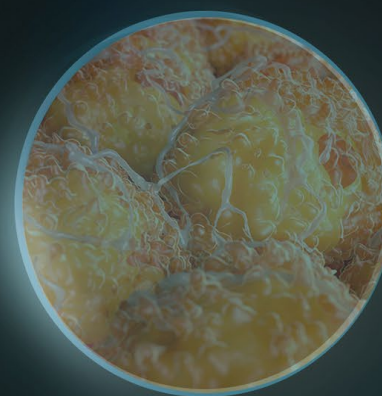
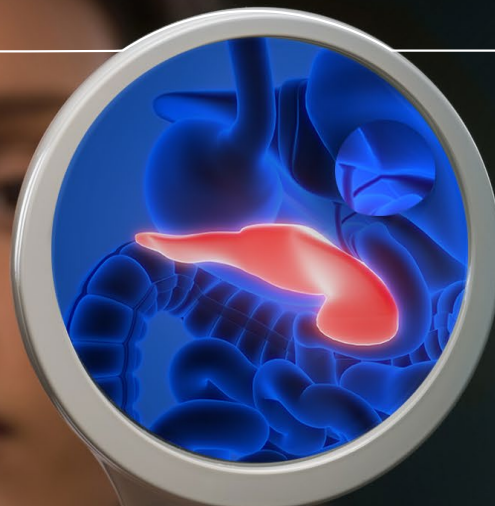
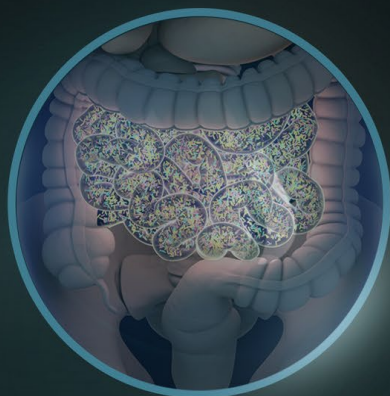


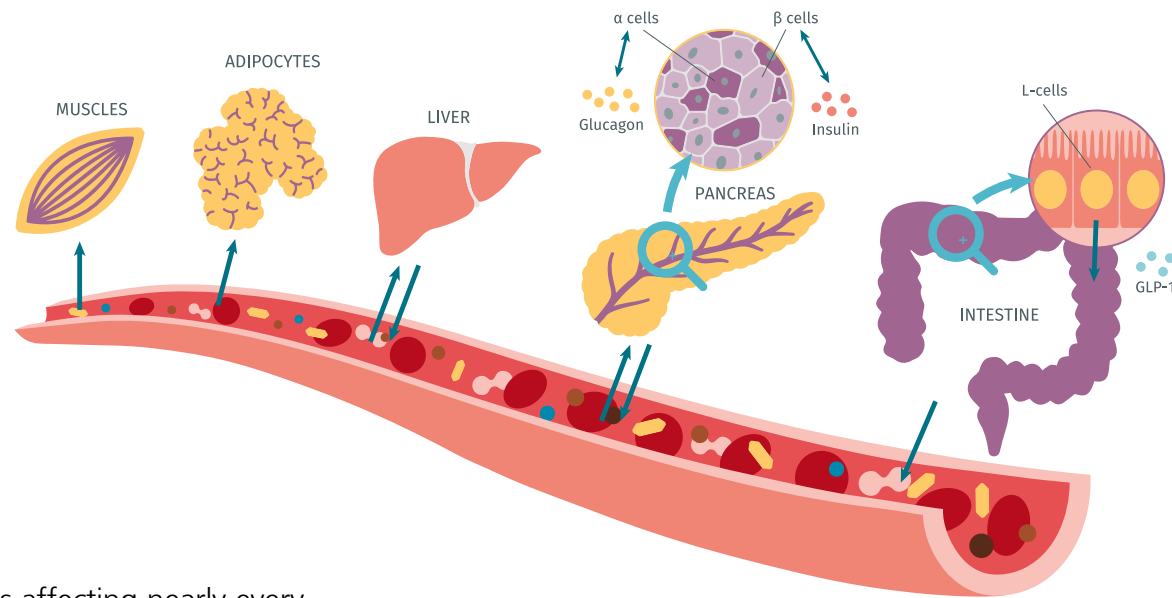
# THE PATH TO DECIPHERING **DIABETES**



Complete Solutions for Diabetes Research

  
**PerkinElmer**<sup>®</sup>  
*For the Better*

# DIABETES PATHWAYS TO PREVENTION AND THERAPIES



Type 1 and type 2 diabetes are complex diseases affecting nearly every major bodily organ and impacting the lives of millions of people worldwide. Studies show that around 1.6 million deaths per year can be attributed directly to diabetes. That's why finding a cure, and adding to our arsenal of effective therapeutics, is so vitally important.

We're committed to helping you understand the complex cellular and molecular pathways involved in diabetes and translating these findings into new prevention and treatment strategies. Our solutions are helping you to:

- Examine the impact genetic and environmental factors have on molecular functions in cell models and effects *in vivo* and how epigenetics are mediating the interaction between these two factors.
- Determine the genetic basis for diabetes through identification and functional analysis of rare mutations associated with beta cell function (types 1 and 2), immune dysregulation (type 1), and metabolism and obesity (type 2).
- Discover biomarkers associated with the onset of diabetes and improve understanding of underlying pathways to reveal potential therapy targets.

