PEPTIDES FOR DIABETES RESEARCH

In 2014, according to data from the WHO, 422 million adults (or 8.5% of the population) had diabetes mellitus, a chronic metabolic disorder characterized by hyperglycemia, compared with 108 million (4.7%) in 1980. Diabetes mellitus can be divided into two main types, type 1 or insulin-dependent diabetes mellitus (IDDM) and type 2, or non insulin-dependent diabetes mellitus (NIDDM). The absolute lack of insulin, due to destruction of the insulin producing pancreatic β-cells, is the particular disorder in type 1 diabetes. Type 2 diabetes is mainly characterized by the inability of cells to respond to insulin. The condition affects mostly the cells of muscle and fat tissue, and results in a condition known as „insulin resistance“.

Introduction
Diabetes was already known in ancient times. The name of this disease was created by the Graeco-Roman physician Aretaeus of Cappadocia (approx. 80 - 130 AD) and is derived from the Greek word diabainein that means „to flow through“. The adjective melilitus, which comes from Latin and means „honey-sweet“, was added by the German physician Johann Peter Frank (1745-1821). It was introduced in order to distinguish diabetes mellitus, also called „sugar diabetes“, from diabetes insipidus, where an excessive amount of urine is produced as a result of a disturbance of the hormonal control of reabsorption of water in the kidneys. In 1889, pancreatic secretions were shown to control blood sugar levels. However, it took another 30 years until insulin was purified from the islets of Langerhans. In the following 50 years scientists detected the system-wide effects of insulin in liver, muscle, and adipose tissues. In the 1970s, the insulin receptor was discovered, and 10 years later, its tyrosine kinase activity was demonstrated. Despite this steady progress, one of the most challenging health problems of the 21st century remains the dramatic increase in diabetes mellitus that
is occurring throughout the world. Today diabetes mellitus is one of the main causes of death in most developed countries. According to data from the International Diabetes Federation, more than 382 million people around the world suffered from diabetes in 2013. This alarming number could reach 592 million by 2035. Further 316 million people have impaired glucose tolerance, a condition that can signal oncoming diabetes. 85 - 95 % of the diabetics have type 2 diabetes, a chronic disease associated with insulin deficiency and insulin resistance. Complications seen with diabetes range from heart disease (2 to 4 times higher occurrence than in non-diabetics) to blindness, kidney disease, amputations, nerve damage and erectile dysfunction. As obesity spreads, the number of type 2 diabetics rises. Over 80% of diabetics are obese. Consequently, the treatment of risk factors such as obesity, hypertension, and hyperlipidemia assumes major importance and must be coordinated with a good glycemic control for the reduction in total mortality in type 2 diabetes mellitus. In this monograph, we describe the pancreatic and gastrointestinal peptide hormones that are involved in the control of blood glucose, the classification, and the treatment of diabetes mellitus.

Pancreatic Peptide Hormones

The islets of Langerhans contain four main cell types: β-cells secreting insulin, α-cells secreting glucagon, δ-cells secreting somatostatin and γ-cells secreting pancreatic polypeptide (PP). The core of each islet contains mainly the β-cells surrounded by a mantle of α-cells interspersed with δ-cells or γ-cells. Insulin is synthesized as a preprohormone in the β-cells of the islets of Langerhans. Removal of its signal peptide during insertion into the endoplasmic reticulum generates proinsulin which consists of 3 domains: an amino-terminal B-chain, a carboxy-terminal A-chain and a connecting peptide known as C-peptide. Within the endoplasmic reticulum proinsulin is exposed to several specific endopeptidases. These enzymes excise the C-peptide, thereby generating the mature form of insulin, a small protein consisting of an A-chain of 21 amino acids (containing an internal disulfide bridge) linked by two disulfide bridges to a B-chain of 30 amino acids. β-Cells secrete insulin in response to a rising level of circulating glucose. The normal fasting blood glucose concentration in humans and most mammals is 80 to 90 mg per 100 ml, associated with very low levels of insulin secretion. After a meal, excess sugars must be stored so that energy reserves will be available later on. Excess glucose is sensed by β-cells in the pancreas, which respond by secreting insulin into the bloodstream. Insulin causes various cells in the body to store glucose (see Fig. 1):

