



GLP-1

Animal models were essential to discovering and developing GLP-1 receptor agonists, drugs now transforming treatment for type 2 diabetes and obesity. These therapies mimic a hormone that regulates blood sugar, insulin and appetite. Here's how animal research played a role.

Discovery Phase: A Fishing Expedition Leads to a Breakthrough

- In the late 1970s, Dr. Joel Habener's team at Mass General sought precursors for **pancreatic hormones** like glucagon. NIH rules restricted early recombinant DNA use in warm-blooded animals, so the [team studied anglerfish](#), a cold-blooded species exempt from the rules.
- In anglerfish, pancreatic endocrine cells are concentrated in the **Brockmann body**, making hormones easier to isolate. Habener's team identified proglucagon — the precursor to glucagon — and discovered it also encoded a new hormone, **glucagon-like peptide-1 (GLP-1)**. GLP-1 stimulates insulin and blocks glucagon — the foundation of today's GLP-1–based therapies.

Drug Design and Mechanism Testing

- **Diabetic rats** helped show how GLP-1 signals pancreatic endocrine cells to control blood sugar and appetite. **Obese mice** showed how GLP-1 impacts weight loss, satiety and metabolism.
- A key discovery came from an unlikely source: **the Gila monster**. In the 1990s, scientists found a compound in its saliva called exendin-4, a naturally occurring GLP-1 receptor agonist. This led to the development of exenatide, the first GLP-1 receptor agonist the FDA approved.

Nonhuman Primate Preclinical Studies

- **Nonhuman primates (NHPs)** helped determine how long-acting GLP-1 drugs are metabolized and cleared, guiding dosing and delivery.
- NHPs were also key to confirming drug safety, including the safety of long-acting GLP-1 drugs like **semaglutide**. They helped identify side effects to meet FDA safety requirements.
- **Long-tailed and rhesus macaque monkeys** helped test **metabolism, pancreatic function and cardiovascular effects**.

Additional Preclinical Studies

- **Dogs and pigs** were studied for cardiovascular and gastrointestinal safety. **Rabbits and hamsters** also contributed key safety and **pharmacokinetic data** supporting FDA approval.
- The FDA approved **exenatide** in 2005, followed by **liraglutide** and **semaglutide** (such as Ozempic and Wegovy). These drugs now **help millions** manage diabetes and obesity.

2024 Lasker Award Recognizes GLP-1 Breakthrough

- In 2024, **Drs. Joel Habener, Svetlana Mojsov and Lotte Bjerre Knudsen** received a [Lasker-DeBakey award](#) for discovering and developing GLP-1–based therapies.
- Their achievement rested on decades of research with animal models — from **anglerfish** to **primates** — that made GLP-1 therapies possible.