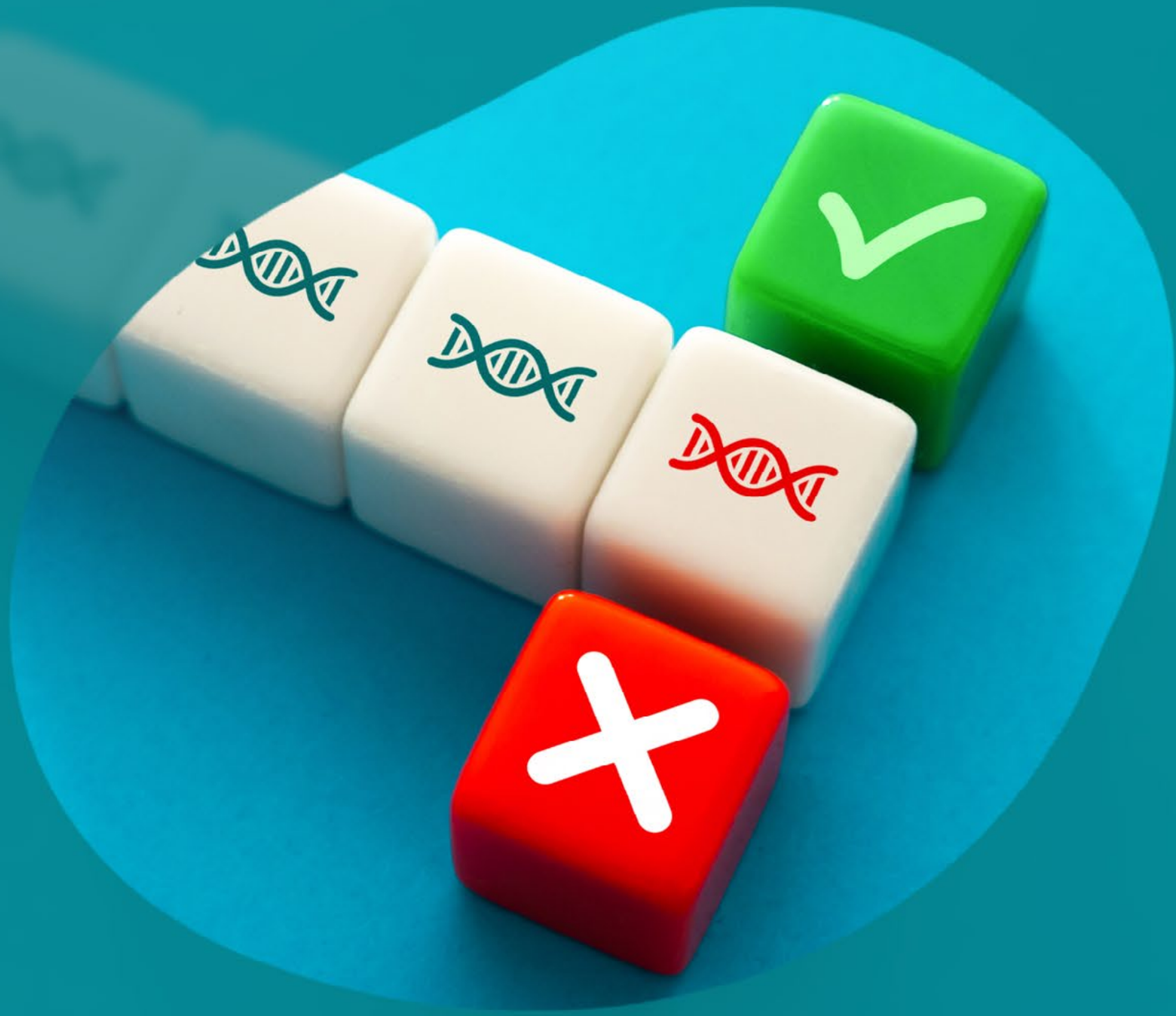
Identify targets others miss.



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Pooled functional genomic screening solutions and services

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- FGS overview
- FGS applications
- FGS approaches
- Choosing the right tool
- Pooled workflow challenges
- Pooled workflow read out
- FGS services
- Contact us