• Insulin stimulates skeletal muscle fibers to convert glucose into glycogen. It also induces the synthesis of proteins from amino acids circulating in the blood.
• Insulin acts on liver cells. It stimulates them to take up glucose from the blood converting it into glycogen while inhibiting the production of the enzymes involved in glycogenolysis.
• Insulin acts on fat cells to stimulate the uptake of glucose and the synthesis of fat.

C-Peptide is applied as a diagnostic tool. It is released in amounts equal to insulin, so the level of C-peptide in the blood indicates how much insulin is being produced by the pancreas. The concentration of C-peptide is measured in diabetics to differentiate between endogenous (produced by the body) and exogenous (injected into the body) insulin, since synthetic insulin does not contain the C-peptide. Inappropriate use of insulin in persons with a low blood sugar level results in a low C-peptide level. The C-peptide level can also be determined in patients with type 2 diabetes showing how much insulin is produced by the β-cells. Abnormal high amounts of C-peptide can indicate the presence of a tumor called insulinoma which secretes insulin. β-Cells also secrete a peptide hormone known as islet amyloid polypeptide (IAPP).
Peptides and Diabetes

or amylin. This 37 amino acid peptide is structurally related to calcitonin and has weak calcitonin-like effects on calcium metabolism and osteoclast activity. Amylin shows about 50% sequence identity with calcitonin gene-related peptide (CGRP). It is stored together with insulin in the secretory granules of β-cells and is co-secreted with insulin. Amylin’s most potent actions include the slowing of gastric emptying and the suppression of postprandial glucagon secretion. The hormone also reduces food intake and inhibits the secretion of gastric acid and digestive enzymes.

Thus, there is therapeutic potential of IAPP agonists for the treatment of patients with absolute amylin deficiency (type 1 diabetes) or relative amylin deficiency (type 2 diabetes).

In addition, amylin is the major component of the pancreatic amyloid deposits occurring in the pancreas of patients with type 2 diabetes.

Glucagon secretion is stimulated by low, and inhibited by high concentrations of glucose and fatty acids in the plasma (see Fig. 1). It counterbalances the action of insulin, increasing the levels of blood glucose and stimulating the protein breakdown in muscle. Glucagon is a major catabolic hormone, acting primarily on the liver. The peptide stimulates glycogenolysis (glycogen breakdown) and gluconeogenesis (synthesis of glucose from non-carbohydrate sources), inhibits glycogenesis (glycogen synthesis) and glycolysis, overall increasing hepatic glucose output and ketone body formation. In people suffering from diabetes, excess secretion of glucagon plays a primary role in hyperglycemia (high blood glucose concentration). Glucagon is clinically used in the treatment of hypoglycemia in unconscious patients (who can’t drink). Somatostatin release from the pancreas and gut is stimulated by glucose and amino acids. In diabetes, somatostatin levels are increased in pancreas and gut, presumably as a consequence of insulin deficiency. Somatostatin inhibits secretion of growth hormone, insulin and glucagon.
Gastrointestinal Peptide Hormones

Glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide 1 (GLP-1) have significant effects on insulin secretion and glucose regulation. They are released after ingestion of carbohydrate- and fat-rich meals and stimulate insulin secretion postprandially. Both gut hormones constitute the class of incretins and share considerable sequence homology. GIP is a single 42 amino acid peptide derived from a larger 153 amino acid precursor (see Fig. 2). The peptide was originally observed to inhibit gastric acid secretion (hence it was designated gastric inhibitory polypeptide). Subsequent studies have demonstrated potent glucose-dependent insulin stimulatory effects of GIP administration in dogs and rodents. GIP also regulates fat metabolism in adipocytes, including stimulation of lipoprotein lipase activity, fatty acid incorporation, and fatty acid synthesis. Unlike GLP-1, GIP does not inhibit glucagon secretion or gastric emptying. The peptide promotes β-cell proliferation and cell survival in islet cell line studies.