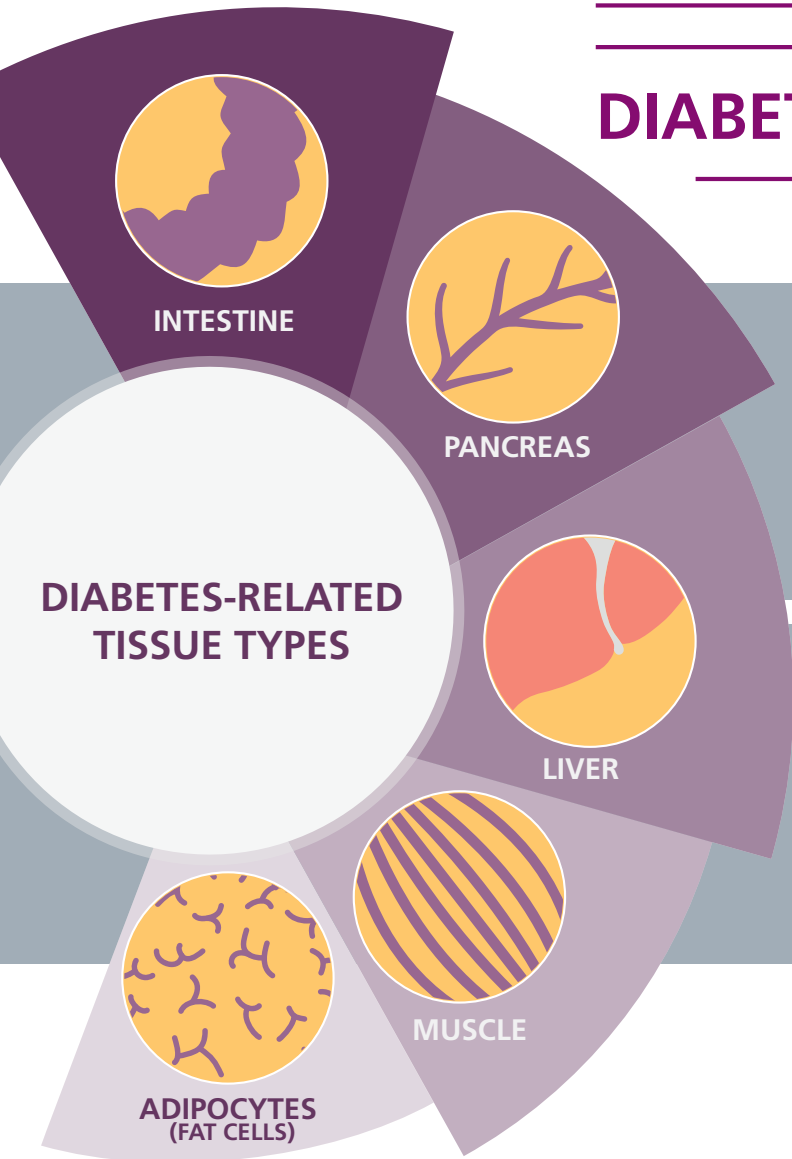
# GETTING AHEAD OF A GLOBAL HEALTH CHALLENGE

Diabetes is characterized by high levels of blood glucose, which can lead to serious damage to vital organs in the body – heart, kidneys, blood vessels, and nerves among them. The most common form of diabetes is type 2 (about 90% of cases), which occurs when the body stops producing enough insulin or becomes resistant to it. Type 1 diabetes is a chronic condition in which the pancreas by itself produces no insulin or makes it in insufficient quantities.

All types of diabetes can lead to health complications and increase the risk of dying prematurely. There's still no cure for any type of diabetes; however, most treatments aid in the management of symptoms and address the long-term health risks.



# DIABETES AROUND THE WORLD: 5 KEY FACTS



In 2016, an estimated 1.6 million deaths were directly caused by diabetes.<sup>2</sup>



**463 MILLION PEOPLE WORLDWIDE** have diabetes (1 in 11 adults) and this number is expected to grow to 642 million by 2040.<sup>4</sup>



Global diabetes-related health expenditures: \$760 billion.<sup>4</sup>

**TYPE 1** 8%

**TYPE 2** 90%

About 90% of people with diabetes have type 2, 8% have type 1, and 2% have rarer types.<sup>1</sup>