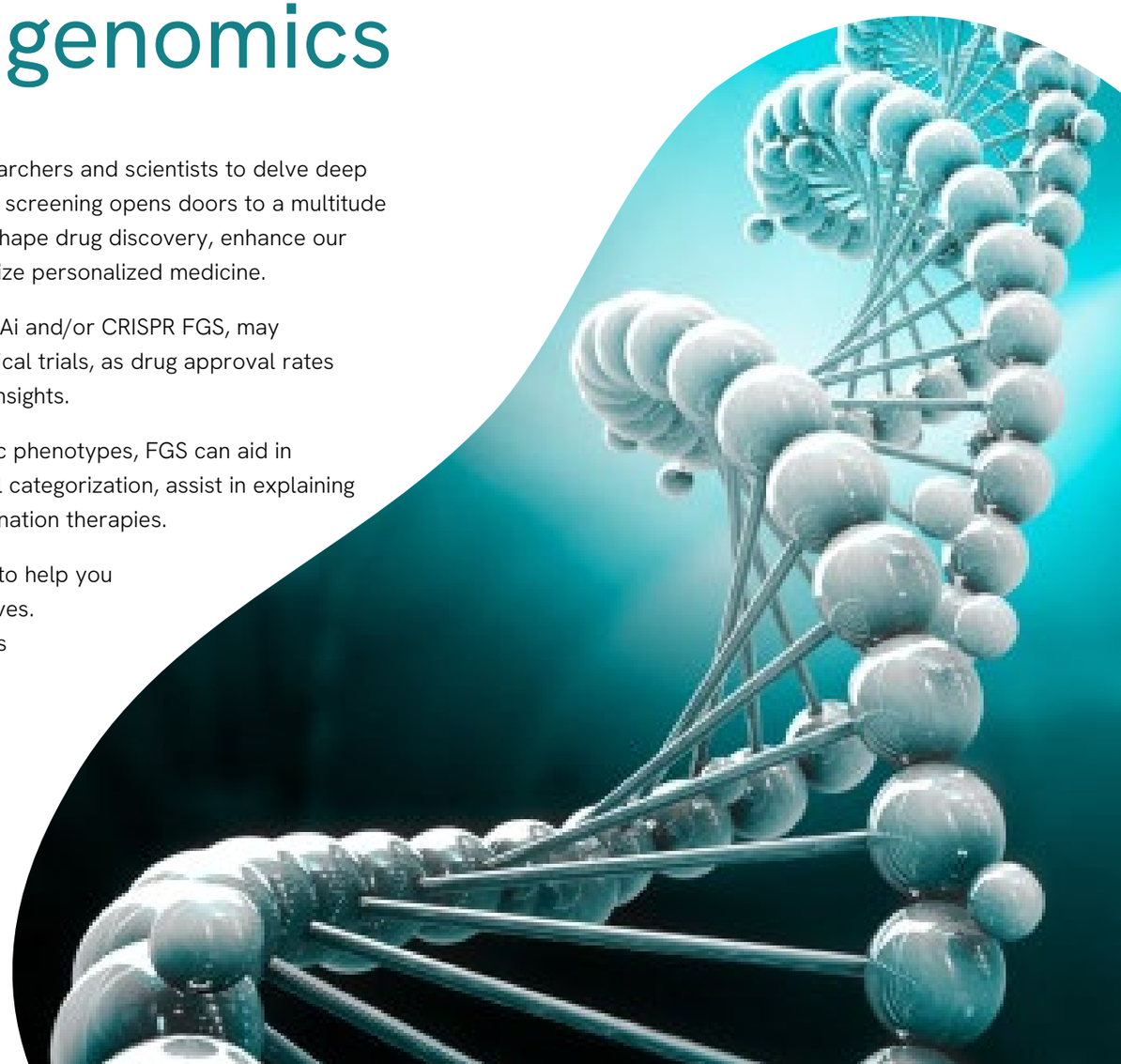
A dynamic, transformative approach to genomics

Functional genomic screening (FGS) empowers researchers and scientists to delve deep into the intricate world of genomics. This method of screening opens doors to a multitude of applications, each with its unique potential to reshape drug discovery, enhance our understanding of biological systems, and revolutionize personalized medicine.

Performing genetic profiling on drug targets with RNAi and/or CRISPR FGS, may potentially enhance the likelihood of successful clinical trials, as drug approval rates may see improvement when supported by genetic insights.

Through systematic analysis linking genes to specific phenotypes, FGS can aid in discovering novel gene targets, facilitating individual categorization, assist in explaining mechanism of action, and revealing potential combination therapies.

We offer a range of tailored services and solutions to help you customize your screenings to your research objectives. Get ready to discover the power of genomic insights that could take your research to the next level.



revvity

- FGS overview
- FGS applications
- FGS approaches
- Choosing the right tool
- Pooled workflow challenges
- Pooled workflow read out
- FGS services
- Contact us

Multiple applications for infinite discoveries

Explore how FGS may enhance drug discovery pipelines. Collectively, these applications lead to groundbreaking insights and innovative therapies that could help realize a brighter future in healthcare.

Basic research

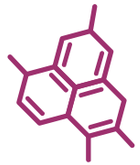
FGS may help uncover novel genes, pathways, and cellular processes that may assist in expanding our understanding of biology.

Target discovery

New promising targets may be identified by assessing gene function and relevance with large-scale loss- or gain-of-function screens.

