CRISPR QC Analytics Platform: Precisión, eficacia y control de calidad en el editado génico.

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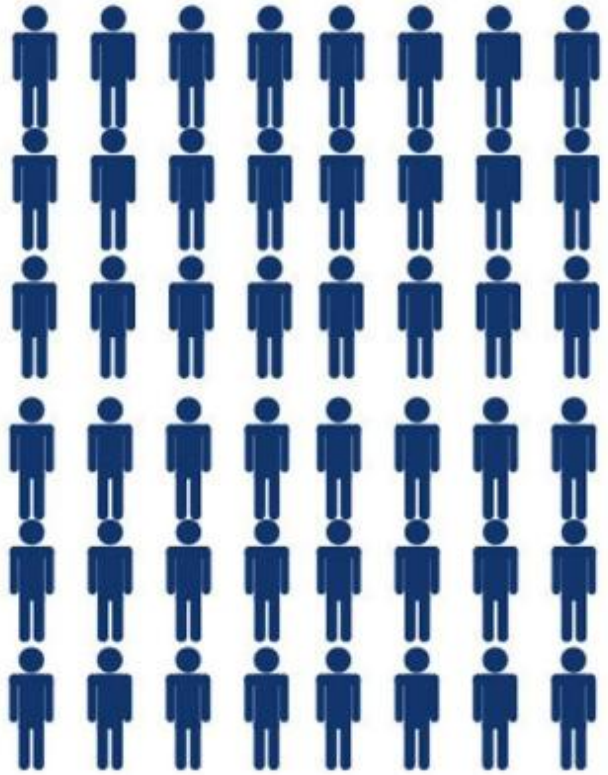
Feeding the World in a Sustainable Manner



WORLD'S POPULATION

11.0 Billion

by 2050

70%

beyond today's level

FOOD DEMAND SURGING

La presión actual sobre la agricultura representa una amenaza importante para la producción de cultivos y la soberanía biotecnológica y agroalimentaria.

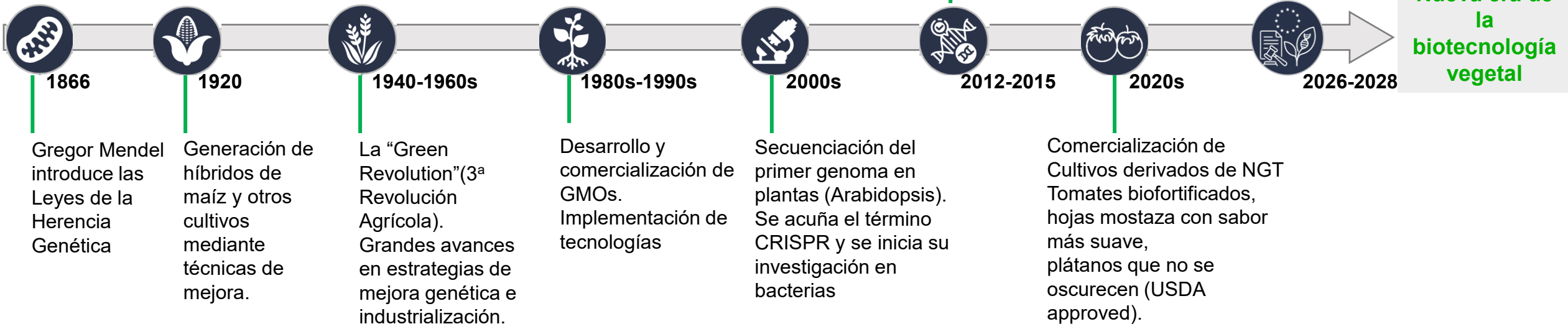
Esta situación nos está obligando a encontrar con urgencia soluciones biotecnológicas eficientes y respetuosas con el medio ambiente.

Las aproximaciones NGT basadas en CRISPR están allanando el camino para acelerar la ingeniería de cultivos y la agricultura de precisión

CRISPR

THE DEFINING TECHNOLOGY OF THE 21st CENTURY

Los grandes puntos de inflexión en la agricultura durante los últimos 150 años han sido impulsados por la genética y la ingeniería genómica.
CRISPR representa el próximo gran salto en la industria.



Las Nuevas Tecnologías Genómicas en Agricultura no están exentas de desafíos.

Diversity in Species and Cultivars

- Variety in crops species with: corn, tomato, strawberry, etc.
- Variety in cultivars

Challenging Polyploids

- Major crops are polyploids

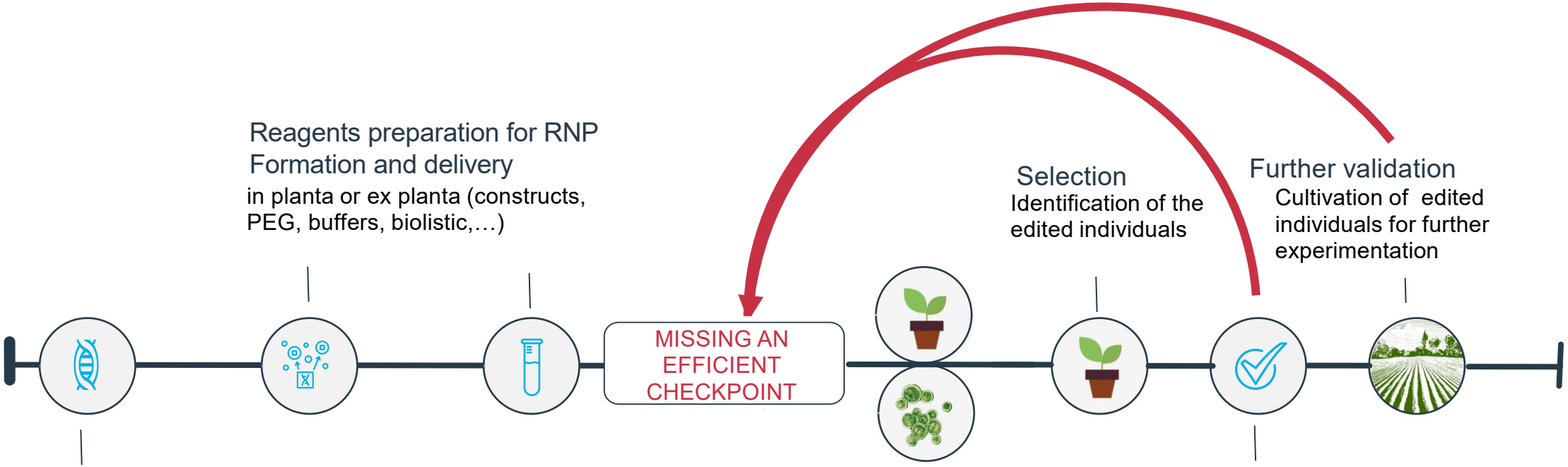
Varied Editing Methods

- Varied editing methods make it difficult to determine which are most efficient and effective for use

Lack of Speed in R&D and Translational approaches

- Loss of money, resources, due to lag in bringing products to market caused by editing inefficiencies

CRISPR Editing Workflow



Why CRISPR Development Fails

Quality requires measuring the source of failure so it can be corrected

Delivery is difficult to measure

- Intracellular delivery is rarely measured directly
- Uptake varies by cell type and modality
- Population averages hide delivery heterogeneity

“Dosing” windows are undefined

- Effective dose is determined empirically
- Delivered RNP concentration is unknown
- Higher dose increases off-target risk

In/Del Scores hide sources of variation

- % indels conflate delivery and activity
- Similar scores mask different mechanisms
- Bulk metrics obscure heterogeneous outcomes

Off-targets can be detected, but not fixed

- Sites identified, but risk not quantified
- Assessed late in development
- “Undetected” does not mean safe/accurate