## IN THE USA

**1 in 7 health-care dollars (\$327 billion)** is spent treating diabetes and its complications.<sup>3</sup>

1. [www.diabetes.org.uk/resources-s3/2019-02/13628\\_Facts%20and%20stats%20Update%20Jan%202019\\_LOW%20RES\\_EXTERNAL.pdf](https://www.diabetes.org.uk/resources-s3/2019-02/13628_Facts%20and%20stats%20Update%20Jan%202019_LOW%20RES_EXTERNAL.pdf) <https://www.cdc.gov/diabetes/basics/type2.html>  
2. [www.who.int/news-room/fact-sheets/detail/diabetes](https://www.who.int/news-room/fact-sheets/detail/diabetes)  
3. [www.diabetes.org/resources/statistics/cost-diabetes](https://www.diabetes.org/resources/statistics/cost-diabetes)  
4. [www.diabetesatlas.org/upload/resources/material/20200302\\_133351\\_IDFATLAS9e-final-web.pdf](https://www.diabetesatlas.org/upload/resources/material/20200302_133351_IDFATLAS9e-final-web.pdf)

# UNDERSTAND AND MANAGE GENETIC RISK

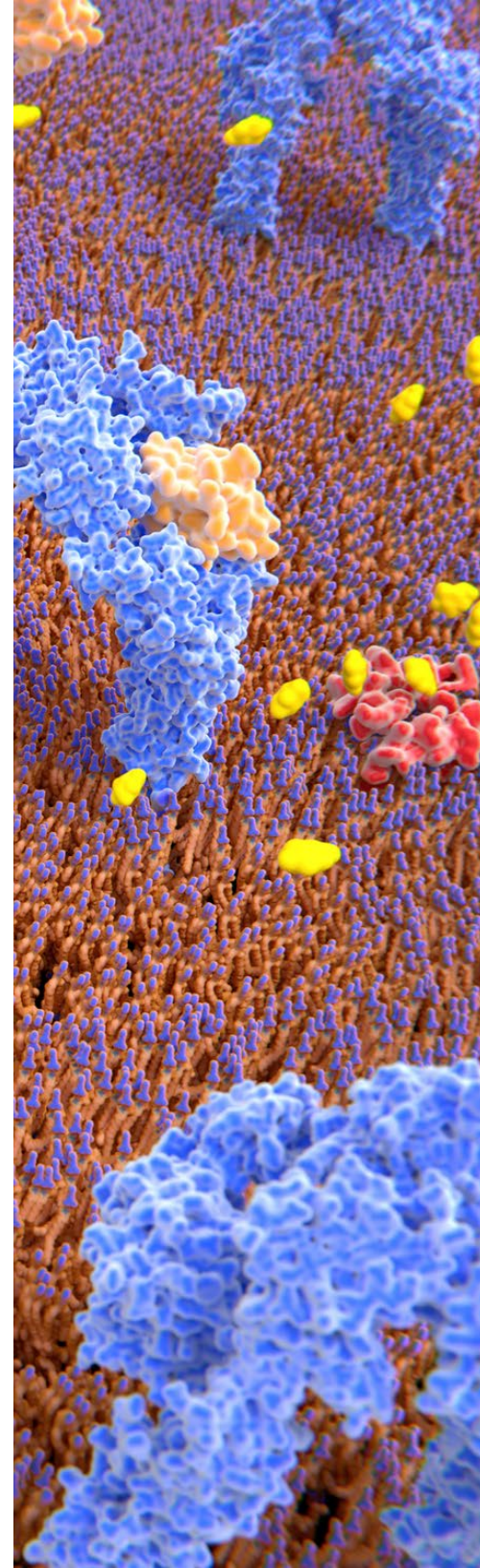
Though diabetes types 1 and 2 have different causes, genetic predisposition plays a critical role in both variations of the disease. Not everybody with genetic risk factors develops the disease – but the combination of environmental triggers and genetics always plays a part in its genesis.

For type 1 diabetes, scientists have identified a major association of disease risk with variants of the HLA-DQA1, HLA-DQB1, and HLA-DRB1 genes, important in immune regulation. Variations in HLA genes seem to increase the risk for an autoimmune response, resulting in the destruction of  $\beta$  cells in the pancreas. But this class of genes only accounts for a portion of genetic risk – variations in other genes are associated with risk of developing the disease.

Type 2 diabetes results from a combination of genetic and lifestyle factors. Though there's no clear pattern of inheritance, there's a strong link to family history and lineage. Hundreds of DNA variations associated with developing type 2 diabetes have been identified, and the difficulty is in understanding how these gene variations contribute to it.

Researchers need advanced tools for large-scale genomic studies of mutations associated with diabetes and obesity, helping us develop personalized medicine.

[Click to read how the European Genomic Institute for Diabetes at the Institut Pasteur de Lille is focusing on the epigenetics and genomics of type 2 diabetes and obesity.](#)

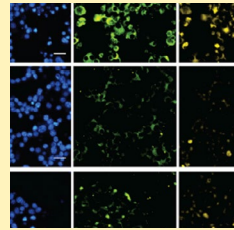


# VISUALIZE MOLECULAR UNDERSTANDING

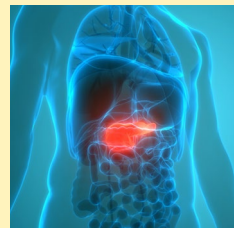
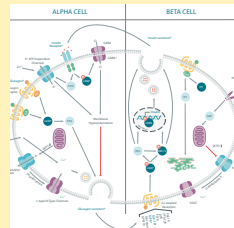
The pathogenesis of diabetes is complex, with various molecular pathways affecting and contributing to disease progression. Diabetes' pathophysiology is still not thoroughly understood, and more insight into molecular processes is needed to spur development of new therapeutics. Besides metabolic pathways, immune-response pathways and inflammatory processes also play key roles in understanding the disease.