GLP-1 is derived from the product of the proglucagon gene. This gene encodes a preproprotein (see Fig. 3) that is differentially processed dependent on the tissue in which it is expressed. In pancreatic α-cells, prohormone convertase 2 action leads to the release of glucagon. In the gut, prohormone convertase 1/3 action leads to the release of several peptides including GLP-1. Bioactive GLP-1 consists of two forms: GLP-1 (7-37) and GLP-1 (7-36) amide. The latter form constitutes the majority (80%) of the circulating GLPs.

The primary physiological responses to GLP-1 are glucose-dependent insulin secretion, inhibition of glucagon secretion and inhibition of gastric acid secretion and gastric emptying. All effects of GLP-1 are exerted by activation of the GLP-1 receptor, a seven transmembrane spanning G-protein-coupled receptor (GPCR), leading to increased cAMP production and enhanced protein kinase A (PKA) activity.

The potential use of GLP-1 for the treatment of diabetes has been considered. GLP-1 exerts antidiabetogenic properties in subjects with type 2 diabetes by stimulating insulin secretion, increasing β-cell mass, inhibiting glucagon secretion, delaying gastric emptying, and inducing satiety, thus slowing the entry of sugar into the blood. However, GLP-1 is rapidly degraded by the enzyme dipeptidyl peptidase IV (DPP IV), making it unattractive as a therapeutic agent. Successful strategies to overcome this difficulty are the use of DPP IV-resistant GLP-1 receptor agonists, such as liraglutide (NN2211, a fatty acid-linked DPP IV-resistant derivative of GLP-1) or exendin-4 (ex-
enatide). An alternative approach is the use of inhibitors of DPP IV, such as sitagliptin, P32/98 (H-Ile-thiazolidide hemifumarate), NVP DPP 728 (N-[2-[(5-Cyanopyridin-2-yl-amino)ethyl]-Gly-Pro-nitrile) and the Gly-Pro-nitrile-derived compounds vildagliptin and saxagliptin.

Exendin-4 is a peptide hormone found in the saliva of the Gila monster, a lizard native to several Southwestern American states. Like GLP-1 exendin-4 exerts its effects through the GLP-1 receptor but is much more potent than GLP-1. Exenatide, a synthetic form of exendin-4 has been approved by the FDA as an antidiabetic drug. In contrast to most drugs that work by only one mechanism, exendin-4 acts by multiple mechanisms, such as stimulation of insulin secretion, slowing gastric emptying, and inhibiting the production of glucose by the liver. Furthermore, exendin-4 was shown to suppress appetite and promote weight loss.

Classification of Diabetes Mellitus

The International Diabetes Federation distinguishes between three main types of diabetes mellitus. This division is based upon whether the ‘blood sugar problem’ is caused by insulin deficiency or insulin resistance:

Type 1 diabetes (formerly known as insulin-dependent diabetes mellitus or juvenile-onset diabetes) is a β-islet cell specific, T-lymphocyte-mediated autoimmune disorder. It is characterized by a failure of the pancreas to produce sufficient insulin. Without insulin to promote the cellular uptake of glucose, the blood glucose concentrations reach high levels. At concentrations above 10 mM, renal tubular reabsorption is saturated and glucose is passed into the urine. The classic symptoms are excessive secretion of urine, thirst, weight loss and tiredness.

It is known that multiple genes contribute to the familial clustering of this disease, the major histocompatibility complex (MHC) being the most important of these. The MHC class 2 genotype is one of the strongest genetic factors determining disease susceptibility.