Target validation

Potential drug targets may be confirmed whether you're testing the role of specific genes in different cell models or using RNAi and CRISPR orthogonal methods.



Lead identification

The search for potential drug candidates may be accelerated when you understand their genetic interactions.

Lead optimization

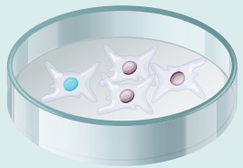
Help fine-tune drug candidates using better *in vitro* and *in vivo* models.

- FGS overview
- FGS applications
- FGS approaches
- Choosing the right tool
- Pooled workflow challenges
- Pooled workflow read out
- FGS services
- Contact us

Navigating FGS

When choosing a screening approach, consider your research objectives and the scale of your screen. Explore the differences between pooled and arrayed methods to determine the right one for your research.

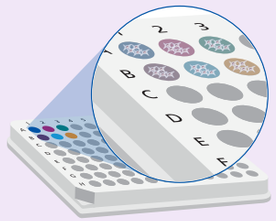
Pooled vs. arrayed screening



Pooled screening using CRISPR technology is a high-throughput approach that allows researchers to simultaneously target multiple genes within a cell population. In this method, a diverse library of CRISPR guide RNAs (gRNAs) is introduced into a cell population. The gRNAs guide the CRISPR system to specific DNA sequences, resulting in the knockout or modulation of target genes.

Pooled screening can help with:

- Identifying essential genes
- Uncovering gene interactions
- Understanding complex biological pathways
- Conducting large-scale functional genomics research



Arrayed screening is a focused approach to CRISPR-based gene regulation. In this method, individual gRNAs are placed in separate wells or positions within microplates, creating an array. Each well or position corresponds to a specific gene target.

Arrayed screening can help with:

- Investigating the effects of altering individual genes
- Conducting detailed reserach of gene function and target validation
- Exploring the specific impact of each gene on cellular processes
- Researching a limited number of genes in-depth using multiplexed readouts
- Research complex models like organoids and co-cultures

View our arrayed screening solutions and services brochure.

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- FGS overview
- FGS applications
- FGS approaches
- Choosing the right tool
- Pooled workflow challenges
- Pooled workflow read out
- FGS services
- Contact us

Choosing the right gene editing platform

Gene expression can be regulated using either RNAi or CRISPR technology. RNAi represses gene expression at the mRNA level, while CRISPR works at the DNA level and can permanently knockout, modulate, or knock-in genes.

Which one is best for your unique research? Sometimes both. In many ways, they are complementary technologies and using them synergistically can lead to superior results.

	RNAi	CRISPR
Definition	Gene silencing	Gene editing
Benefits	▪ Easy-to-use, one-step protocol ▪ Essential genes can be researched ▪ Reversible — temporary loss-of-function research	▪ Higher editing efficiencies ▪ Different formats available: CRISPRko, CRISPRi, CRISPRa ▪ Fewer off-target effects
Drawbacks	▪ Off-target effects ▪ Shorter assay window ▪ Incomplete silencing	▪ Cas9 and sgRNA needed — often a two-step approach ▪ Lethality when researching essential genes

- FGS overview
- FGS applications
- FGS approaches
- Choosing the right tool
- Pooled workflow challenges
- Pooled workflow read out
- FGS services
- Contact us

A workflow that works for you

Pooled screening is a powerful and versatile approach to FGS, offering distinct advantages in various research contexts. Consider leveraging pooled screening when your research goals include:

Detecting genes involved in sensitivity or resistance to a potential therapeutic candidate

Pooled screening may be preferable for identifying genes that play a crucial role in determining a cell's response to a potential therapeutic candidate. By modulating a diverse set of genes in a population, researchers can pinpoint those involved in sensitivity or resistance to a potential therapeutic candidate, paving the way for more effective drug development.

Uncovering genes involved in synthetic lethality

When the combination of two gene alterations results in cell death, synthetic lethality is a key concept in cancer research and targeted therapy research. Pooled screening may help enable the systematic exploration of gene interactions, making it an invaluable tool for discovering synthetic lethal gene pairs.

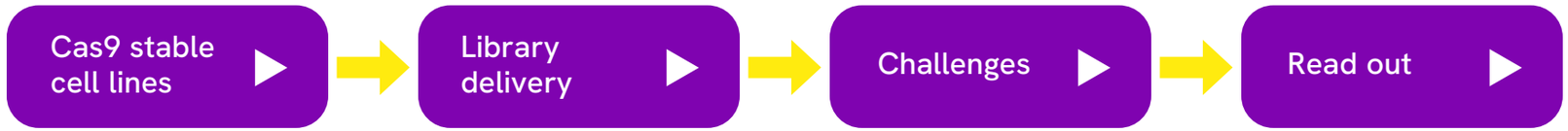
Enabling individual categorization

Understanding the genetic factors that influence individual response to treatments is paramount. Pooled screening may help categorize individuals based on their genetic profiles.