We offer an extensive range of reagents and assays, as well as detection platforms, to study diabetes-related pathways and interactions, including GPCRs, kinases, cytokines, and hormones for target identification, screening, and more.

Researchers also benefit from technologies such as live-cell and high-content imaging that deliver more physiologically relevant insights. Molecular processes can also be monitored and visualized by *in vivo* preclinical imaging, perfect for noninvasive real-time studies.



[Learn about noninvasive bioluminescence imaging of  \$\beta\$ -cell function in obese-hyperglycemic \[ob/ob\] mice.](#)

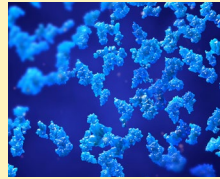


[Read more about the organs affected by or contributing to type 2 diabetes.](#)

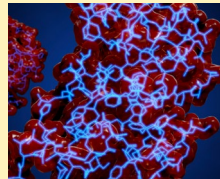
# BIOMARKER AND DRUG DISCOVERY FOR EARLY DIAGNOSIS AND TREATMENT

Early diagnosis of diabetes is essential for predicting disease risk, progression, and response to treatment. Although several biomarkers are associated with diabetes, no single biomarker on its own is sensitive or specific enough to diagnose diabetes accurately in most cases. So you need access to robust, easy-to-use assays that can detect the wide range of biomarkers, enabling you to examine underlying pathways and discover novel drug targets.

Our solutions can help you detect and quantify many key biomolecules in diabetes research and gain precise insight on disease biomarkers such as C-reactive protein, fibrinogen, IGF, FGF, insulin and glucagon, leptin and ghrelin, adiponectin, and factor VIII. And we enable you to target diabetes-related complications such as heart disease and stroke, blindness, kidney failure, and nerve damage.



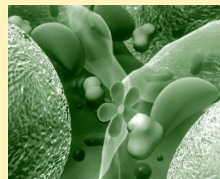
[See how AlphaLISA technology provides a homogeneous, bead-based assay for quantification of TNFR1 in urine.](#)



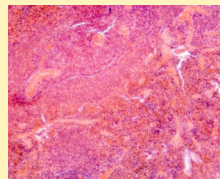
[Learn how AlphaPlex™ offers a complete assay for all-in-one-well measurement of insulin and glucagon in biological samples.](#)



[This brochure describes the functionality and benefits of three assay kits available for insulin quantification.](#)



[Read how the Alpha-enabled VICTOR® Nivo™ plate reader meets critical assay parameters testing human insulin and p24 \(human HIV\).](#)



[Learn how AlphaLISA® technology can help you gain more relevant data from studies of molecular pathways.](#)



[Learn about novel approaches to addressing the short shelf life of liraglutide for type 2 diabetes.](#)