Type 2 diabetes (formerly named non-insulin-dependent diabetes mellitus or maturity-onset diabetes) is associated with insulin resistance rather than the lack of insulin as seen in type 1 diabetes. This lack of insulin sensitivity results in higher than normal blood glucose levels.

Type 2 diabetes is not HLA-linked and no autoimmune destruction of the pancreatic cells is observed. The development of type 2 diabetes seems to be multifactorial. Genetic predisposition appears to be the strongest factor. Other risk factors are obesity and high caloric intake. Pancreatic α-cell mass is increased, followed by an exaggerated response of glucagon to amino acids and an impaired suppression of glucagon secretion by hyperglycemia. Increased hepatic production of glucose with a failure of the pancreas to adapt to this situation and resistance to the action of insulin are characteristic features of this disorder. Another important morphological feature is the amyloid deposition in islets. These deposits consist of islet amyloid polypeptide or amylin, that is believed, to originate in the β-cell secretory granule.

Type 2 diabetes occurs most frequently in adults, but is being noted increasingly in adolescents as well. Type 2 diabetes develops slowly and the symptoms are usually less severe than in type 1. Sometimes the disease is only diagnosed several years after its onset, when complications are already present. Common late microvascular complications include retinopathy, nephropathy, and peripheral and autonomic neuropathies. Macrovascular complications include atherosclerotic coronary peripheral arterial disease.

Gestational diabetes may be observed in non-diabetic women during late pregnancy. They develop a resistance to insulin and, subsequently, high blood glucose. This type of diabetes is probably caused by hormones produced by the placenta. The blood glucose level has to be carefully controlled as to minimize risks for mother and child, it will return to the normal value after birth.

Treatment of Diabetes Mellitus

Insulin is essential for the treatment of type 1 diabetes. The effects of insulin and its mechanism of action are described above. For clinical application, either porcine or bovine insulin was given formerly. Today, human insulin (produced recombinantly) is used. A new approach is the production of
orally active insulin using modifications to make insulin resistant to enzymatic breakdown, facilitating absorption. Most of the vascular consequences of insulin resistance are due to the hyperglycemia seen in type 2 diabetes. For this reason a major goal of therapeutic intervention in type 2 diabetes is to reduce circulating glucose levels. There are many pharmacological strategies to accomplish these goals:

1) The use of α-glucosidase inhibitors (e.g., acarbose) leads to a reduction in digestion and thereby minimizes the consequent absorption of glucose into the systemic circulation. The reduction in glucose uptake allows the pancreatic β-cells to regulate the insulin secretion more effectively. The advantage of α-glucosidase inhibitors is that they function locally in the intestine and have no major systemic action. Plants are rich sources of α-glucosidase inhibitors, some of which are being evaluated for their therapeutic potential.

2) The sulfonylureas (e.g., glibenclamide) are referred to as endogenous insulin secretagogues because they induce the pancreatic release of insulin and thus reduce plasma glucose. Sulfonylureas function by binding to and inhibiting the pancreatic ATP-dependent potassium channels normally involved in the glucose-mediated insulin secretion. Unwanted side-effects of sulfonylureas are appetite stimulation, probably via their effects on insulin secretion and blood glucose, often leading to weight gain.

3) The biguanides (e.g., metformin) are a class of drugs that lower blood glucose levels by enhancing insulin-mediated suppression of hepatic glucose production (gluconeogenesis) and by enhancing insulin-stimulated glucose uptake by skeletal muscle. Metformin is currently the most widely prescribed insulin-sensitizing drug in clinical use. The major site of action for metformin is the liver. Its use can be contraindicated in patients with liver dysfunction.