Data Is Complex to Interpret

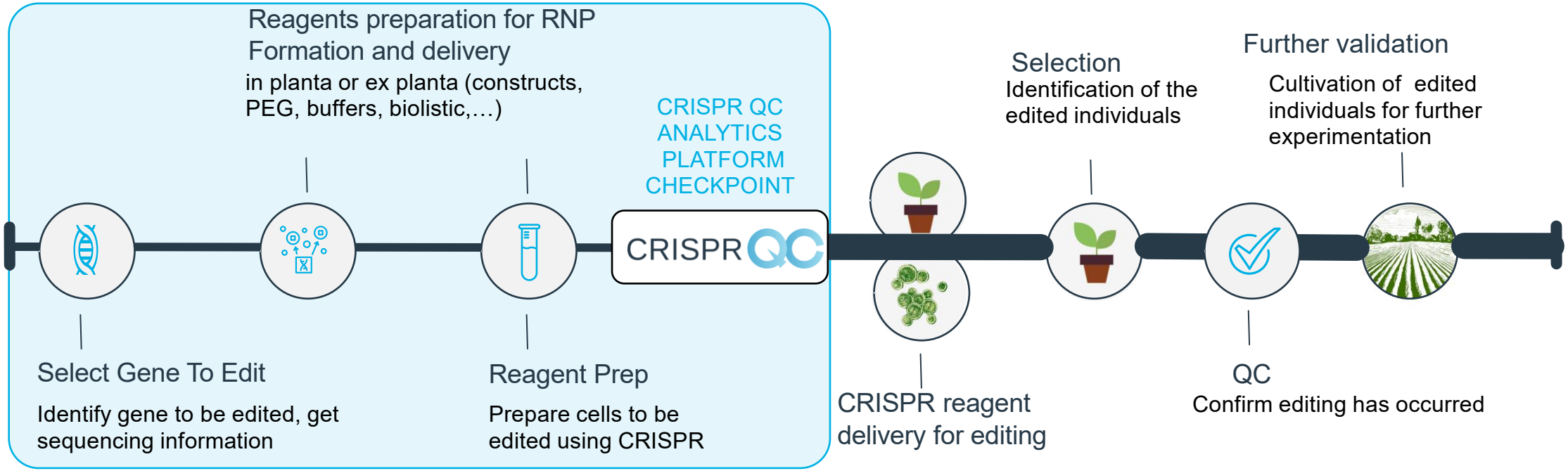
- Delivery and biology are tightly coupled
- Failure modes are difficult to isolate
- Results depend on assay and thresholds

Scale-up breaks what worked in Lab

- Delivery efficiency changes with scale
- Lot-to-lot, source, Cas-type differences are hard to detect
- Lab-optimized processes fail to translate

Optimal CRISPR Editing Workflow

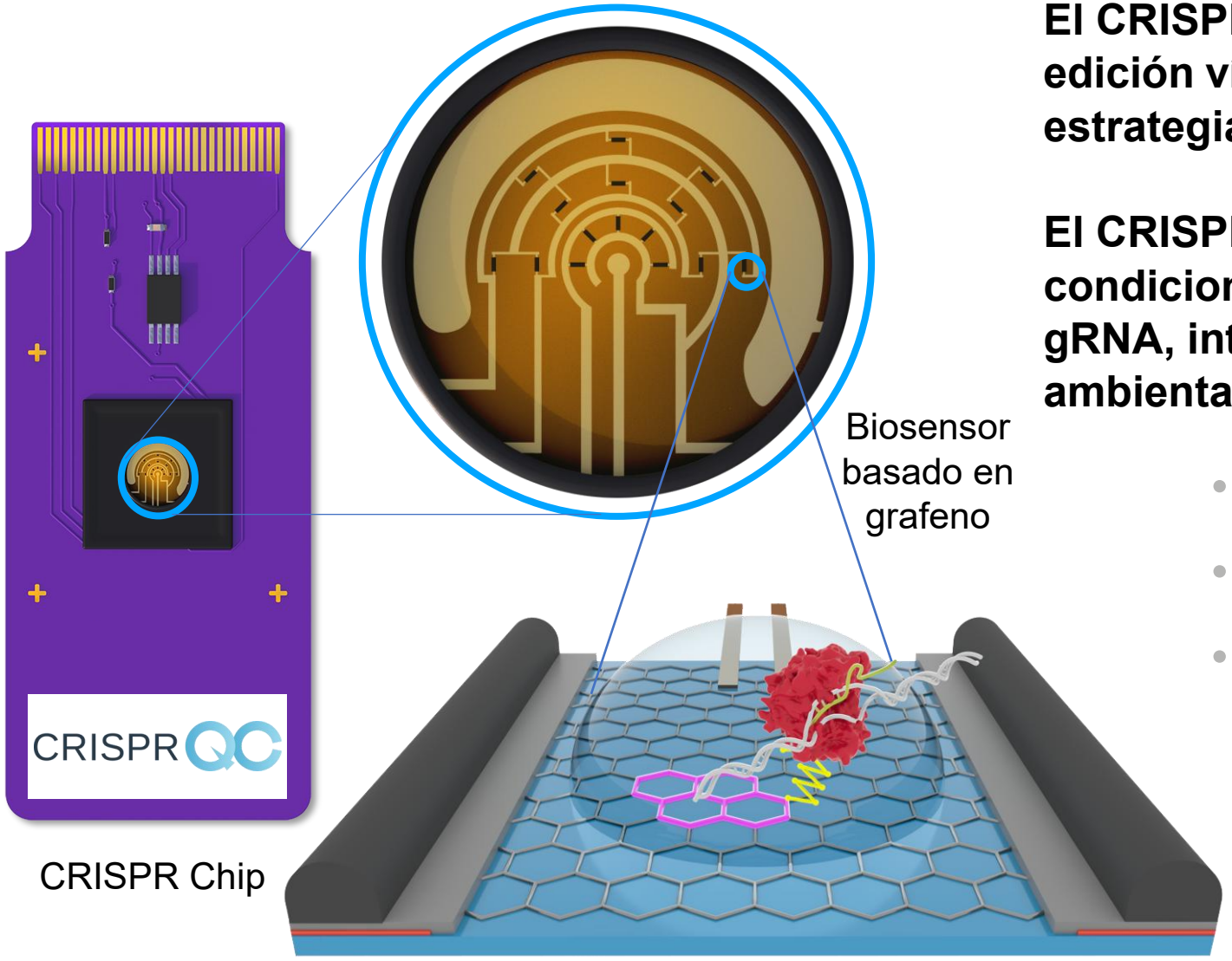
Optimized, more efficient gene editing process