## CASE STUDY

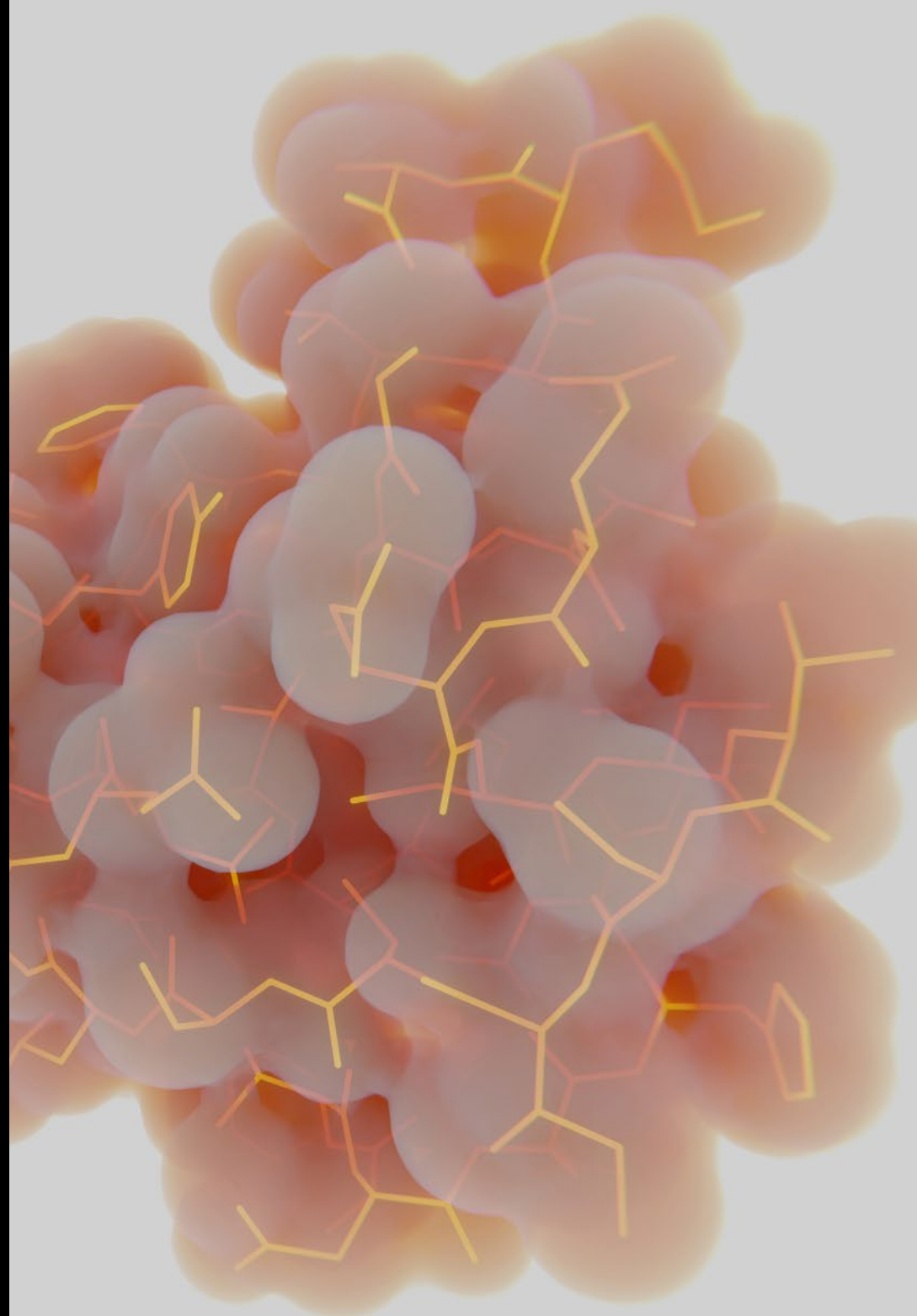
# MEASURING PK/PD AND BIOMARKERS IN ANIMAL PLASMA AND CELL-CULTURE SUPERNATANTS

*Research Bioanalysis Group, Novo Nordisk*

Novo Nordisk is using AlphaLISA technology to measure thousands of samples for bioactive peptides and proteins, which are needed for PK/PD studies. AlphaLISA is a homogenous, easy-to-use technology that's simple to automate, and with a dynamic range of more than three orders of magnitude and superior sensitivity and superior sensitivity, it allows the quantification of biomarkers in the low pM range. AlphaLISA can determine insulin concentrations in a large number of samples during the drug discovery process, while saving time and sample compared to ordinary ELISA assays.

Novo Nordisk is using AlphaLISA® technology on two fully automated analysis lines with a throughput of 25,000 datapoints per six-hour run, as well on partially automated EnVision™ plate readers, Biotek dispensers, and several pipetting workstations.