Addressing diverse biological questions

Pooled screening is not limited to a single application; it can be employed to address a wide array of biological questions. Whether you're looking for mechanistic insights into the action of drugs, toxins, and pathogens or aiming to define gene essentiality in a particular context, pooled screening may help provide a high-throughput and budget-tailored means to exploring diverse facets of genomics.

Click each step to read more.



- FGS overview
- FGS applications
- FGS approaches
- Choosing the right tool
- Pooled workflow challenges
- Pooled workflow read out
- FGS services
- Contact us

Step 1: choose or create a Cas9 stable cell line

Back to workflow

When using CRISPR technology for gene editing or modulation, you first need a Cas9 nuclease. This enzyme is responsible for generating the cut in the dsDNA.

Before initiating the pooled screening experiment, you must decide whether to use an existing Cas9-expressing stable cell line or create one specifically for your research. This step involves engineering the cells to stably express the Cas9 protein. Once you have a stable Cas9-expressing cell line, you can move on to the next step of the workflow.

Read more

Lentiviral Cas9 nucleases
For a pooled screen, lentiviral Cas9 nucleases are recommended with an optional fluorescent marker for optimization or enrichment.

Read more

Stably expressing Cas9 cell lines
Shorten the workflow by starting with stably expressing Cas9 cell lines. Choose from a range of popular cell line backgrounds.

Read more

Inducible Cas9 nuclease
Use our inducible Cas9 nuclease when temporal control over the expression of Cas9 is required.

Read more

CRISPRmod systems
Both CRISPR activation (CRISPRa) and CRISPR interference (CRISPRi) use a deactivated Cas9 construct to leverage the specificity of the CRISPR system without the cut.

Read more

- FGS overview
- FGS applications
- FGS approaches
- Choosing the right tool
- Pooled workflow challenges
- Pooled workflow read out
- FGS services
- Contact us

Step 2: library delivery

Help enhance your chances of success with pooled lentiviral libraries — reliable pools, complete analysis tools, and tested protocols for bulk sequencing read outs.

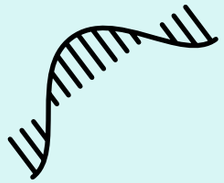
CRISPR knockout

Read more

CRISPR modulation

Read more

RNA interference



Read more

Back to workflow

- FGS overview
- FGS applications
- FGS approaches
- Choosing the right tool
- Pooled workflow challenges
- Pooled workflow read out
- FGS services
- Contact us

Close window

CRISPR knockout

In a pooled CRISPR screen, hundreds and even thousands of genes are knocked out using a lentiviral sgRNA screening library. Though lentiviral transduction requires appropriate safety measures, this ensures that after proliferation, successive generations of cells carry the lentiviral guide RNA expression cassette. The goal is to infect each cell with only one virion, so the multiplicity of infection (MOI) is important to consider. Since cutting efficiency varies among different targets, we offer libraries containing 5-10 sgRNAs per gene to enhance your confidence in achieving successful hits. Our guides are algorithm-designed to assist in amplifying functionality and specificity.

See our predefined gRNA screening libraries

Discover our cherry pick clone libraries

View our custom design lentiviral guide RNAs

- FGS overview
- FGS applications
- FGS approaches
- Choosing the right tool
- Pooled workflow challenges
- Pooled workflow read out
- FGS services
- Contact us

Close window

CRISPR modulation

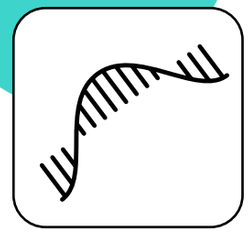
Before embarking on your FGS journey, carefully consider additional CRISPR systems such as CRISPRi and CRISPRa. These innovative approaches allow you to control gene expression without entirely knocking out essential genes. It's a strategic decision which may enable you to uncover the nuanced contributions of genes to your biological system, and support the deeper insights and more tailored discoveries.

Dive deeper into CRISPRi lentiviral sgRNA

Discover more about CRISPRa lentiviral sgRNA

- FGS overview
- FGS applications
- FGS approaches
- Choosing the right tool
- Pooled workflow challenges
- Pooled workflow read out
- FGS services
- Contact us

Close window



RNA interference

RNA interference (RNAi) remains one of the simplest yet highly effective methods for target gene knockdown in loss-of-function experiments. Dharmacon™ Reagents is a pioneer in developing novel siRNA, shRNA, and microRNA technologies for nearly 30 years, offering a broad portfolio of trusted synthetic and expressed reagents. With Dharmacon™ Reagents, you gain access to highly specific and efficient gene silencing tools, which could help enhance the reliability of your research. For your pooled screening approach, choose from our shRNA and miRNA libraries.

