parallel genome editing experiments.



# A Biofoundry on Your Benchtop

Welcome to the new era of CRISPR-based genome engineering. With the **Onyx Digital Genome Engineering Platform**, you can design and generate libraries, track results, and evaluate findings right on your benchtop—all with the push of a button.

It's a complete benchtop solution, consisting of design and analysis software, custom consumables, assays, and a fully automated instrument.

## Unprecedented scale

- Build complex libraries with the push of a button.
- Make diverse edits including insertions, deletions, and substitutions.
- Library sizes from 100 to 10,000 in *E. coli* and up to 6,000 in *S. cerevisiae*.

## Superior performance

- High edit rates ensure your designs are integrated.
- Barcode every cell, track every design.
- Rational design approach affords you precise control of genomic edits.

## Greater access

- Perform advanced genome engineering, even without extensive gene-editing experience.

View the video, [Onyx Platform Introduction](#).





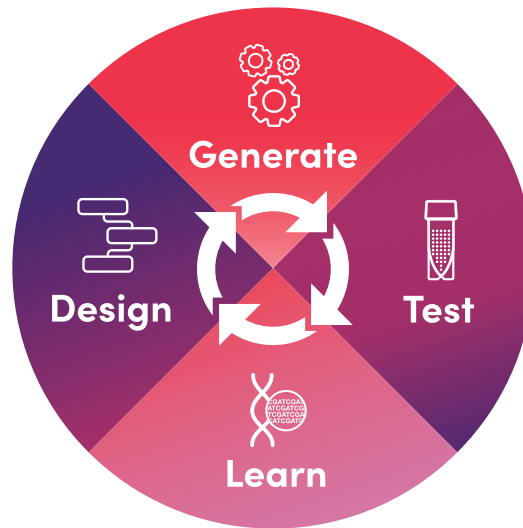
# Accelerate Forward Engineering Using the Design-Generate-Test-Learn Cycle

## Generate

Build an edited Onyx cell library on the Onyx Instrument using your customized order of **Onyx Genome Engineering Kit**.

## Design

Design your library in a few clicks with **InscriptaDesigner™ Software**.



## Test

Characterize the Onyx Library, plan your phenotype experiment, and identify the edits of interest using the **Onyx Genotyping Assays** and **InscriptaResolver™ Software**.

## Learn

Data analysis of hundreds of thousands of data points to drive your next experiment.

## Example: Lysine Metabolic Engineering

Inscripta Applications Development team used lysine biosynthesis in *E. coli* to demonstrate how Onyx technology can rapidly generate diversity to improve production. A saturation mutagenesis library was designed to probe every residue of every protein in the lysine biosynthesis pathway, along with the knock-out and stepwise expression modification of every open reading frame. Three cycles of editing, screening, analysis, and stacking of successful mutations led to a 14,000-fold improvement in lysine production over 4 months of experiments.

View the video, ***A New Era in Forward Engineering of Proteins, Pathways and Genomes.***

## Other Forward Engineering Applications:

- Directed Evolution
- Heterologous Pathway Engineering
- Natural Product Synthesis
- Protein Production
- ...and more.



# Explore the Genome with the Onyx Digital Genome Engineering Platform

## Discover and map functions at unprecedented scale and pace

In addition to forward engineering, diversity generation by Onyx facilitates genomic discovery: from probing the function of essential genes to discovering novel antimicrobial drug targets, the possibilities are limitless.

### Example: Mapping of essential residues in four different essential genes

In collaboration with Dr. Liselot Dewachter from VIB-KU Leuven Center for Microbiology, Inscripta used the Onyx chemistry to perform saturation mutagenesis on four essential genes involved in cell envelope synthesis in *E. coli*. In total, 22,790 edits were designed to replace every amino acid of these proteins by every other amino acid. Novel positions that could not tolerate amino acid changes were discovered, as well as known essential positions validated.



View the webinar-on-demand, *High-throughput CRISPR editing using the Onyx platform identifies essential residues in proteins.*

### Other Genomic Discovery Applications:

- Antibiotic Resistance
- Adaptive Laboratory Evolution
- Cell-free synthesis
- Directed evolution
- Functional Genomics
- Microbial Genetics
- Quantitative Trait Loci
- Systems Biology
- ...and more.



# The Onyx Genome Engineering Instrument

The **Onyx Instrument** automates every aspect of large-scale, massively parallel genome engineering experiments—including cell transformation, CRISPR-based genome editing, cell growth, and cell recovery.

## Easy to use

Install the ready-to-use reagents and consumables, push go, and walk away.