*Journal of Biomolecular Screening 12(2); 2007*





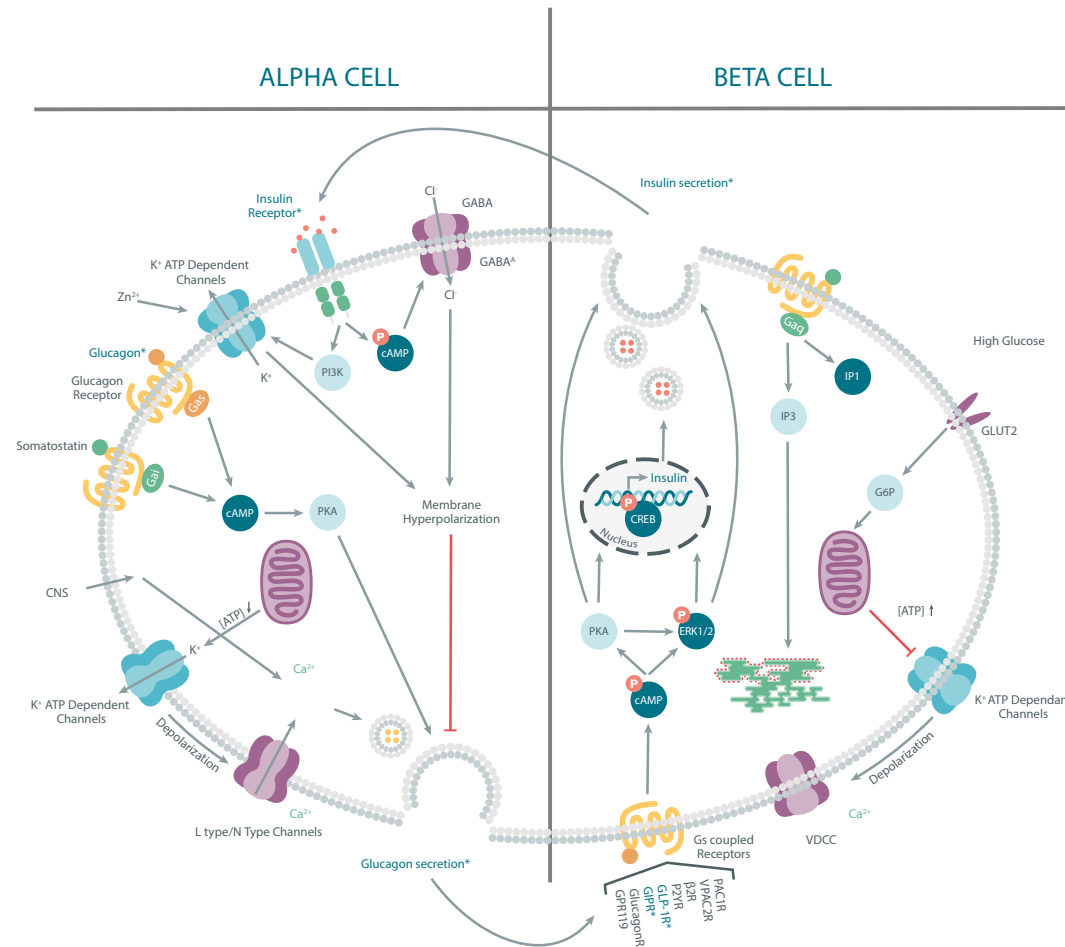
## CASE STUDY

# STUDYING MOLECULAR PATHWAYS USING ALPHALISA

Dr. Jonathan Campbell, Duke University

Pancreatic  $\alpha$  and  $\beta$  cells play critical roles in type 2 diabetes. While  $\beta$  cells lose the ability to release insulin,  $\alpha$  cells increase production of glucagon. However, the role of  $\alpha$ -to- $\beta$  cell communication is not fully understood. This study suggests an essential contribution of proglucagon-derived peptides (PGDPs) to  $\alpha$ -cell regulation of  $\beta$  cells and the control of insulin secretion.

Insulin and glucagon content and secretion were assessed by AlphaLISA<sup>®</sup> technology and assayed using the EnVision<sup>®</sup> plate reader.



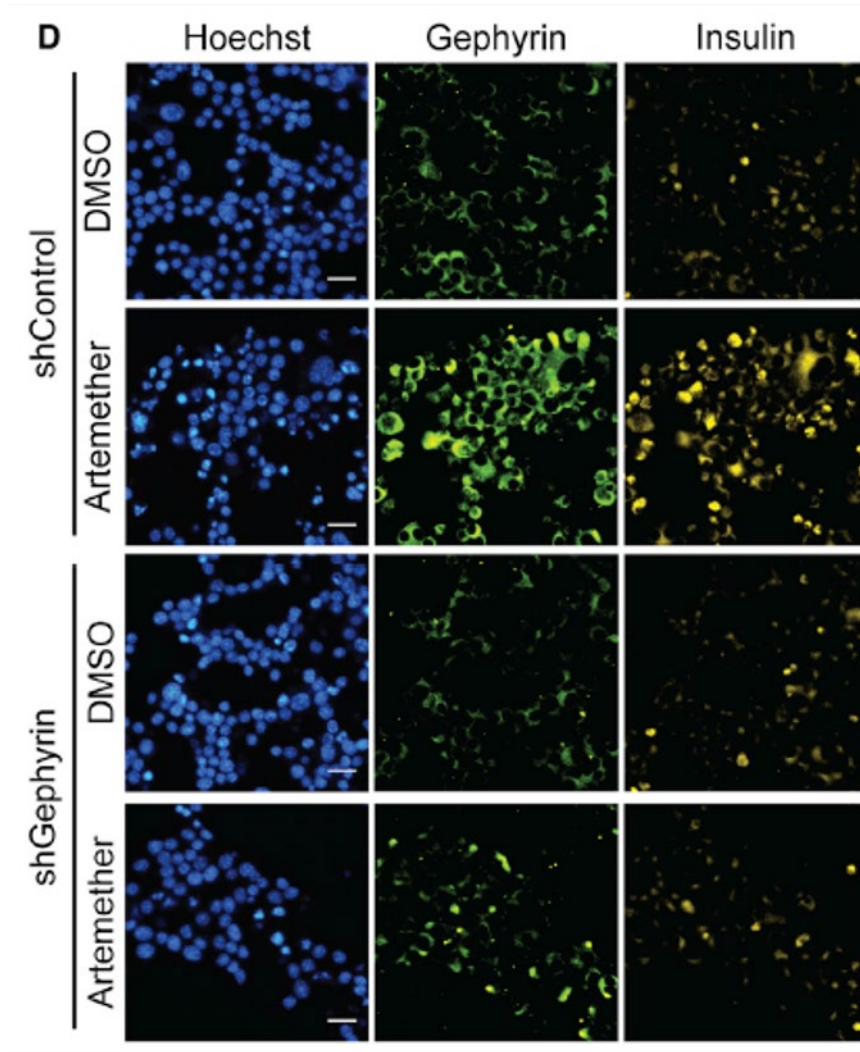
## CASE STUDY

# IDENTIFICATION OF NEW DRUG TARGETS USING HCS

Stefan Kubicek, CeMM Research Center for Molecular Medicine, Austrian Academy of Science

Type 1 diabetes is caused by the destruction of pancreatic  $\beta$  cells. One way to treat the disease would be to generate insulin-producing cells from other cell types. Researchers from the CeMM Research Center show that a glucagon-producing  $\alpha$  cell can be converted in a functional  $\beta$ -like cell by repression of the regulatory transcription factor ARX.