4) The thiazolidinediones (e.g., pioglitazone) have been proven useful in treating the hyperglycemia associated with insulin resistance in both type 2 diabetes and non-diabetic conditions. These products function as agonists for the peroxisome proliferator-activated receptor-γ (PPAR-γ). PPARs are members of a nuclear receptor superfamily that has important roles in carbohydrate and lipid metabolism. Thiazolidinediones enhance peripheral sensitivity to insulin and, to a lesser degree, decrease hepatic glucose production by binding to and activating the PPAR-γ. Adverse effects of thiazolidinediones include weight gain, anemia, and abnormalities in liver and enzyme levels. Resistin, an adipocyte-derived peptide, first identified during a search for targets of thiazolidinediones, has been found to be downregulated by thiazolidinediones.

5) GLP-1 analogs stimulate insulin release, inhibit glucagon secretion, slow gastric emptying and stimulate β-cell proliferation. One of the most promising GLP-1 receptor agonists is exenatide (exendin-4) which is 53% identical to human GLP-1 at the amino acid level. The main advantage of exenatide

According to the WHO, the number of people living with diabetes has almost quadrupled since 1980 to 422 million adults.
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is its resistance to cleavage and inactivation by dipeptidyl-peptidase IV (DPP IV). In 2005, the FDA approved exenatide as adjunctive therapy to improve blood sugar control in patients with type 2 diabetes who have not achieved adequate control with metformin and/or a sulfonylurea. Use of the peptide as primary monotherapy was approved in 2009, and a sustained release formulation in 2014. The long-acting GLP-1 agonist liraglutide was approved by the authority for the treatment of type 2 diabetes in 2010. Albilglutide, a DPP IV-resistant GLP-1 dimer bound to albumin was approved by both FDA and European authorities in 2014. FDA-approved dulaglutide is a GLP-1 dimer linked to human immunoglobulin G4. Their half-lives, 4 - 7 days, are in the same range as the half-life of the recently developed GLP-1 analog semaglutide. These peptides are considerably more stable than exenatide.

6) DPP IV inhibitors represent another approach for the treatment of diabetes. Sitagliptin is the first candidate of this novel class of antihyperglycemic agents that has been approved by the FDA. Alogliptin, linagliptin, saxagliptin, and vildagliptin have been approved in the USA and in various countries worldwide. These DPP IV inhibitors can be used either alone or in combination with other oral antihyperglycemic agents (such as metformin or a thiazolidine-dione) for treatment of diabetes mellitus type 2.

7) Pramlintide, a soluble amylin analog, has gained FDA approval as an adjunct to insulin therapy in type 1 and type 2 diabetes. Like amylin, pramlintide acts centrally and decreases glucagon secretion, slows gastric emptying and induces satiety.

8) Insulin therapy is also indicated in the treatment of type 2 diabetes for the management of severe hyperglycemia after failure of oral agents. Long-acting insulin analogs could be obtained by replacement of Asn21 (A-chain) by glycine and addition of two arginine residues (insulin glargine) or acylation of lysine29 (B-chain) with long-chain fatty acids. Insulin degludec was approved in Europe in 2015 for treatment of children and adolescents with diabetes.

9) C-Peptide is biologically active. Clinical studies showed that administration of C-peptide to diabetes type 1 patients lacking the peptide alleviates nerve and renal dysfunctions associated with the disease. A long-acting analog, PEGylated C-peptide, is under evaluation.

Prospects

Although some of the agents described above are still in the early phases of investigation, there is little doubt that the therapy of diabetes will undergo major changes in the near future. It is important to diagnose all type 2 diabetics at an earlier stage (for example by making self-monitoring of blood glucose easier) and begin treatment in an attempt to minimize the diabetes-associated complications.

The identification of the genetic components of type 1 and type 2 diabetes is an important area of research, because elucidation of the diabetes genes will influence all efforts towards an understanding of the disease, its complications, and its treatment, cure, and prevention. For this reason, genomic DNA from subjects with severe insulin resistance has been screened for mutations in genes that are implicated in insulin signaling. Indeed, a mutation in the gene encoding the serine/threonine kinase AKT2 (also known as PKBβ) could be identified. AKT2 is highly expressed in insulin-sensitive tissues and has been implicated in insulin-regulated glucose uptake into muscle and fat cells by promoting the translocation of glucose transporter 4 (GLUT4) to the cell surface.