CRISPR QC
REIMAGINING CRISPR EDITING

- Fewer repeats
- Time & money savinngs

CRISPR-CHIP, la herramienta

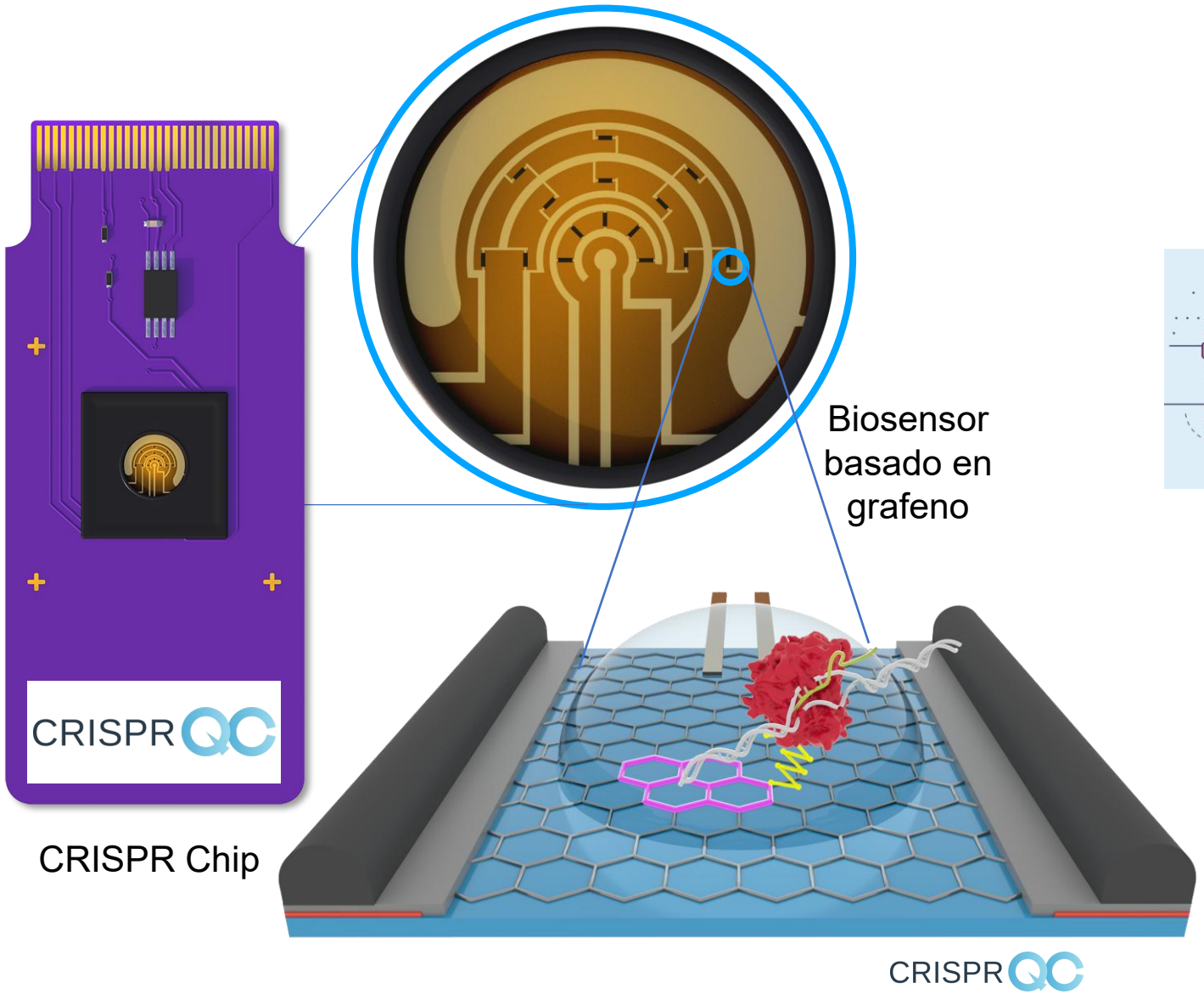


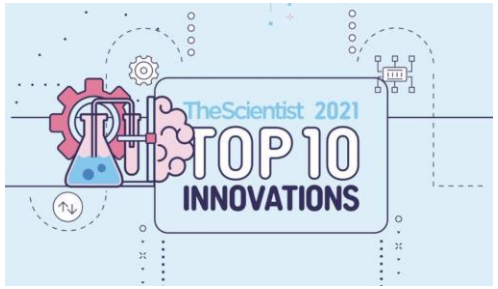
El CRISPR-Chip™ analiza varios elementos de la edición vía CRISPR y ayuda a diseñar la mejor estrategia de edición genómica.

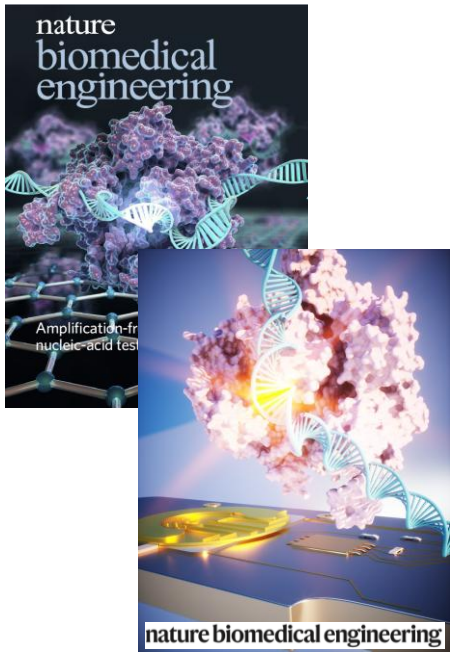
El CRISPR-Chip, permite identificar las condiciones óptimas de edición (calificación de gRNA, interrogación del complejo RNP, estabilidad ambiental, etc.) y agilizar sus flujos de trabajo.

- Matriz de micro-sensores organizados
- Datos por triplicado en cada medición
- Seguimiento y obtención de los datos en tiempo real

CRISPR-CHIP, nuestra herramienta



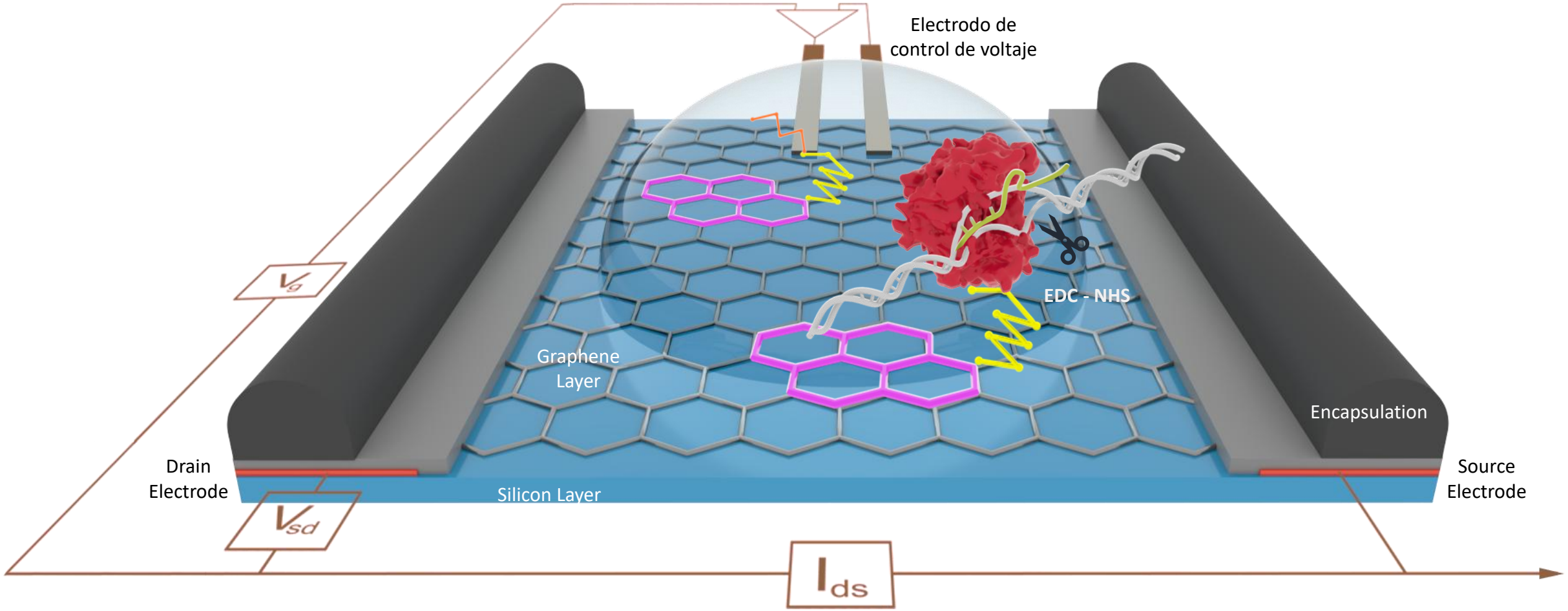




Nature BME (2019, 2021)-Front Cov

CRISPR-chip is now featured in museum of science, Dresden, Germany

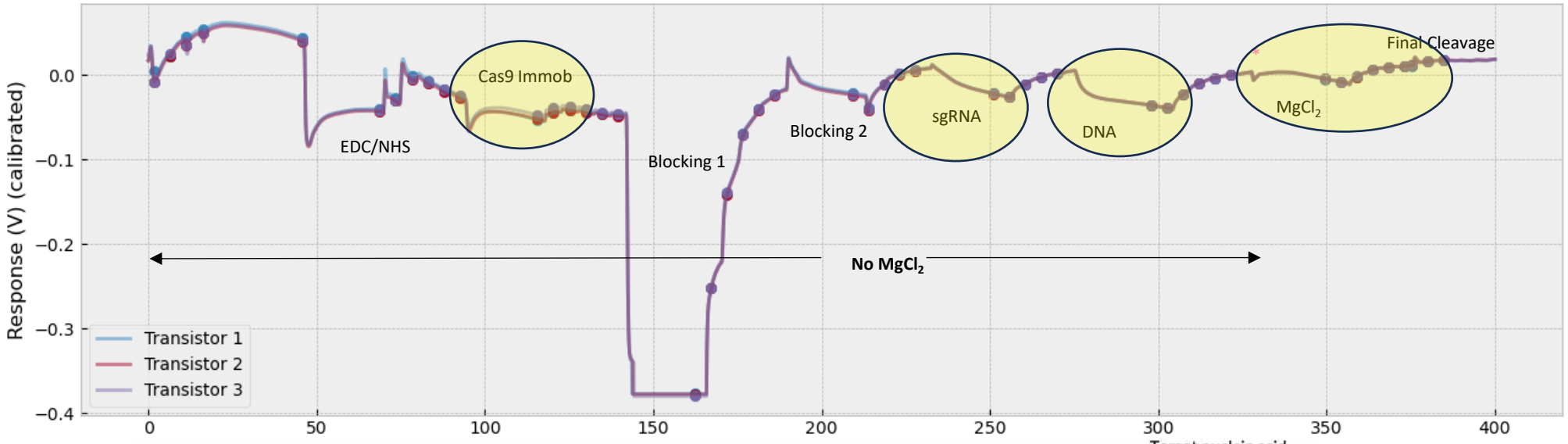
CRISPR COMPLETE – Monitorización de los pasos de la maquinaria CRISPR

