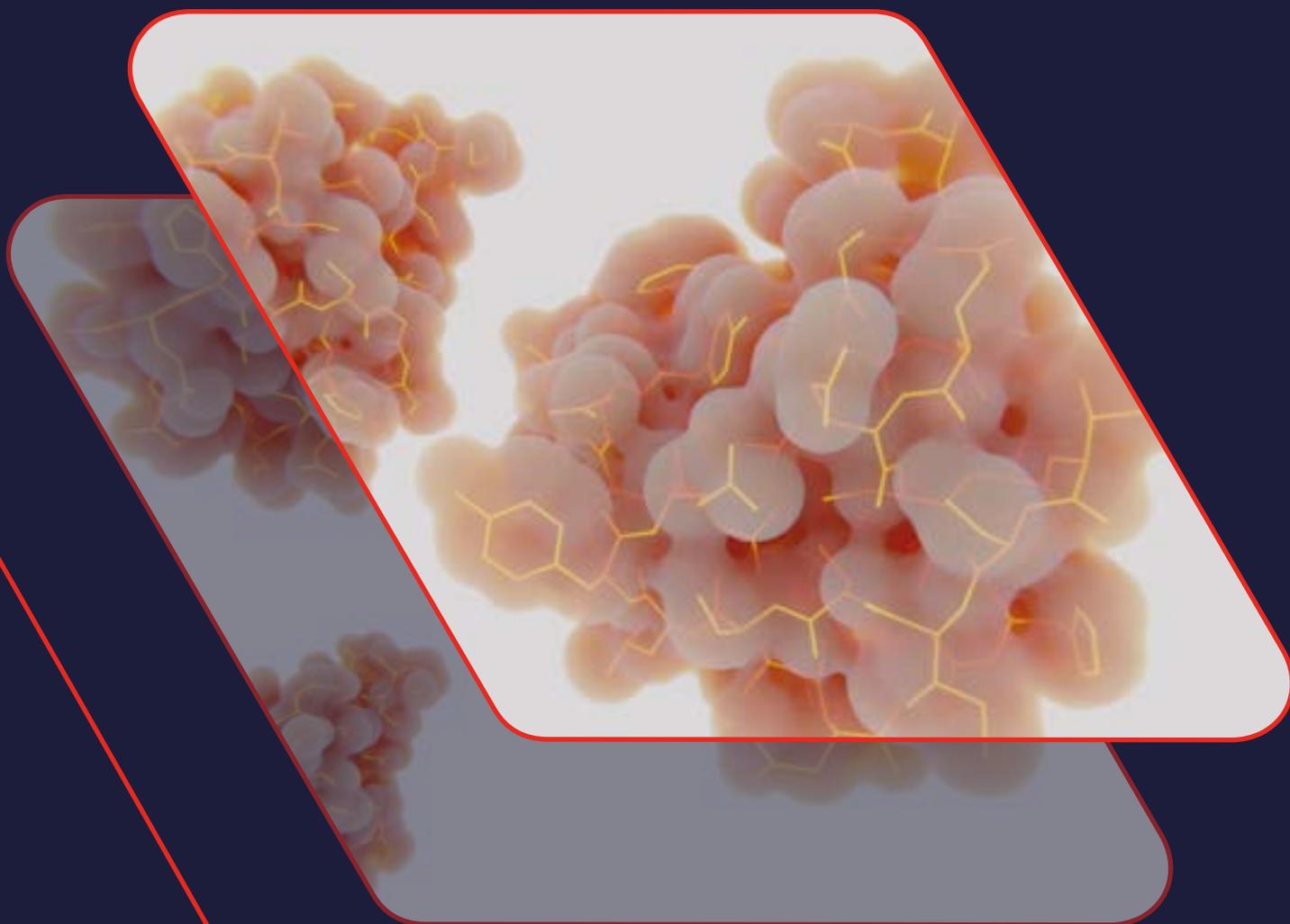
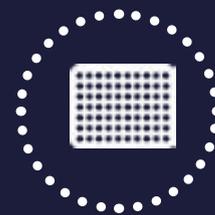


METABOLISM GHRELIN



- Unique set of assays
- Compatible with any blood collection process
- Recognized technology

GHRELIN

AN EXCITING SCIENTIFIC STORY...