## Reduces errors

Instrument automatically reads the consumables' barcodes and downloads the corresponding protocol, ensuring every instrument run is set up for success.

## Fully automated

The benchtop instrument performs every step of the engineering process while providing real-time monitoring from anywhere using the **Incripta Engineering Portal**.

## Unmatched throughput

CRISPR-edited cell libraries with thousands of programmed edits are generated in 2–4 days.

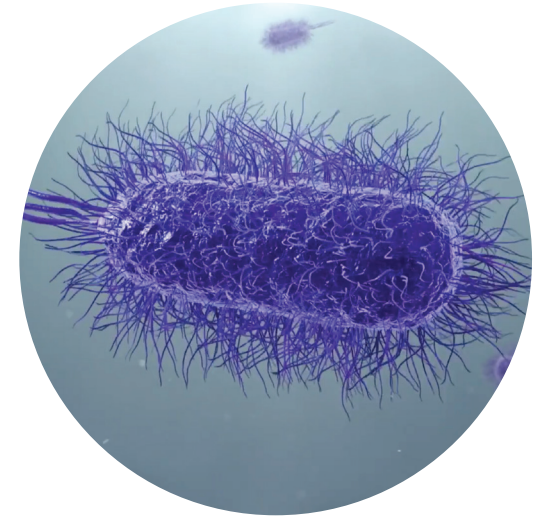
View the video, *[Get to Know the Onyx Platform](#)*.





# Innovative Microfluidics for Precise Editing

Onyx is unlike any other instrument. It features four innovative microfluidic devices used to precisely manage time and temperature, monitor cell growth, and control for the non-linearities of biological variability during the editing process. These microfluidic devices provide cell-type normalization across millions of cells. Contamination is minimized through self-contained design and dry instrument technology.



Cell Growth Cuvette



Microfluidic Cell Controller



Microfluidic Cell Transformer



Cell Growth Cuvette



Digital Engineering Processor

## 1 Cell Growth

Measure and manage optimal cell growth in real time.

## 2 Electrocompetency

Exchange media and prepare cells for electroporation.

## 3 Electroporation

Efficiently electroporate Design DNA into the cells.

## 4 Cell recovery

Measure and manage optimal cell growth in real time.

## 5 Outgrowth

Manage and normalize cell editing and growth.



# Onyx Genome Engineering Kits



Simply design and order your kit from the **Inscripta Engineering Portal**, and three to four weeks later you'll receive a ready-to-use library of up to 10,000 Design DNAs, plus all necessary consumables and reagents. Each Design DNA contains a unique gRNA-Donor DNA-Barcode combination and all other components, such as the MAD7™ and repair proteins, required to perform DNA editing *in vivo*.

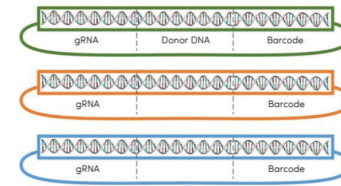
## Onyx chemistry enables thousands of edits in a single tube.

In a traditional CRISPR experiment, one edit is performed per reaction, and multiplexing is tedious at scale. With Onyx technology, up to 10,000 edits can be multiplexed in a single experiment, contained to a single tube. This saves time and greatly reduces the use of plastic.

## Using your own strain.

**Onyx Genome Engineering Kits** are designed for compatibility with widely used and validated *E. coli* and *S. cerevisiae* strains, but you can use your own similar strain. The **Onyx Strain Assessment Kit** can determine if your strain of interest is compatible with the Onyx Platform.

## One Design DNA per cell



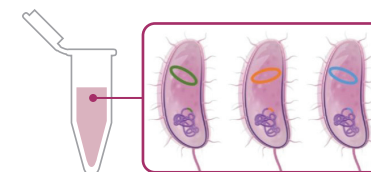
Linking the gRNA with the donor template means each transformed cell receives only one Design DNA, generating one edit per cell, even in a complex multiplexed experiment.

## One component set per experiment



Along with your custom Design DNA library, each **Onyx Genome Engineering Kit** comes with new microfluidic components to ensure against cross-contamination.

## Thousands of edits in a single tube

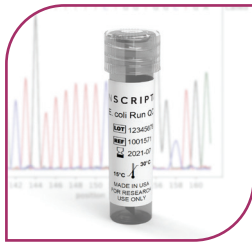


The Onyx Cell Library obtained at the end of the Onyx run contains millions of cells with up to 10,000 unique, complete, and intended edits.