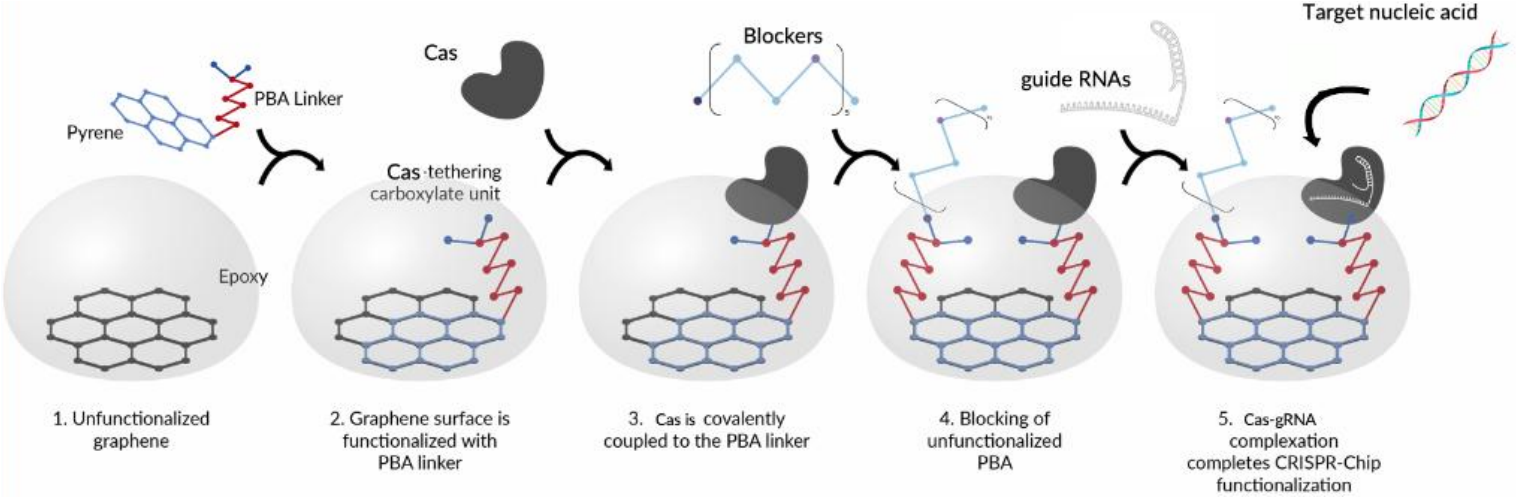


Sensitivity determined by optimized sensor design and operation parameter

CRISPR QC Data

The Genome Sensor™ by **CRISPR QC to reimaging CRISPR**





CRISPR QC

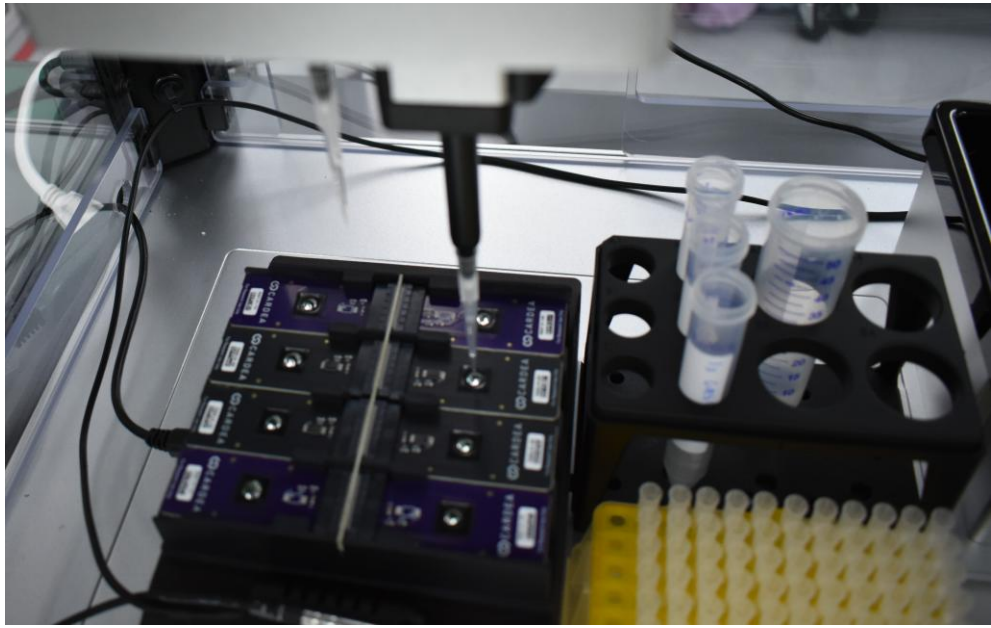
CRISPR QC Analytics Platform. Technology benefits.

- Sistema electrónico y en tiempo real:
  Detección de la señal a través de métodos electrónicos y analizar diferentes parámetros eliminando la necesidad de amplificación molecular y etiquetas.

- Medición directa de las señales derivadas de la acción e interacción Cas-gRNA-ácido nucleico.

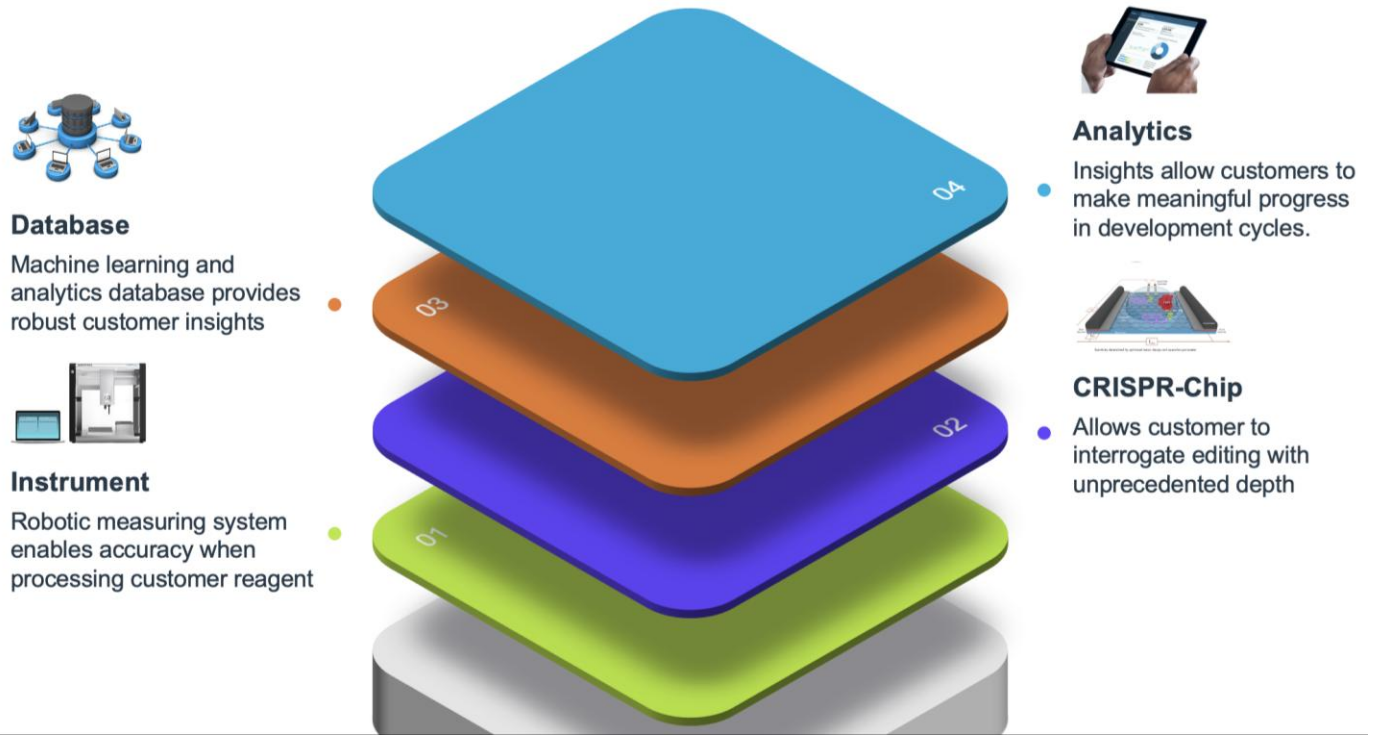
- Simulación de factores del entorno celular para entender el impacto en los resultados de edición.

