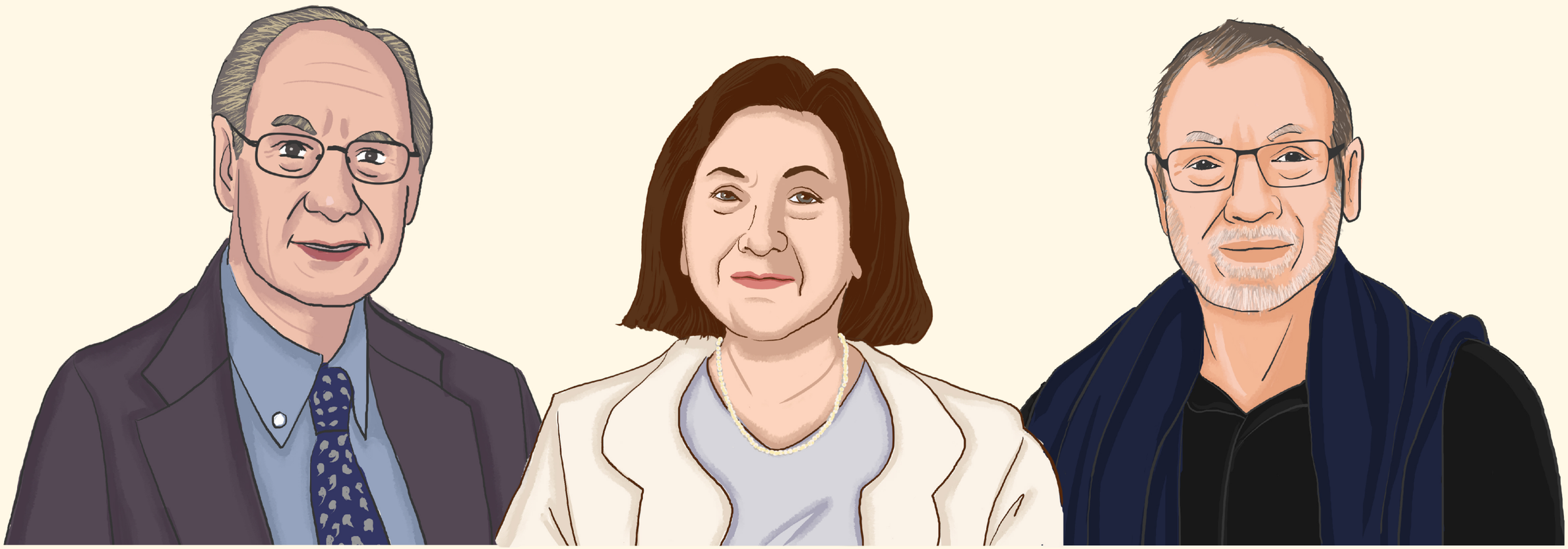
TANG PRIZE

2024 Tang Prize

Biopharmaceutical Science



Joel F. Habener　**Svetlana Mojsov**　**Jens Juul Holst**

Diabetes and Obesity are Eating Our World Away

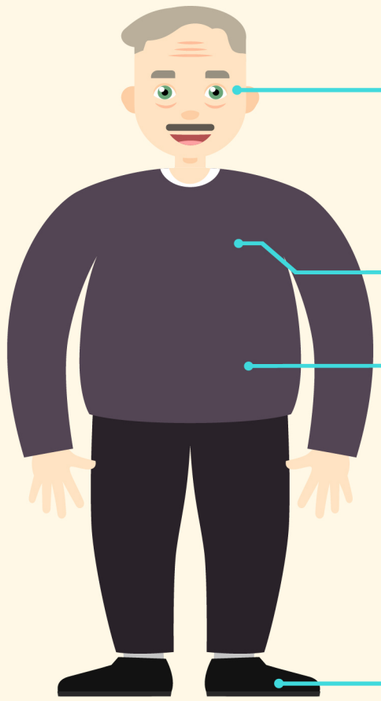
- There are more than 500 million people worldwide suffering from diabetes and nearly 1 billion living with obesity, posing a great threat to human health.
- Over 90% of all diabetes are Type 2 diabetes, caused by the beta-cells of the pancreas not secreting enough insulin and the body not responding to insulin properly, resulting in high blood sugar.