# Onyx Genotyping Assays

We offer three genotyping assays to assess the instrument run and analyze the composition of the Onyx Cell Library pre-phenotyping, help to plan the phenotyping experiment, and identify the edit of interest post-phenotyping.



## The Control Edit Assay

This assay, included in every **Onyx Engineering Kit**, is a Sanger sequencing experiment managed by Inscripta. It detects the presence or absence of internal control edits in the genome in order to confirm if the engineering run was successful.



## The Onyx Barcode Diversity Assay

This assay is designed to detect the Onyx barcodes, allowing you to derive the distribution of designs within their cell population using an Illumina™ platform. The kit contains everything necessary to make an Illumina-ready library.



## The Onyx Edit Identification Assay

This assay contains everything required to create an Illumina-ready library for Whole Genome Sequencing. It can be run either on clonal isolates or pooled cells.





# Inscripta Engineering Portal

With our cloud-based portal, you can design hundreds of thousands of precise genomic edits and analyze large quantities of data with maximum speed and efficiency. You can also navigate and monitor every step of the Design-Generate-Test-Learn cycle.

## Use the Portal to:

- Design your edit library using **InscriptaDesigner Software**.
- Order your **Onyx Genome Engineering Kit**.
- Monitor the **Onyx Instrument** run in real-time.
- Order your **Onyx Genotyping Assay** to characterize the Onyx Cell Library and analyze the results using the **InscriptaResolver Software**.





# InscriptaDesigner. Design your edits at scale.

You can create customized edit design libraries within the portal with **InscriptaDesigner Software**. Select your genome, the type of edit, and location on the genome, and **InscriptaDesigner** takes care of the rest, including PAM site identification, plus gRNA and donor DNA design. With **InscriptaDesigner's** innovative scoring function, you can gain insight into the probability that a design will result in an edit, helping you create meaningful edits at scale without the drudgery of manual design and review.

## Large variety of designs

Design multiple edit types across the genome for diverse library strategies such as genome-wide knock-outs and saturation mutagenesis. You have ultimate control over your library design and can even elect to have redundant designs created at a locus, depending on your experimental goals.

## Unprecedented speed

Create hundreds to thousands of edit designs across the genome within hours, and sometimes even minutes.

## Worry-free, reliable design

The highly efficient design algorithm has been informed by hundreds of thousands of editing experiments.

## Ease of review

The innovative scoring mechanism built into **InscriptaDesigner** is complete with a visual genome viewer—enabling you to see your designs in their relevant genomic context.

View the video, [Introduction to InscriptaDesigner Software](#).





# InscriptaResolver. Analyze your library at scale.

With **InscriptaResolver**, you can characterize the Onyx Edit Library. It provides easy-to-use bioinformatics pipelines to process next generation sequencing files. Results are graphically displayed for quick and easy review of genotypic metrics.

## Robust analysis

**InscriptaResolver** features state-of-the-art algorithms to quickly analyze data and characterize your library.

## Intuitive dashboards

Upload your data and **InscriptaResolver** will automatically generate a series of dashboards for easy data review.

## Streamlined phenotyping

Use the screener's and selector's curves to plan your phenotyping experiments.

## Clear experimental insights

After the phenotyping experiment, genotype isolated cells or pooled cells using the **Onyx Edit Identification Assay** or the **Onyx Barcode Diversity Assay** to select genotypes of interest and add them to your design library list for your next run.

View the video, *[A Quick Guide to InscriptaResolver Tools.](#)*

The screenshot shows the InscriptaResolver web interface. At the top, it says 'INSCRIPTA | Resolver | Experiment - NEBexpress\_liftover'. Below this is a navigation menu with 'ACTIVE EXPERIMENTS', 'ACCOUNT', 'INTERNAL - BUILDER', 'PROJECTS', 'CSA ECOLOGY KITS', 'ORGANISM', 'ECOLI', 'DATA', 'NEBEXPRESS', and 'SHARING'. A large circular badge with the number '1' is next to 'Libraries in Experiment'. The main content area is titled 'ANALYSES' and contains a table with columns: 'ID', 'Name', 'Analysis', 'Design Library Name', 'Version', 'Status', '# Files Loaded', 'Last Edit Date', and 'Created By'. The table lists three analyses: '72 p900 Edit Identification Analysis', '71 Singleplex Edit Identification Isolate Analysis', and '70 Amplicon Barcode Diversity Analysis'. Below the table is an 'ANALYSIS SAMPLE DETAIL' section with a table of sample data. To the right, there are 'DASHBOARDS' and 'CHARTS' sections. A play button is overlaid on the screenshot. Below the screenshot is a physical device with a screen displaying a circular progress indicator and a line graph.