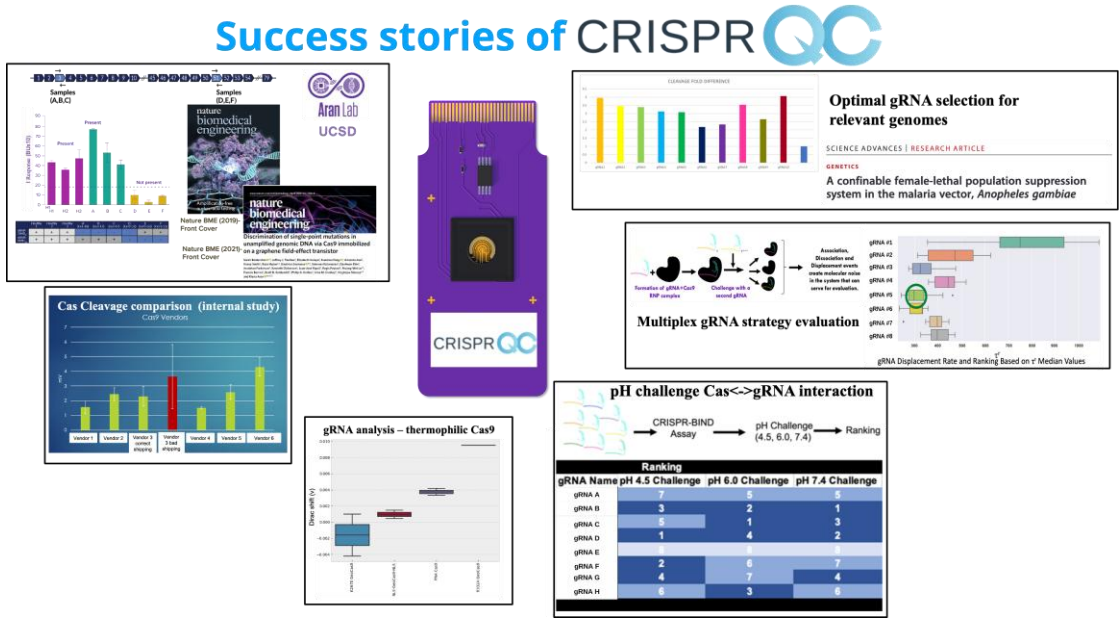
- Evaluación de puntos críticos para solucionar problemas y optimizar los resultados en la implementación de NGTs



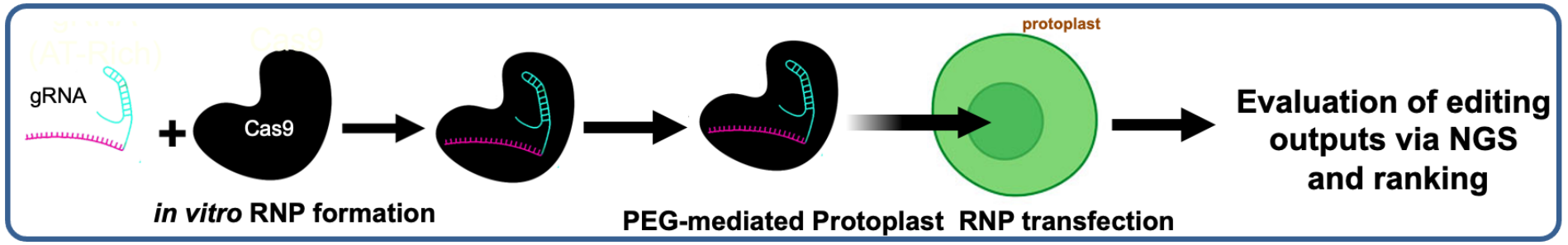
CRISPR QC

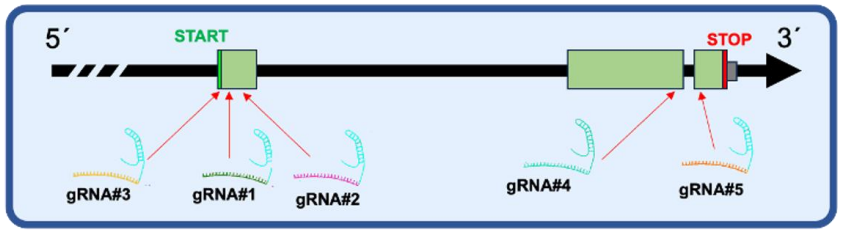
Ejemplos del uso de la Plataforma CRISPR QC





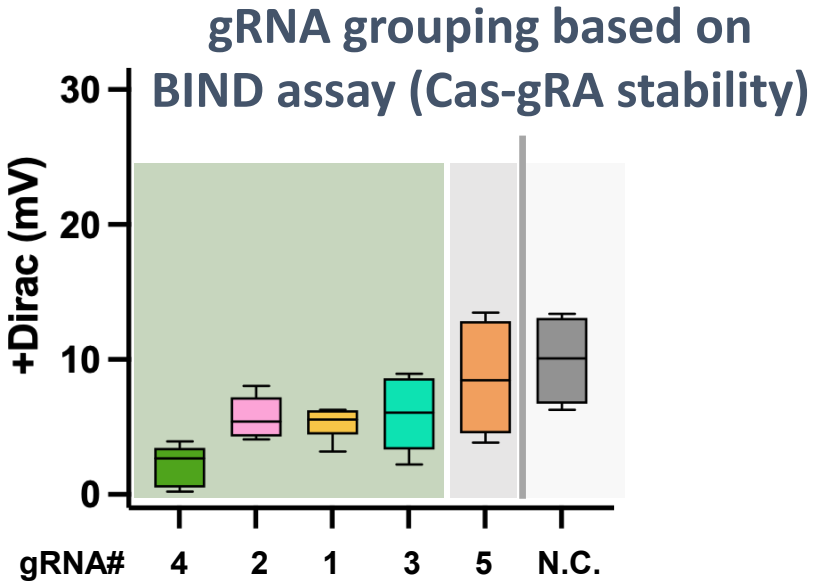
Transfección de protoplastos y resultados (Solanáceas)





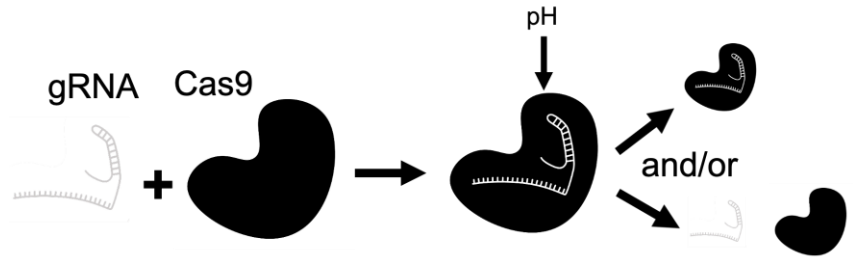
Table

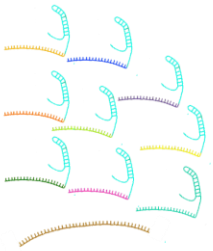
Locus	gRNA#	gRNA sequence	PAM	GC %	-4 nt from PAM	TOTAL EDITS
[illegible]	gRNA#4	[illegible]	AGG	45%	G	8175
[illegible]	gRNA#2	[illegible]	TGG	55%	G	1659
[illegible]	gRNA#1	[illegible]	GGG	50%	T	1477
[illegible]	gRNA#5	[illegible]	CGG	45%	T	421
[illegible]	gRNA#3	[illegible]	AGG	45%	A	11



- gRNA#5 behaves similarly as our negative control suggesting that stability of gRNA#5-RNP is compromised.
- Correlative results for gRNAs#1,2,3 and 4 show similar behavior being #4 the gRNA that can be considered the top in terms of RNP stability.