Risk factors for type 2 diabetes

Overweight and obesity

Family history

Age

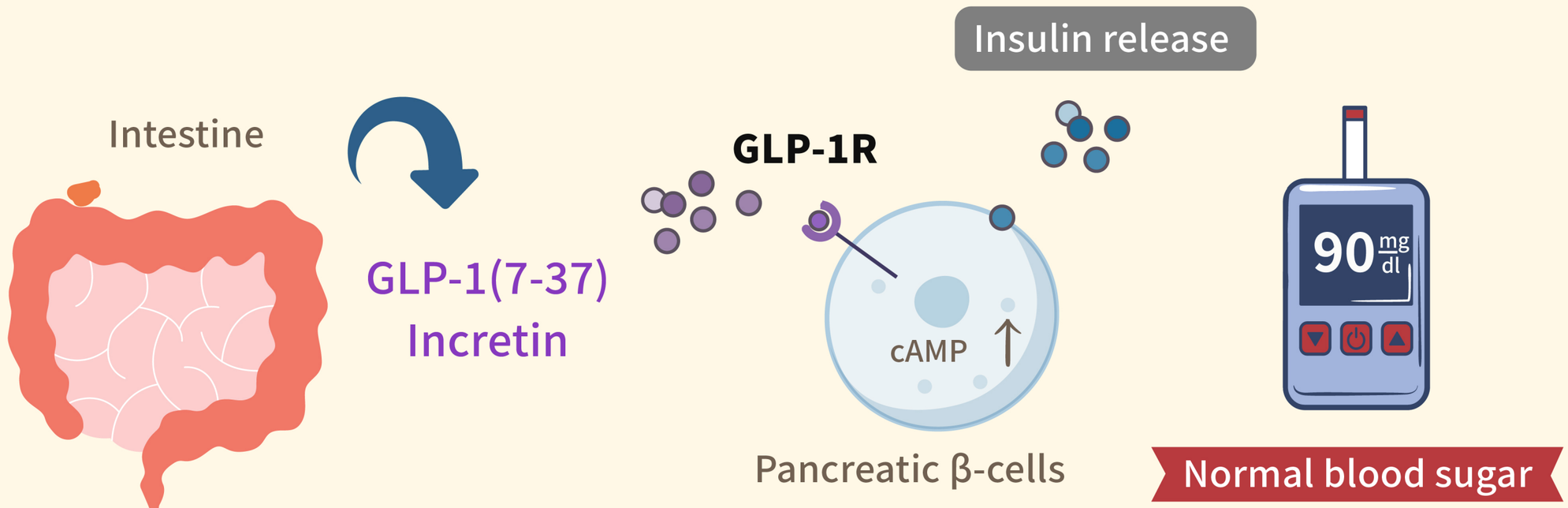


Complications of type 2 diabetes

- Retinopathy
- Cardiovascular diseases
- Nephropathy
- Neuropathy

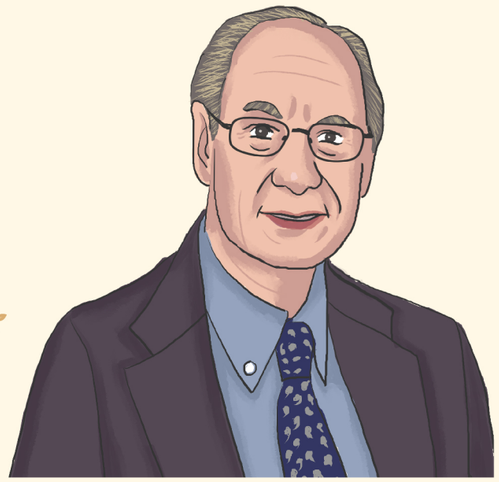
GLP-1 (7-37)

GLP-1 (glucagon-like peptide-1) is an intestine-secreted hormone, also known as “incretin”. When blood sugar levels rise in the body, it stimulates the secretion of GLP-1. Once the bioactive GLP-1(7-37) binds to its receptor GLP-1R on β-cells of the pancreas, it triggers insulin release, regulating glucose levels in the blood.