The compound artemether could be identified as a functional ARX inhibitor by targeting the protein gephyrin using the Operetta<sup>®</sup> CLS HCS system.



Immunofluorescence for insulin and gephyrin in  $\alpha$ TC1 cells treated with artemether in the presence (shControl) or absence (shGephyrin) of the multifunctional protein gephyrin. In contrast to control treated  $\alpha$  cells, cells with significant reduction of gephyrin (shGephyrin) failed to increase intracellular insulin levels after artemether treatment.

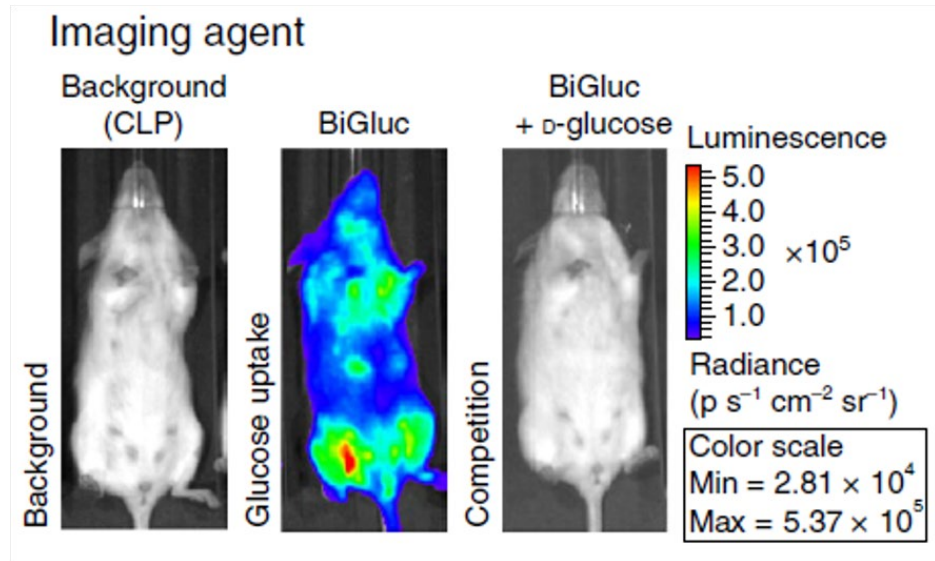
## CASE STUDY

# VISUALIZING GLUCOSE UPTAKE

Tamara Maric, Institute of Chemical Sciences and Engineering, École Polytechnique Fédérale de Lausanne (EPFL)

To date, there's a lack of easy-to-use optical tools to image glucose uptake *in vivo* and *in vitro*, which limits our knowledge of disease-associated glucose flux. The goal of this study was to develop a new bioluminescent imaging probe (BiGluc) for real-time noninvasive longitudinal imaging studies. BiGluc technology is based on a reaction of two components (CLP and GAZ4) resulting in the release of luciferin. Animals injected with BiGluc components were imaged using IVIS® Spectrum imaging system.

The signal is specific to the D-glucose and can be used to quantify physiological fluxes of D-glucose in a noninvasive way.



It could be shown that the BiGluc probe was D-glucose specific by administering the probe in the presence or absence of high concentrations of D-glucose (competition experiment).

## CASE STUDY

# TOWARD GENOMIC MEDICINE IN COMMON TYPE 2 DIABETES

*Dr. Philippe Froguel and Dr. Amelie Bonnefond,  
European Genomic Institute for Diabetes,  
Institut Pasteur de Lille*

Researchers at Institut Pasteur de Lille are focusing on the epigenetics and genomics of type 2 diabetes and obesity (monogenic and polygenic forms).

Molecular diagnosis of monogenic forms of diabetes and obesity is crucial for personalized care, and recent studies reveal that pathogenic mutations of actionable genes linked with monogenic diabetes are more prevalent than previously thought in patients with polygenic-like type 2 diabetes.

The goal of this study is to confirm these results by sequencing all patients with type 2 diabetes passing through the Department of Diabetology at Liege Hospital in Belgium. The Sciclone™ G3 NGS workstation is used for automating library prep processes.

# SMARTER QUESTIONS BETTER ANSWERS

With all the advances in therapeutics discovery and development, we're generating vast amounts of data. Making sense of it all is perhaps the challenge of our time. So our informatics solutions are designed to speed identification of vaccine or therapeutic candidates; help you import, align, and analyze biological sequences; and manage experimental, instrument, and outsourced pharmacology data.