Cas9 RNP activity and stability are impacted by by environmental conditions (temperature, pH,…)





Collection of gRNA
(negative control)

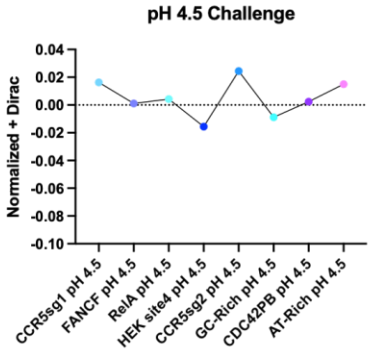
CRISPR-BIND Assay → pH Challenge (4.5, 6.0, 7.4) → Ranking

RNP response upon pH Challenge

	Ranking		
gRNA Name	pH 4.5 Challenge	pH 6.0 Challenge	pH 7.4 Challenge
CCR5_sg1	7	5	5
FANCF	3	2	1
RelA	5	1	3
HEK Site 4	1	4	2
CCR5_sg2	8	8	8
GC-Rich	2	6	7
CDC42BPB	4	7	4
AT-Rich	6	3	6

High Performer
Intermediate
Poor Performer

A)



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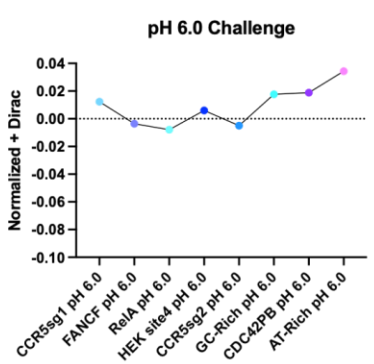

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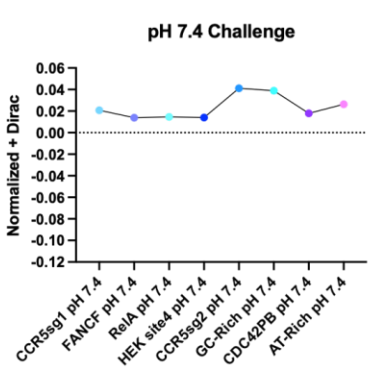
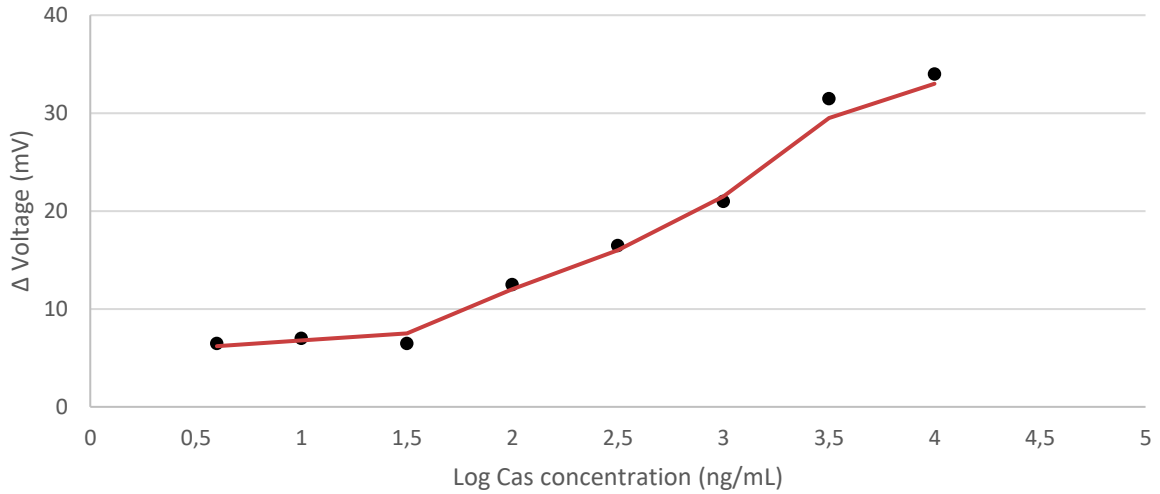


CRISPR QC

Application 1: Know Your True Delivered Cas-gRNA RNP abundance

- Measure absolute Cas abundance inside cells
- Separate delivery failure from editing failure
- Compare delivery modalities quantitatively
- Stop troubleshooting downstream biology prematurely

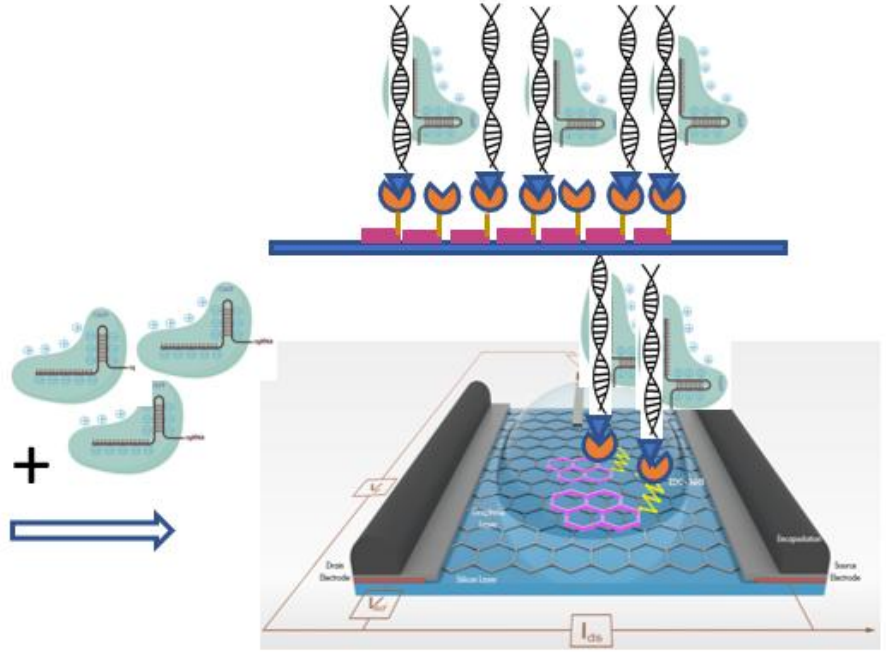
Quantitative detection of Cas protein in cell lysate *via anti-Cas antibody titration*

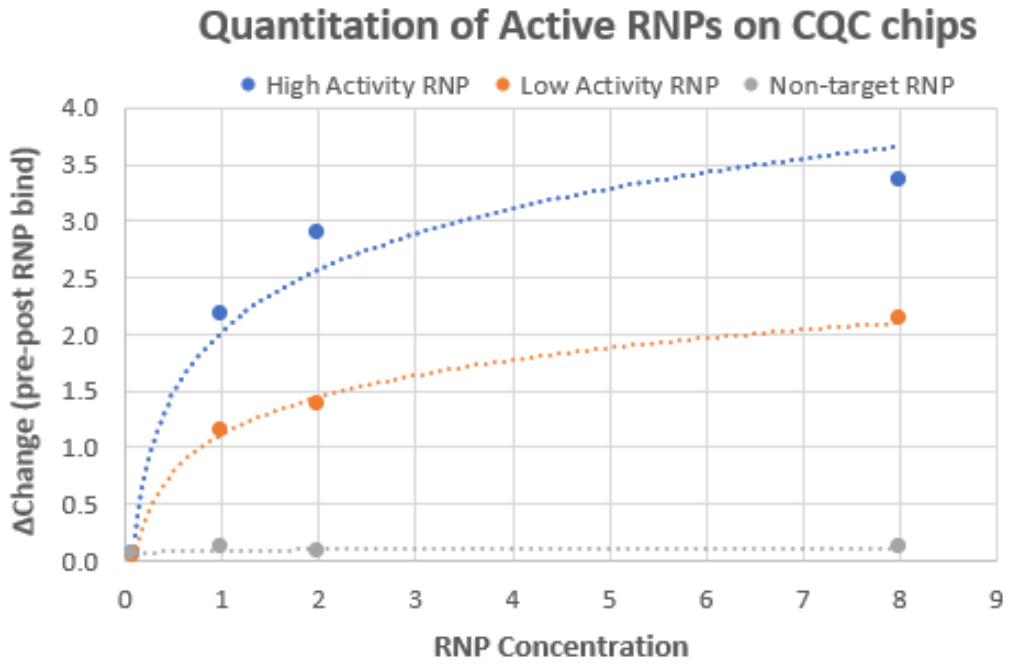


CRISPR QC

Application 2: Measure Functional Editing Efficiency

- Quantifies active, cleavage-capable RNP
- Distinguishes intact RNP from inactive cargo
- Supports reagent qualification and scale-up decisions
- Identifies reagent-driven failure early