Obesity and diabetes are amongst the greatest public health issues for this century. Indeed, over the last 30 years, obesity has more than doubled, achieving 1.5 million persons. It affects people in every age group (children, adults, and elderly people), and every socioeconomic class. Obesity is a complex condition which poses a major risk for serious diet-related, non-communicable diseases, including type 2 diabetes.

Ghrelin is fast becoming an endocrinology target of the millennium. It has been discovered in 1999 almost concomitantly by two teams using different approaches:

- The first one in Japan (Kojima & Kangawa) used a reverse pharmacological approach and submitted a patent on their discovery. This was the first time a peptidic hormone was shown to become activated by acylation.
- The second one in France (Tomasetto et al) used molecular biology techniques and published their discovery of the Ghrelin (Motilin like peptide) one day after Kojima's team submitted their patent anteriority.

From the discovery of both teams, we learned that this peptide would potentially be a good candidate to study growth but also a gut peptidic hormone with an important role in appetite, food intake and glucose homeostasis (diabetes/obesity).

Very quickly after Kojima's publication, scientists became interested in measuring the circulating concentration of the hormone in biological samples (blood/plasma). Assays were quite

rapidly set-up but often without caring about the reliability of Acylated Ghrelin values and mixing content of both forms (Acylated and Unacylated Ghrelin).

Assays put early on the market were either non-specific (measuring Acylated and Unacylated forms) or leading to falsely low values due to Ghrelin deacylation/degradation. Despite those biased results, the existence of a Ghrelin pulse has been established, and has been characterized to manifest as a peak before meal times, followed by a rapid decrease postprandial. However, a number of inconsistencies remain between the different results obtained in clinical studies due to a lack of reliable tools to measure Acylated Ghrelin.

This led many scientists to dismiss Ghrelin as a reliable biomarker. However, for those still interested, sample collection remained a major challenge.

The first assay distinguishing between the two Ghrelin forms only appeared on the market five years later and was developed and produced by Bertin Technologies, under the SPI-Bio brand name.

While Acylated Ghrelin is known as the active form of the peptide, and as the only form for which a receptor has been identified, clinical trials have shown positive results using the Unacylated form. The underlying mechanisms are not yet well understood, and several teams in the world are currently working on this topic.

In 2014, Bertin Bioreagent launched, under the brand name SPI-Bio, a new set of assays called Ghrelin Easy Sampling ELISA kits that are compatible with any blood collection process.

...AND CLINICAL CHALLENGES

Ghrelin is now a well-known orexigenic hormone (an hormone which leads to an increase in appetite). It has become an obvious target for treatment of eating disorders like obesity or anorexia nervosa.

However, we know that Ghrelin is also implicated in many other physiological systems like the cardiovascular, bone, gastrointestinal and immune

BERTIN BIOREAGENT KNOW-HOW

Bertin Bioreagent's expertise is to develop analytical tools for biomarkers. As such, in 2004, Bertin Pharma launched its first Ghrelin Biomarker assay kits, under the SPI-Bio brand name, as a result of its state-of-the-art R&D research teams.

Bertin Technologies was the first company to provide bioanalytical tools to assay Acylated and Unacylated Ghrelin with a very high sensitivity.

Today, in addition to their existing Ghrelin Express ELISA kits, Bertin Bioreagent offers a set of assays that will allow any scientist to measure Acylated & Unacylated Ghrelin in samples collected with any blood collection process.

This range of assays was called "Easy Sampling" as the assays are compatible with any kind of blood sample collection process. The assays can be used to measure ghrelin in blood samples collected with any kind of protease inhibitors, with or without an acidification step. While there is not yet a consensus on the collection procedure, we are quite confident that the scientific community will gradually establish standards for the blood collection procedure for Ghrelin studies, especially in the context of clinical trials or later on in clinical settings. It is today largely accepted that a study

BERTIN BIOREAGENT KNOW-HOW

Bertin Bioreagent uses the Acetylcholinesterase (AChE[®]) technology in most of its ELISA kits. Acetylcholinesterase, the enzymatic label for ELISA, has the fastest turnover rate of any enzymatic label. The use of AChE[®] as enzymatic label for ELISA has been patented by the CEA (French Alternative Energies & Atomic Energy Commission) and Bertin Bioreagent, formerly known as SPI-Bio which has over 20 years expertise developing and producing ELISA kits using this technology.

systems as well as some physio-pathological states like mood or muscle mass maintenance, heart failure, myocardial infarction, cachexia, cancer, Prader Willi syndrome...