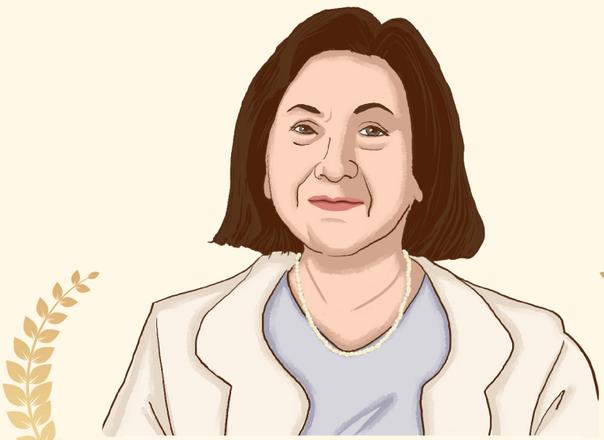


Their Contributions

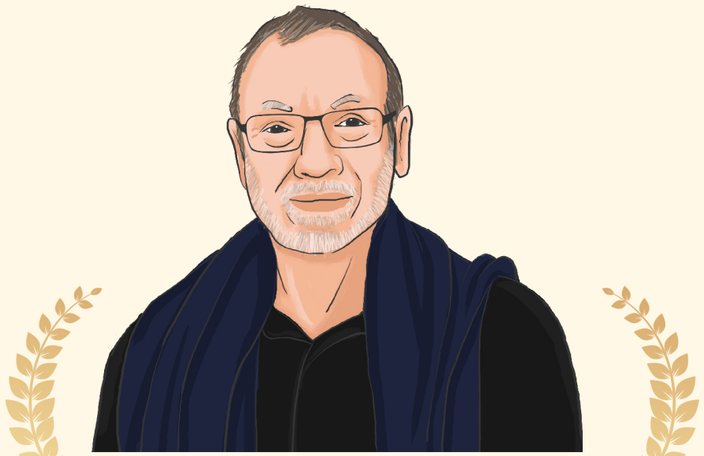
- They are awarded for the discovery of GLP-1(7-37) as an incretin and development of GLP-1(7-37)-based anti-diabetic and anti-obesity drugs.



Joel F. Habener



Svetlana Mojsov

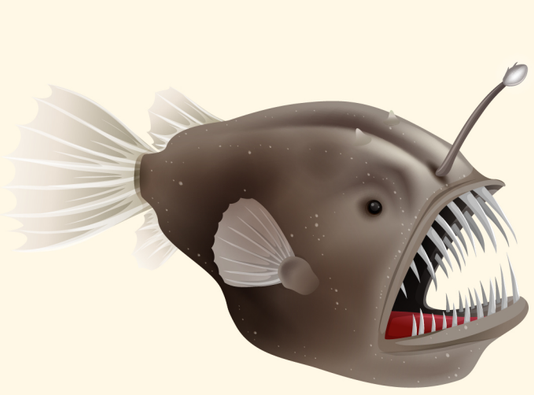


Jens Juul Holst

- Their groundbreaking discoveries redefined the long-sought incretin, leading to its application as an antidiabetic strategy.

Joel F. Habener

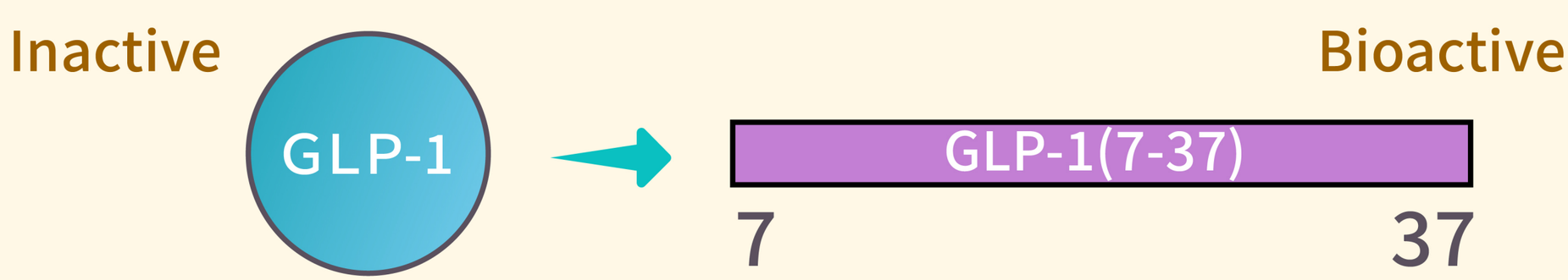
- In the early 1980s, Dr. Habener first cloned the "preproglucagon" gene from anglerfish and discovered this precursor protein contains glucagon and a GRP. Subsequent cloning of the rat preproglucagon gene showed that it contained glucagon and two additional peptides designated GLP-1 and GLP-2, and that the anglerfish GRP is a GLP-1.



- Dr. Habener then collaborated with Dr. Mojsov to show that GLP-1(7-37) can induce insulin release from the pancreas rather than the entire GLP-1 (1-37), and further confirmed its insulinotropic effect in clinical trials.