Explore our custom shRNA libraries

Browse our smartvector shRNA libraries

View our inducible shRNA libraries

Read about microRNA (miRNA)

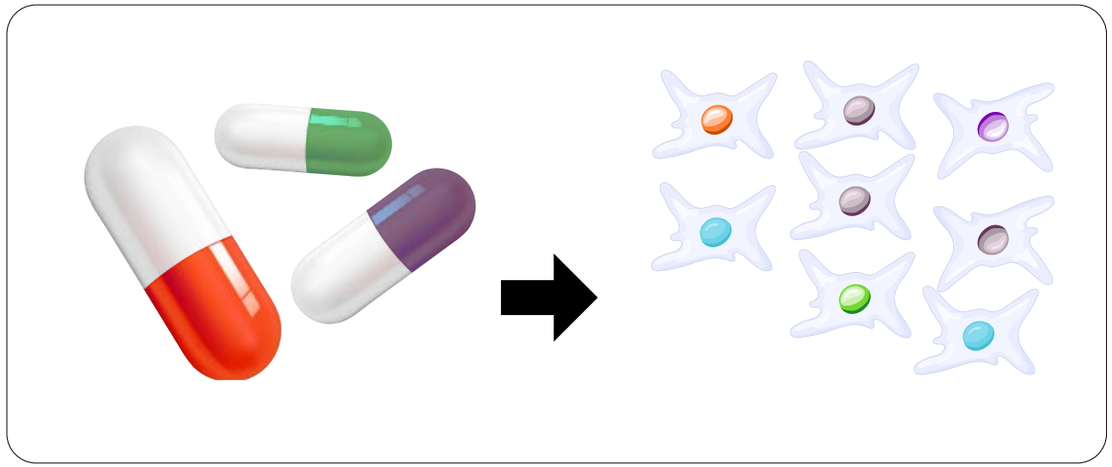
Back to workflow

Step 3: challenges

- FGS overview
- FGS applications
- FGS approaches
- Choosing the right tool
- Pooled workflow challenges
- Pooled workflow read out
- FGS services
- Contact us

With the genetic perturbations in place, it's time to subject your cell pool to a challenge. This includes assessing cell survival or proliferation and, in certain cases, exposing the cells to specific drugs, radiation, or pathogens.

The challenge step is a critical moment in the screening workflow. You can observe how the genetic modifications influence the cellular response. It's an opportunity to uncover genes essential for processes like cell growth, survival, or drug sensitivity.



Cell survival/proliferation or optional drug treatment in cell pool

- FGS overview
- FGS applications
- FGS approaches
- Choosing the right tool
- Pooled workflow challenges
- Pooled workflow read out
- FGS services
- Contact us

Back to workflow

Step 4: readout

The final step of your FGS workflow is the read-out phase. Here, advanced next-generation sequencing (NGS) techniques come into play. Sequencing the genetic material from your challenged cell pool may assist you in gaining invaluable insights into which guides have been depleted or enriched.

This critical last step provides the data needed to identify the genes involved in your biological pathway, shedding light on gene function, interactions, and potential therapeutic targets.

Advanced sequencing techniques

Bulk RNA sequencing

Offering a high-throughput, comprehensive identification of guide depletion and enrichment, this process may enable you to uncover the most subtle shifts in your cellular model.

See readout

Single cell sequencing

This technique may assist you in dissecting the heterogeneous responses within your cell population, potentially revealing unique cell behavior and gene expression patterns.