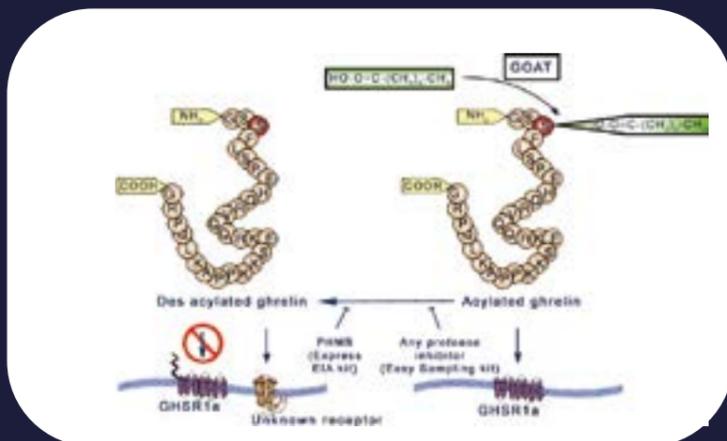
Since bioanalysis tools such as the SPI-Bio Ghrelin ELISA assay kits are now available, it will become progressively easier to elucidate the role of this new hormone as well as its therapeutic implications.

involving Ghrelin should include both Acylated and Unacylated forms, while total Ghrelin is almost irrelevant.

Bertin Bioreagent has a solution, from early discovery programs using our 384-well plate format to select your GOAT inhibitor, to pre-clinical or clinical stages.

Overview

- +100 assays available in various therapeutic areas
- Specific expertise in:
 - **Fit-to-purpose** development assay
 - Analytical platforms: Immunoassays methods, Hyphenated methods
 - Biomarker Assay **Translation from discovery to clinical studies**
 - Capabilities to provide **ready-to-use & customized assay kit** for in-house or central labs implementation
- Over 20 years of experience
- Industrialisation of assays for Pharmaceutical, Cosmectic & nutraceutic R&D



AChE[®] offers several advantages compared to enzymes conventionally used in ELISAs:

- Kinetic superiority and high sensitivity
- Low background
- Wide dynamic range
- Versatility

GHRELIN

LIST OF GHRELIN ELISA KITS

Acylated Ghrelin (human) Easy sampling	Cat No: A05306	Any kind of samples
Unacylated Ghrelin (human) Easy sampling	Cat No: A05319	Any kind of samples
Acylated Ghrelin (human) Express	Cat No: A05106	PHMB, PMSF, Aprotinin samples
Unacylated Ghrelin (human) Express	Cat No: A05119	PHMB, PMSF, Aprotinin samples
Acylated Ghrelin (human) 384 wells	Cat No: A05106	GOAT inhibitor screening
Acylated Ghrelin (mouse, rat) Easy sampling	Cat No: A05317	Any kind of samples
Unacylated Ghrelin (mouse, rat) Easy sampling	Cat No: A05318	Any kind of samples
Acylated Ghrelin (mouse, rat) Express	Cat No: A05117	PHMB, PMSF, Aprotinin samples
Unacylated Ghrelin (mouse, rat) Express	Cat No: A05118	PHMB, PMSF, Aprotinin samples
Acylated Ghrelin (pig)	Cat No: A05401	PHMB, PMSF, Aprotinin samples
Unacylated Ghrelin (pig)	Cat No: A05402	PHMB, PMSF, Aprotinin samples
Unacylated Ghrelin (dog) Easy sampling	Cat No: A05320	Any kind of samples
Acylated Ghrelin (dog) Easy sampling	Cat No: A05321	Any kind of samples
Sampling Tubes with PHMB	Cat No: D31009	Sample preparation