| ID | Name       | Analysis                             | Design Library Name | Version | Status   | # Files Loaded | Last Edit Date | Created By                   |
|----|------------|--------------------------------------|---------------------|---------|----------|----------------|----------------|------------------------------|
| 72 | p900       | Edit Identification Analysis         | Ecoli_CSA_200508    | 3.5     | Complete | 1              | 11/26/2020     | tyson.shepherd@inscripta.com |
| 71 | Singleplex | Edit Identification Isolate Analysis | Ecoli_CSA_200508    | 4.4     | Complete | 36             | 11/26/2020     | tyson.shepherd@inscripta.com |
| 70 | Amplicon   | Barcode Diversity Analysis           | Ecoli_CSA_200508    | 1.4     | Complete | 3              | 11/26/2020     | tyson.shepherd@inscripta.com |

| Sample ID          | Sample Name        | Onyx Design DNA (2000) ID | Number of Designs | Fraction Edited Cells | Fraction Edited Cells Lower 95% CI | Fraction Edited Cells Upper 95% CI | Fraction Edited Cells for Mapped Designs | Fraction Edited Cells Lower 95% CI |
|--------------------|--------------------|---------------------------|-------------------|-----------------------|------------------------------------|------------------------------------|--|------------------------------------|
| SE00000807-DOT_D01 | NEBexpress_Plate   | 125                       | 991               | 0.33                  | 0.29                               | 0.37                               | 0.45                                     | 0.41                               |
| SE00000807-DOT_E01 | NEBexpress_ToxtR   | 125                       | 991               | 0.25                  | 0.22                               | 0.29                               | 0.32                                     | 0.28                               |
| SE00000807-DOT_F01 | NEBexpress_80xT... | 125                       | 991               | 0.35                  | 0.31                               | 0.38                               | 0.48                                     | 0.44                               |



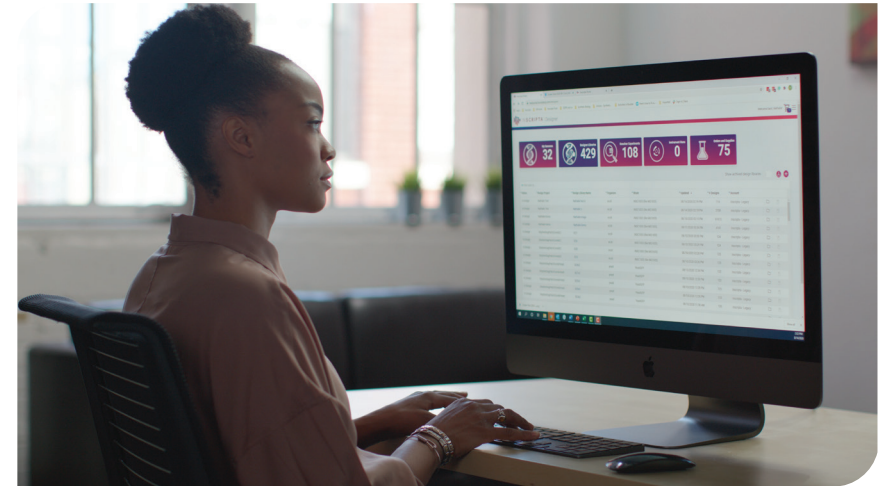
# Service and Support

You're never alone with the **Onyx Digital Genome Engineering Platform**.

Inscripta provides dedicated support through every step of your genome engineering experiments. Training and advice begin before your instrument even arrives. Our Service and Support team will ensure that the platform is set up to meet your specific needs, by providing:

- In-depth project consultation.
- Customized library design.
- Comprehensive installation and training.
- Detailed data analysis and interpretation.

We'll customize a training program to enable your team to take full advantage of the power of Onyx right from the start. From experimental design and optimization, to troubleshooting and diagnostics, we'll work closely with you to ensure that the full potential of the **Onyx Digital Genome Engineering Platform** is unleashed in every experiment you run.