See readout

Imaging-based sequencing

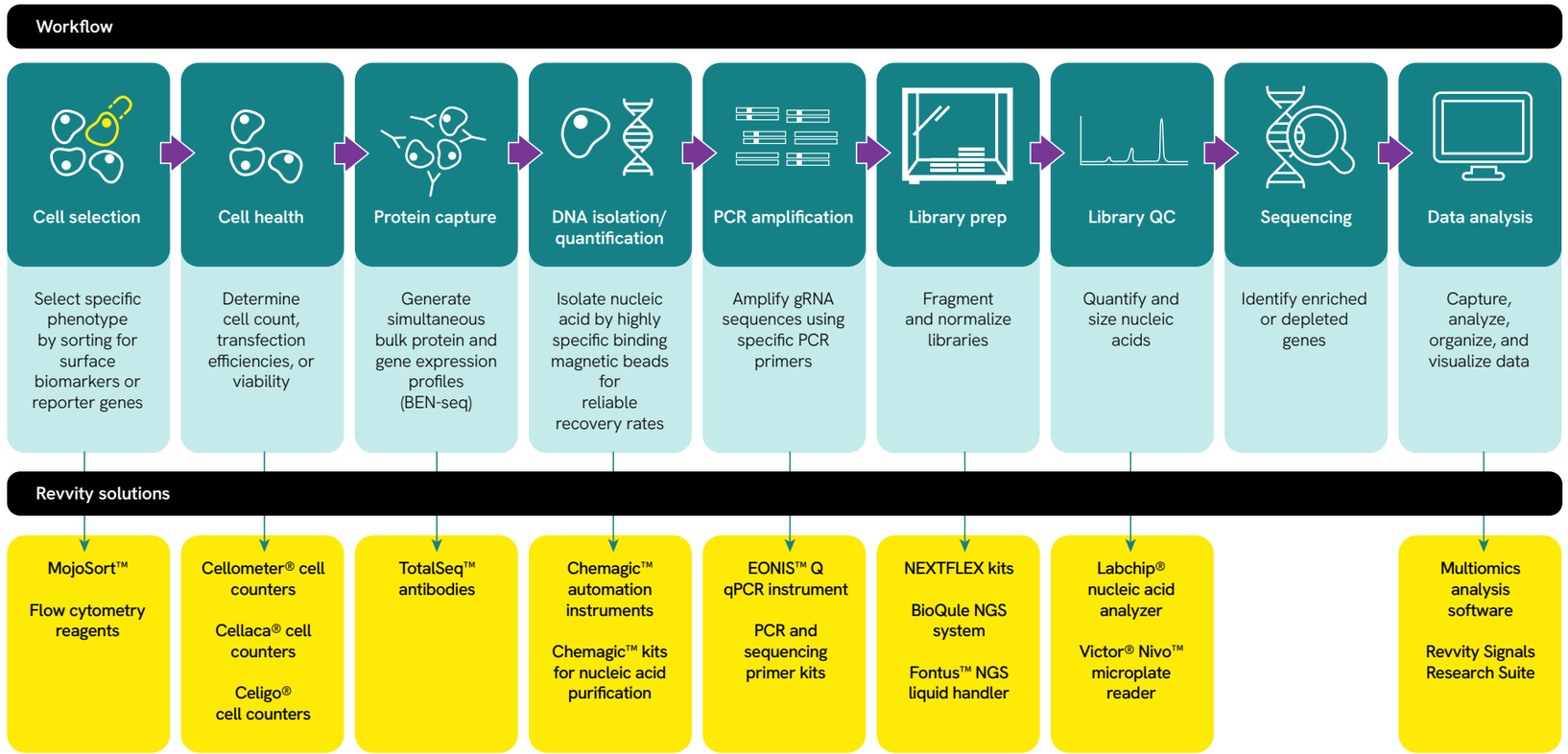
Visualize gene expression within the context of tissue and cell structures for a multidimensional understanding of gene activity.

See readout

- FGS overview
- FGS applications
- FGS approaches
- Choosing the right tool
- Pooled workflow challenges
- Pooled workflow read out
- FGS services
- Contact us