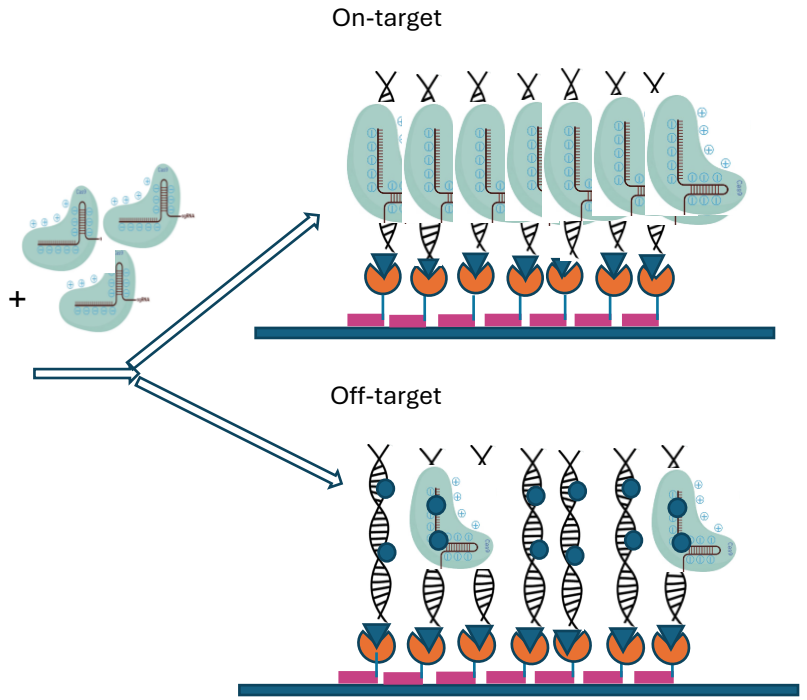


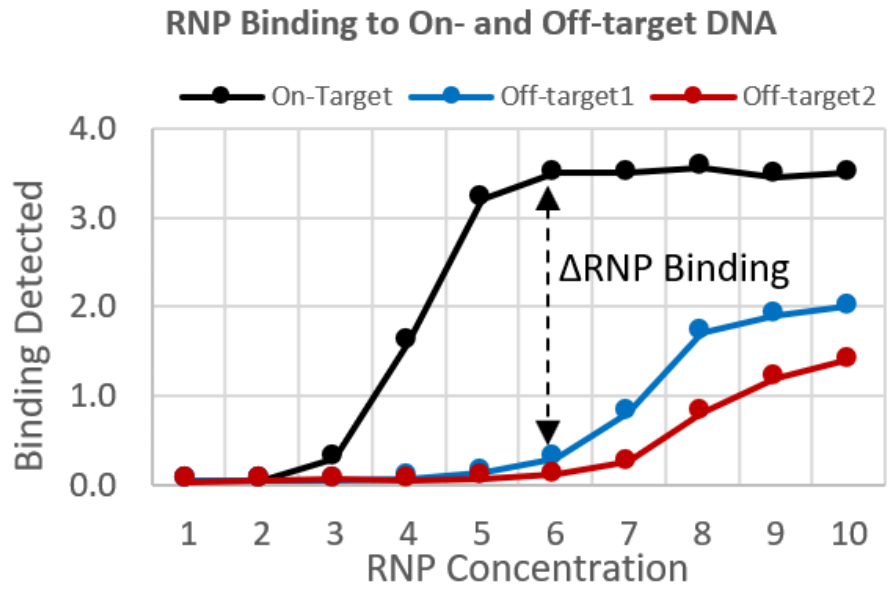


CRISPR QC

Application 3: Quantify Off-Target Risk, Not Just Detect It

- Off-target propensity scales with delivered dose
- Quantitative curves reveal safety ceilings
- Enables dose selection before studies
- Supports rational gRNA and delivery optimization