Svetlana Mojsov

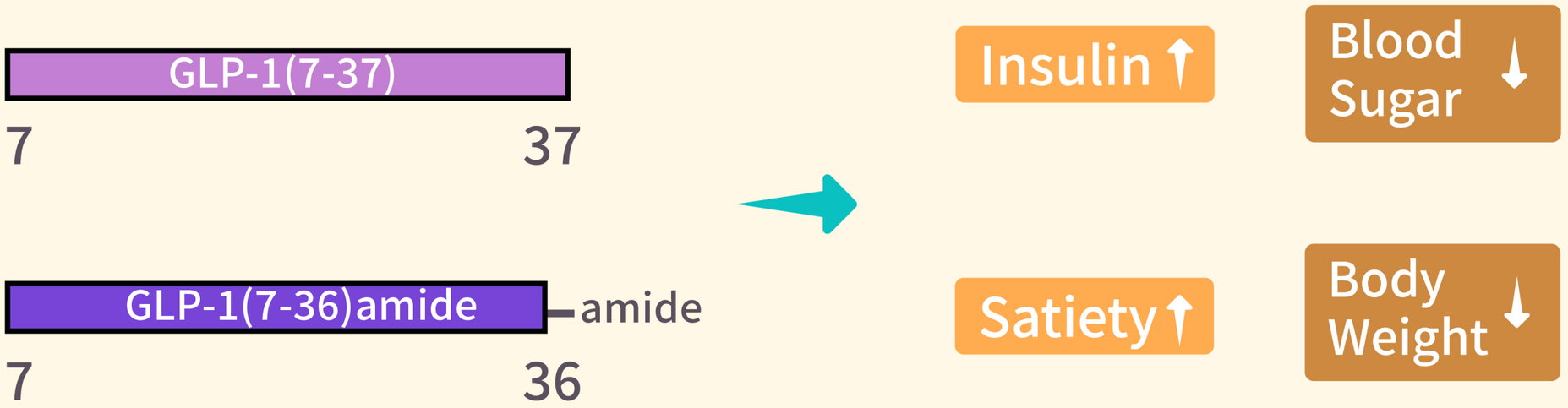
- GLP-1 is a 37 amino-acid peptide. Dr. Mojsov identified the active form of intestinal GLP-1 to be GLP-1(7-37), by truncating its first 6 amino acids. She collaborated with Dr. Habener to show that GLP-1(7-37) exhibits a more potent physiological function in promoting insulin secretion in healthy and type 2 diabetes human subjects.



- Dr. Mojsov's efforts in the synthesis of GLP-1 (7-37) and the development of several experimental approaches to detect the GLPs in the intestines were absolutely critical.

Jens Juul Holst

- Dr. Holst also isolated and identified GLP-1 (1-37), and subsequently GLP-1 (7-36) amide as an active incretin. His lab characterized the biology and physiology of GLP-1 (7-37), demonstrated its therapeutic potential, and has been actively involved in developing anti-diabetic drugs.



- Dr. Holst also reported that GLP-1(7-37) inhibits gastric acid release and slows down gastric emptying, with anti-obesity potential. During clinical trials, it was found that patients receiving GLP-1-based drugs had weight loss tendencies, further promoting its application in the treatment of obesity.

Drug Development and the Future

The short half-life of endogenous GLP-1 poses a significant challenge for drug development. The findings of the three laureates together ushered in an era of GLP-based drugs for treating diabetes and obesity, with contributions by many from academia and industry.

GLP-1 receptor agonist

At least 13 GLP-1RA have been approved by the FDA to treat diabetes and/or obesity. This type of drugs is structurally similar to GLP-1 and can enhance the GLP-1 signaling of insulin release.

DPP-4 inhibitors

The emerging oral drug "DPP-4 inhibitors" can block the degradation of GLP-1 (7-37) by DPP-4, thereby prolonging the function of GLP-1 (7-37) in promoting insulin secretion.

These two types of drugs regulate blood sugar physiologically and can effectively minimize side effects compared to conventional insulin injection therapy!

More possibilities with GLP-1

- GLP-1-based therapeutics have recently become blockbuster drugs to treat obesity and diabetes. Besides the physiological effects on the pancreas and stomach, GLP-1 has also been found to suppress appetite through the hypothalamus.

- Researches on GLP-1 continue to reveal the far-reaching potential of GLP-1 for physiological regulation on many other organs, with promising future prospects.

- This is an exemplary story of translating basic research into pharmaceutical success with major impacts on human health.