Close window

Bulk RNA sequencing



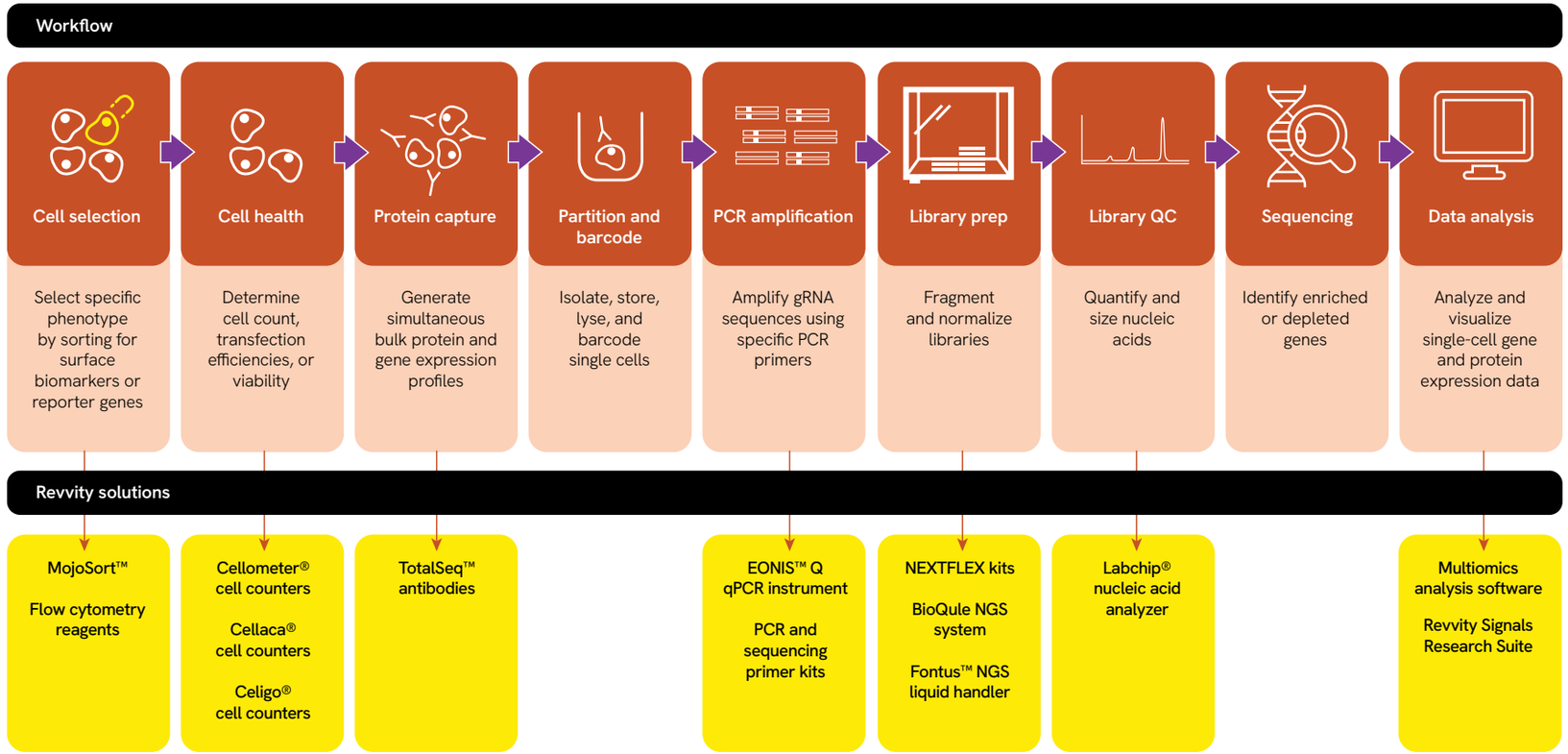
Solutions for advanced sequencing

revvity

- FGS overview
- FGS applications
- FGS approaches
- Choosing the right tool
- Pooled workflow challenges
- Pooled workflow read out
- FGS services
- Contact us

Close window

Single-cell RNA sequencing



Solutions for advanced sequencing

- FGS overview
- FGS applications
- FGS approaches
- Choosing the right tool
- Pooled workflow challenges
- Pooled workflow read out
- FGS services
- Contact us

Close window

Image-based sequencing

Workflow

In situ chemistry

Select from various in situ chemistries for single-modality and highly multiplexed imaging analysis of cell-surface proteins

Automation

Automate the workflow to help increase throughput

Imaging

Conduct in situ sgRNA sequencing using cyclical imaging

Data analytics

Capture, analyze, organize, and visualize data

Revvity solutions

Highly specific antibodies

IBEX antibodies

Automated liquid handlers, robotic arms, or fully integrated solutions

High-content automated imaging solutions

Revvity Signals Research Suite

Solutions for advanced sequencing

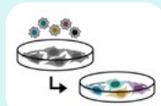
- FGS overview
- FGS applications
- FGS approaches
- Choosing the right tool
- Pooled workflow challenges
- Pooled workflow read out
- FGS services
- Contact us

United in advancing FGS

Outsourcing with our cutting-edge cell-based screening solutions can help you focus on other priorities, reduce obstacles, and accelerate the discovery of new therapeutics. From cell lines to primary or 3D cell cultures, Revvity's screening platform can offer pooled screens using CRISPR knockout, CRISPR activation, CRISPR inhibition, and Pin-point™ technologies. Our libraries can be used either alone or coupled with a variety of assay readouts.

Trust in the established expertise of our service team. Our success depends on your achievements. We're excited to help you enhance your research potential.

CRISPR screening, from target selection to individual categorization



Pooled CRISPR screening
CRISPRa, CRISPRi, CRISPRko, Dual Screening

Single-cell RNAseq-linked CRISPR screening

Pin-point™ base editing services

***In vivo* CRISPR screening**

Complex model screening
Immune cells, organoids, spheroids and primary cells

- FGS overview
- FGS applications
- FGS approaches
- Choosing the right tool
- Pooled workflow challenges
- Pooled workflow read out
- FGS services
- Contact us

Solutions for advanced sequencing

No matter which sequencing technique you're using — NGS, single cell, or in situ — we have the technologies to support your research.