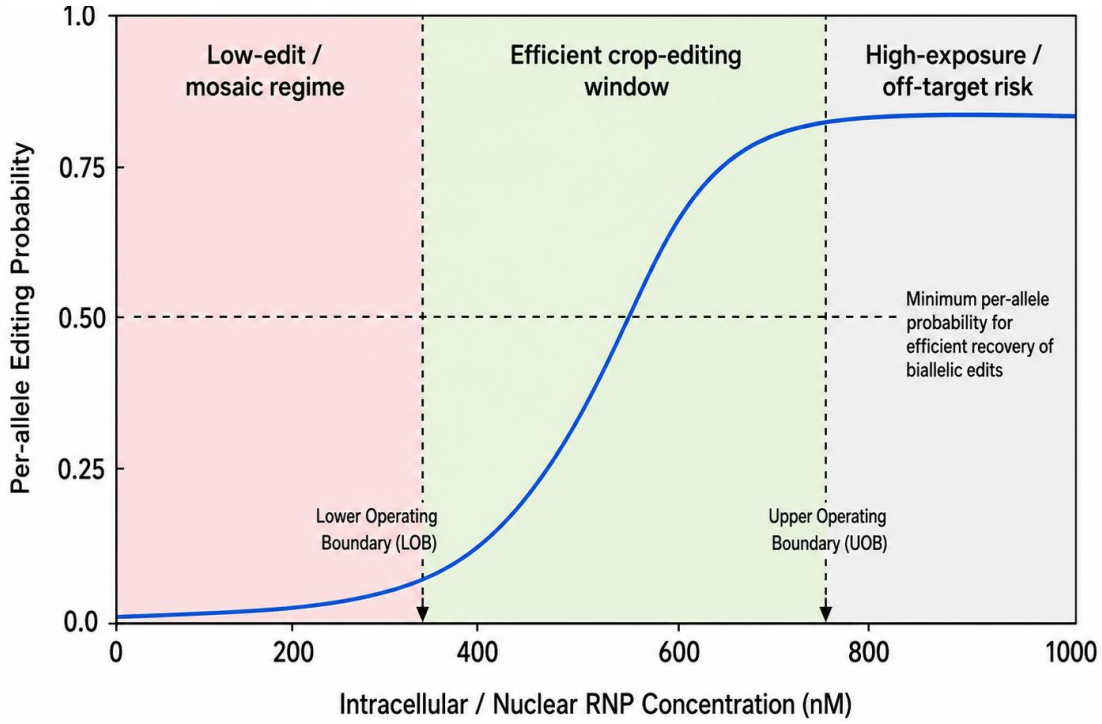


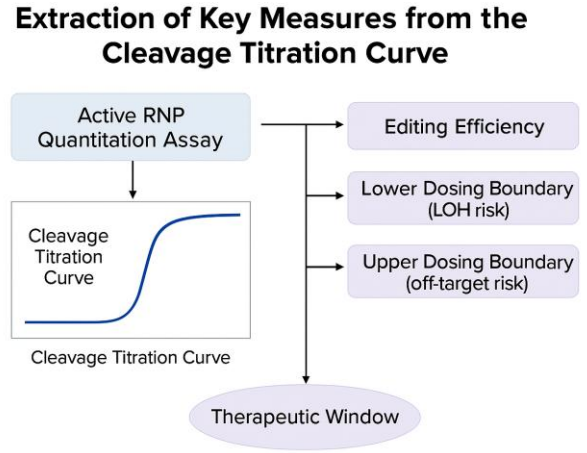
CRISPR QC

Define Effective CRISPR "Dosing" Intervals for

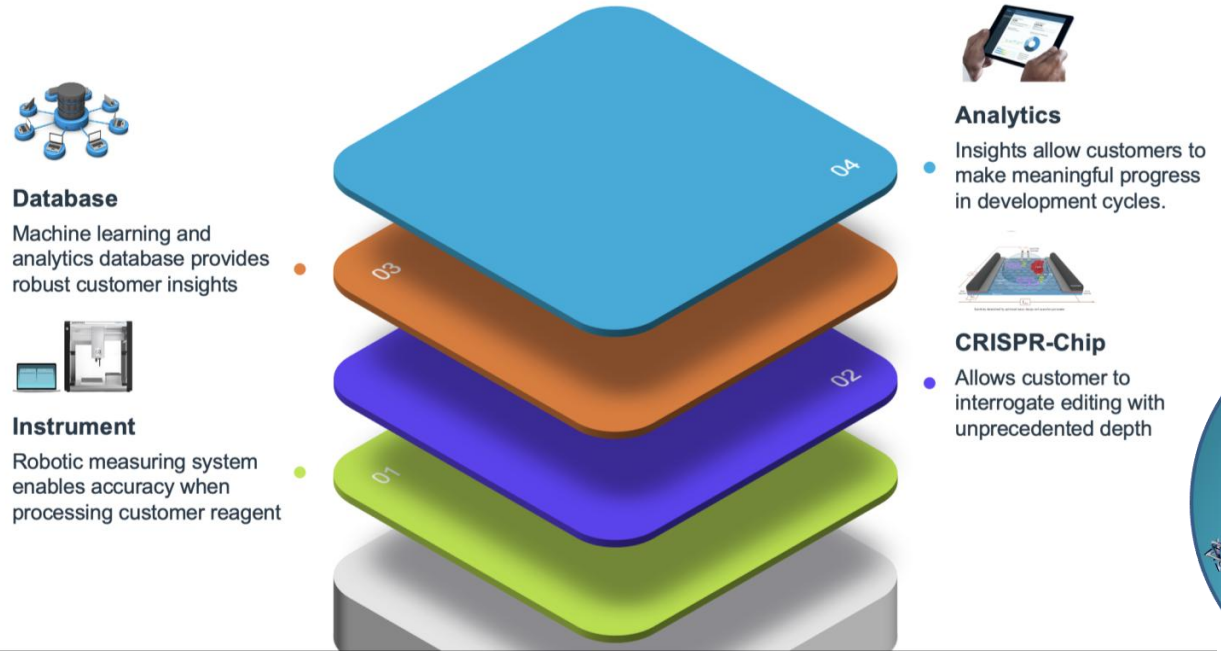
- Lower bounds defined by loss of activity
- Upper bounds constrained by off-target risk
- Identifies therapeutic window early
- Reduces safety surprises later

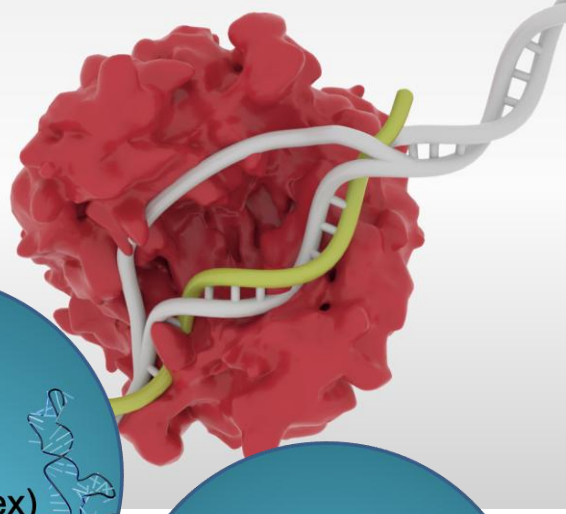
CRISPR PROBABILITY WINDOW FOR PLANT BIOTECHNNOLOGICAL APPLICATIONS

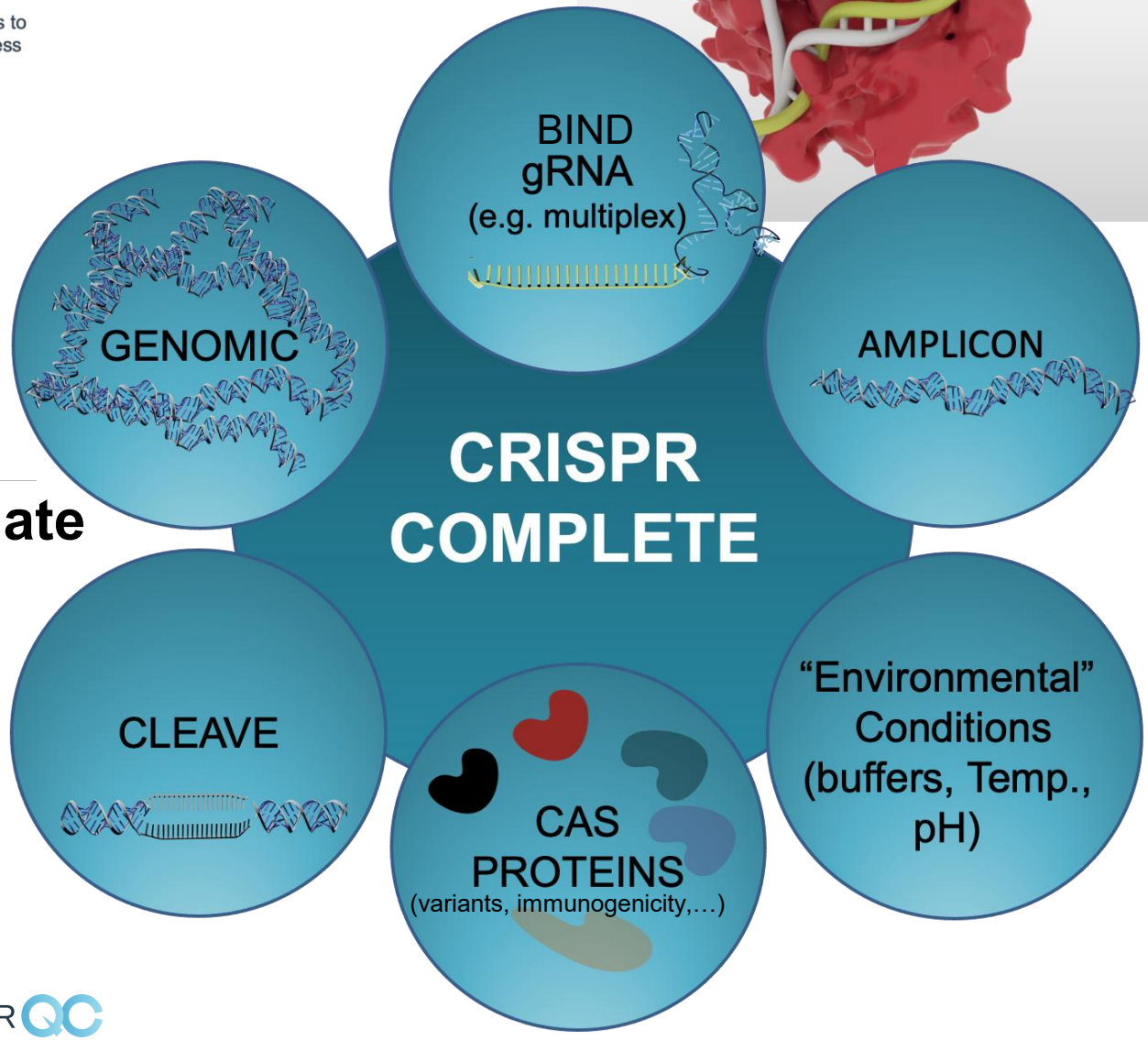




CRISPR QC Analytics Platform







Universal and agnostic platform to evaluate and select CRISPR reagents.

The mission is to provide with the information needed to save time & money bringing crucial solutions to market faster

CRISPR QC