## **ELECTRONIC LAB NOTEBOOKS**

We offer ELNs to meet the needs of scientists and researchers, helping you organize and share experimental data efficiently and communicate seamlessly with the common instruments and devices you use. [READ MORE](#)

## **LEAD DISCOVERY**

Our lead-discovery solutions provide a faster way to help you gain insights through a guided search and analysis workflow that queries and represents data in intuitive, intelligent ways. [READ MORE](#)

## **DATA VISUALIZATION**

Our data visualization platform can empower your team or your entire organization to easily mine scientific and business data and gain insights, in real time. You can create simple dashboard metrics, predictive applications, or dynamic real-time analytics applications with capabilities such as visual, predictive, location, and streaming analytics; data wrangling; and much more. [READ MORE](#)

## **CLINICAL ANALYTICS**

Our solutions streamline clinical trials with real-time access to data during all phases of clinical development, allowing you to interact with information as soon as it's collected. You're better able to explore key aspects of the protocol for specified follow-up, ensure adherence by identifying drop-outs and violations, facilitate data cleaning and data quality, and much more. [READ MORE](#)

# GENOMICS SOLUTIONS

*The study of gene variations in diabetes is critical to our ability to develop personalized medicines. Genomics solutions support your endeavors at every step, from DNA/RNA extraction to automated library quality control.*



HIGH-THROUGHPUT  
NUCLEIC ACID ISOLATION



MICROFLUIDIC DEVICES



AUTOMATED LIQUID HANDLING



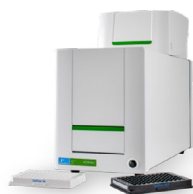
NGS LIBRARY PREP KITS

# DETECTION

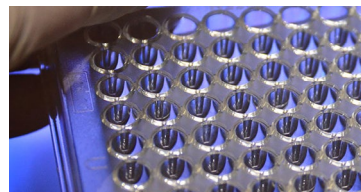
*For basic research, drug discovery screening, PK/IPD, and safety and efficacy studies, reliable detection and quantification of biomarkers and identification of drug compounds are essential. Validated screening assays, multimode plate readers, and radiochemical research solutions accelerate that research.*



RADIOCHEMICALS AND  
RADIOMETRIC DETECTORS



MULTIMODE  
PLATE READERS



MICROPLATES



REAGENTS FOR  
DRUG DISCOVERY

## CELL-BASED ASSAYS

*For researchers trying to better understand metabolic processes or investigating how drugs affect those processes, cell-based assays are proven and powerful tools for gaining more insights in metabolic disease.*



HIGH-CONTENT IMAGING



LIVE-CELL IMAGING

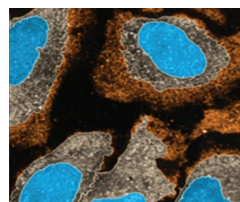


IMAGE ANALYSIS  
AND DATA SHARING



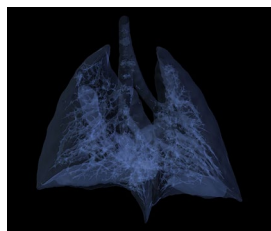
MICROPLATES FOR  
CELL IMAGING

## IN VIVO IMAGING

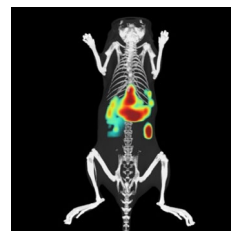
*Small-animal imaging can help drive your next big discovery by giving you the tools to monitor pancreatic  $\beta$ -cell functionality, perform drug efficacy and toxicology studies, enhance your understanding of molecular pathways, and much more.*



OPTICAL IMAGING



MICRO-CT IMAGING



IN VIVO IMAGING REAGENTS

# EXPERT SERVICES WHEREVER YOU NEED THEM



Most labs don't maintain the in-house expertise needed to plan and implement the types of projects that can transform chaotic lab operations into the sleek, efficient, effective lab of the future. After all, you should be concentrating on your core competency – your science – and leaving the infrastructure, operations, and even lab management to the professionals. That's why so many smart labs are looking to outsourcing to help them plan, design, deploy, and manage their lab environments.

## COMPUTER SYSTEM VALIDATION (CSV)

CSV services range from full validation or commissioning for new systems to change-control validation for existing standalone and enterprise systems. Our team follows GAMP 5 templates and aligns with your site's policies and procedures as they relate to the software development lifecycle. At the same time, we provide a range of software IQ/OQ offerings, including enhanced-security instrument software products. [READ MORE](#)

## DATA INTEGRITY

Many regulatory agencies have determined that electronic data is more secure than paper documentation and less likely to be manipulated over the phases of a product's development lifecycle. But that doesn't mean electronic lab data is perfect: It must comply with other stringent regulations, including 21 CFR Part 11 and the EDQM Annex 11. [READ MORE](#)

## INSTRUMENT QUALIFICATION

Our OneSource Instrument Qualification methods maximize your lab productivity while providing ongoing compliance capabilities. We guide your lab through automated, secure electronic or traditional paper qualification procedures with standard recommended OQ protocols customized to your specifications. [READ MORE](#)

## GMP RADIOSYNTHESIS

Our experienced chemists work with you to design and prepare your radiochemical to your exacting specifications. You have access to our extensive technical support resources to help with protocol creation, custom synthesis of radioactive products, stability testing, special packaging, and analytical services. [READ MORE](#)





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Waltham, MA 02451 USA  
P: (800) 762-4000 or  
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[www.perkinelmer.com](http://www.perkinelmer.com)



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