Automation and liquid handling solutions
Flexible and customizable for your throughput needs

BioQule NGS system
For automating library prep for different throughput needs

Cellometer, Cellaca, and Celigo
Chip- or plate-based automatic cell counters for different application and throughput needs

Chemagic automation
Various instruments for automated nucleic acid isolation

Chemagic kits
Nucleic acid purification optimized for Chemagic instruments

EONIS Q qPCR instrument
PCR and sequencing primer kits compatible with Dharmacon pooled libraries

Flow cytometry reagents
Fluorophore-conjugated antibodies

Fontus NGS liquid handler
Automating library prep for various throughput needs

High-content imaging instruments
High-throughput automated imaging for quantitative multiparametric data at the single-cell level

IBEX technique
Antibodies for iterative imaging using photo bleaching

Labchip system
Capillary electrophoresis nucleic acid analyzer

MojoSort system
For magnetic cell separation

Multiomics analysis software
For TotalSeq data analysis

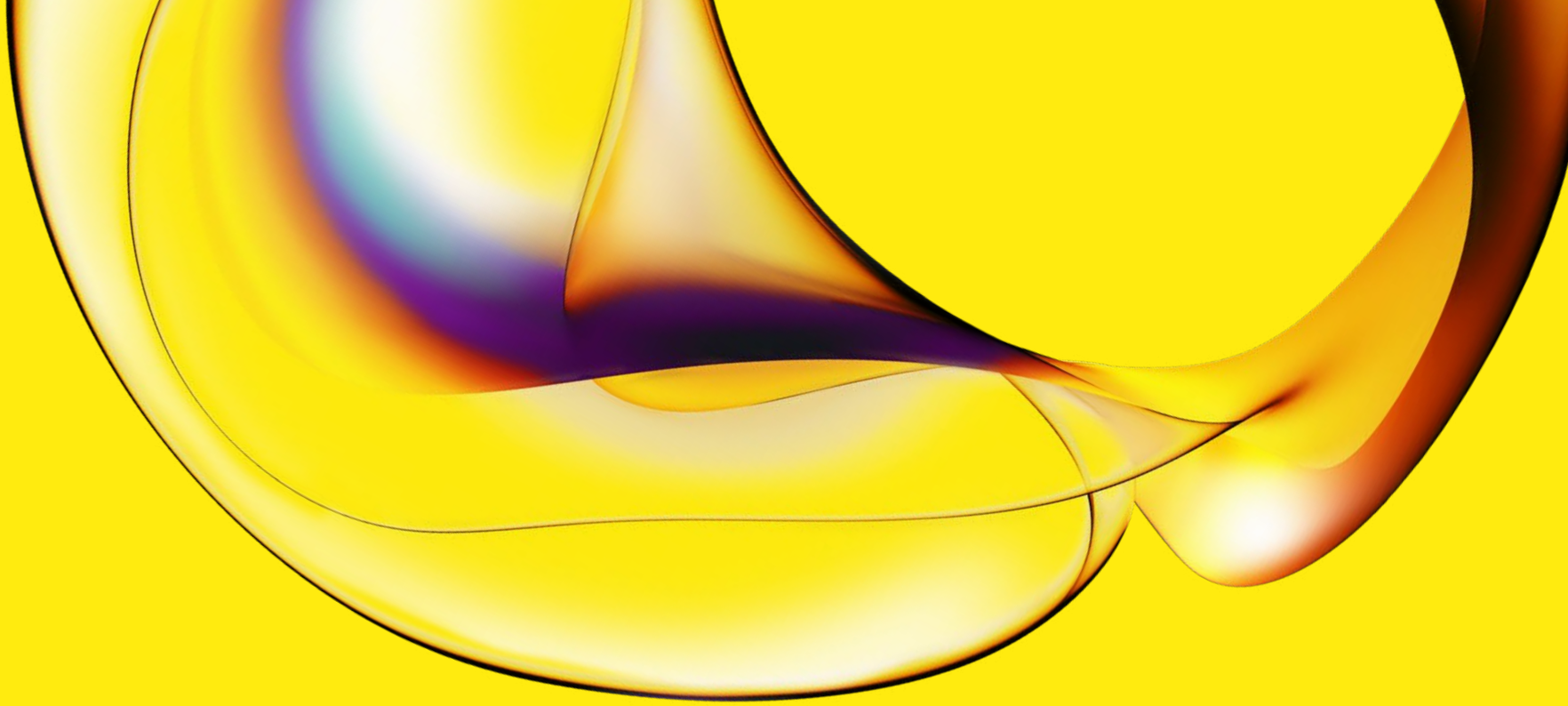
NEXTFLEX Rapid XP DNA-Seq kit or
NEXTFLEX Rapid Directional RNA-Seq kit 2.0
Your choices for whole genome sequencing

Revvity Signals Image Artist platform
Image data analysis and management system

Revvity Signals Research Suite
Scientific data management and workflow platform

TotalSeq reagents
Oligo-conjugated antibodies integrate seamlessly into single cell or bulk sequencing workflows

Victor Nivo microplate reader
Multimode plate reader for high-throughput DNA quantification



www.revvity.com

Revvity, Inc.
940 Winter Street
Waltham, MA 02451 USA
www.revvity.com

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