CONTACT CUSTOMER SUCCESS TEAM | [support@inscripta.com](mailto:support@inscripta.com) | 800-INS-4088



# Onyx Product List

## INSTRUMENT, SERVICE, SUPPORT

| Catalog #   | Name                                       |
|-------------|--|
| INS-ON-1001 | Onyx Digital Genome Engineering Instrument |
| SVC-ON-1014 | Onyx System Delivery                       |
| SVC-ON-1015 | Onyx System Installation North America     |
| SVC-ON-1016 | Onyx Platform Training                     |
| SVC-ON-1017 | Onyx System Installation EU                |
| SVC-ON-1018 | Onyx System Installation UK                |

## ENGINEERING – S. CEREVISIAE

| Catalog #   | Name  |
|-------------|---|
| GEN-SC-1015 | Onyx <i>S. cerevisiae</i> Instrument Setup Kit – INSC1019                       |
| GEN-SC-1002 | Onyx <i>S. cerevisiae</i> Strain Assessment Kit                                 |
| GEN-SC-1016 | Onyx <i>S. cerevisiae</i> Genome Engineering Kit – INSC1019 [100-1000 Designs]  |
| GEN-SC-1017 | Onyx <i>S. cerevisiae</i> Genome Engineering Kit – INSC1019 [1001-2000 Designs] |
| GEN-SC-1018 | Onyx <i>S. cerevisiae</i> Genome Engineering Kit – INSC1019 [2001-4000 Designs] |
| GEN-SC-1019 | Onyx <i>S. cerevisiae</i> Genome Engineering Kit – INSC1019 [4001-6000 Designs] |
| GEN-SC-1009 | Onyx <i>S. cerevisiae</i> Genome Engineering Kit – [100-1000 Designs]           |
| GEN-SC-1010 | Onyx <i>S. cerevisiae</i> Genome Engineering Kit – [1001-2000 Designs]          |
| GEN-SC-1011 | Onyx <i>S. cerevisiae</i> Genome Engineering Kit – [2001-4000 Designs]          |
| GEN-SC-1012 | Onyx <i>S. cerevisiae</i> Genome Engineering Kit – [4001-6000 Designs]          |

## ENGINEERING – E. COLI

| Catalog #   | Name   |
|-------------|--|
| GEN-EC-1001 | Onyx <i>E. coli</i> Instrument Setup Kit – INSC1003                        |
| GEN-EC-1004 | Onyx <i>E. coli</i> Strain Assessment Kit                                  |
| GEN-EC-1006 | Onyx <i>E. coli</i> Edit Competency Kit                                    |
| GEN-EC-1007 | Onyx <i>E. coli</i> Genome Engineering Kit – INSC1003 [100-1000 Designs]   |
| GEN-EC-1008 | Onyx <i>E. coli</i> Genome Engineering Kit – INSC1003 [1001-2000 Designs]  |
| GEN-EC-1009 | Onyx <i>E. coli</i> Genome Engineering Kit – INSC1003 [2001-4000 Designs]  |
| GEN-EC-1010 | Onyx <i>E. coli</i> Genome Engineering Kit – INSC1003 [4001-6000 Designs]  |
| GEN-EC-1011 | Onyx <i>E. coli</i> Genome Engineering Kit – INSC1003 [6001-8000 Designs]  |
| GEN-EC-1012 | Onyx <i>E. coli</i> Genome Engineering Kit – INSC1003 [8001-10000 Designs] |
| GEN-EC-1019 | Onyx <i>E. coli</i> Genome Engineering Kit – [100-1000 Designs]            |
| GEN-EC-1020 | Onyx <i>E. coli</i> Genome Engineering Kit – [1001-2000 Designs]           |
| GEN-EC-1021 | Onyx <i>E. coli</i> Genome Engineering Kit – [2001-4000 Designs]           |
| GEN-EC-1022 | Onyx <i>E. coli</i> Genome Engineering Kit – [4001-6000 Designs]           |
| GEN-EC-1023 | Onyx <i>E. coli</i> Genome Engineering Kit – [6001-8000 Designs]           |
| GEN-EC-1024 | Onyx <i>E. coli</i> Genome Engineering Kit – [8001-10000 Designs]          |

## ASSAYS

| Catalog #   | Name   |
|-------------|--|
| EAS-ON-1001 | Onyx Barcode Diversity Assay – 4 Samples             |
| EAS-ON-1002 | Onyx Barcode Diversity Assay – 48 Samples            |
| EAS-ON-1005 | Onyx Edit Identification Assay (WGS) – 24 Samples    |
| EAS-ON-1006 | Onyx Edit Identification Assay Adapters – 24 Samples |
| EAS-ON-1007 | Onyx Edit Identification Assay Adapters – 96 Samples |

### INSCRIPTA.COM

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### Boulder

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Boulder, CO 80301

### Pleasanton

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Pleasanton, CA 94588

### San Diego

5764 Pacific Center Blvd  
San Diego, CA 92121

### Copenhagen Bio Science Park

Tagensvej 22  
2200 Copenhagen N, Denmark