Advances in genomics, proteomics and metabolomics will help us to further understand the causes of type 1 and type 2 diabetes and could eventually lead to novel therapeutic approaches.
REFERENCES

R.J. Mahler and M.L. Adler

L.B. Knudson et al.

A.D. Baron et al.

D.J. Drucker

J.J. Holst
Gastric inhibitory polypeptide analogues: do they have a therapeutic role in diabetes mellitus similar to that of glucagon-like peptide-1? BioDrugs 16, 175-181 (2002)

J.J. Holst

S. Yakar et al.

B. Ahren

D.J. Drucker

J.M. Egan et al.

R.I.G. Holt et al.

G.G. Holz and O.G. Chepurny

G. Jiang and B.B. Zhang

T.J. Kieffer

L. Marzban et al.

R.G. McTernan et al.

J.J. Meier et al.

N. Moller et al.

T. Perry and N.H. Greig

B. Thorens

T. Vahl and D. D’Alessio

M.F. White

P.E. Wiedeman and J.M. Trevillyan

Y. Dor et al.

E.A. Gale et al.

S. George et al.
Peptides and Diabetes

J.F. List and J.F. Habener
Glucagon-like peptide 1 agonists and the development and growth of pancreatic beta-cells.

L.L. Nielsen et al.
Pharmacology of exenatide (synthetic exendin-4): a potential therapeutic for improved glycemic control of type 2 diabetes.

A. Nourparvar et al.
Novel strategies for the pharmacological management of type 2 diabetes.

S.M. Rangwala and M.A. Lazar
Peroxisome proliferator-activated receptor γ in diabetes and metabolism.

Y. Sato et al.
C-peptide fragments stimulate glucose utilization in diabetic rats.

T.P. Vahl and D.A. D’Alessio
Gut peptides in the treatment of diabetes mellitus.

J.F. Gautier et al.
Biological actions of the incretins GIP and GLP-1 and therapeutic perspectives in patients with type 2 diabetes.
Diabetes Metab. 31, 233-242 (2005)

E.M. Sinclair and D.J. Drucker
Proglucagon-derived peptides: mechanisms of action and therapeutic potential.
Physiology 20, 357-365 (2005)

D.J. Drucker and M.A. Nauck
The incretin system: glucagon-like peptide-1 receptor agonists and dipeptidyl peptidase-4 inhibitors in type 2 diabetes.

K. Fujioka
Pathophysiology of type 2 diabetes and the role of incretin hormones and beta-cell dysfunction.
JAAPA Suppl, 3-8 (2007)

R. Gadsby
New treatments for type 2 diabetes - the DPP4 inhibitors.
Prim. Care Diabetes 1, 209-211 (2007)

J. Meece
Pancreatic islet dysfunction in type 2 diabetes: a rational target for incretin-based therapies.

J. Wahren et al.
C-Peptide is a bioactive peptide.
Diabetologia 50, 503-509 (2007)

A.M. Abbatecola et al.
New approaches to treating type 2 diabetes mellitus in the elderly: role of incretin therapies.
Drugs Aging 25, 913-925 (2008)

S.E. Inzucchi and D.K. McGuire
Circulation 117, 574-584 (2008)

A.M. Lambeir et al.
DPP4 inhibitors for diabetes - what next?
Biochem. Pharmacol. 76, 1637-1643 (2008)

Y. Ng et al.
Rapid activation of Akt2 is sufficient to stimulate GLUT4 translocation in 3T3-L1 adipocytes.
Cell. Metab. 7, 348-356 (2008)

P.R. Flatt et al.
Recent advances in antidiabetic drug therapies targeting the entero-insular axis.
Curr. Drug Metab. 10, 125-137 (2009)

R. Gupta et al.
Emerging drug candidates of dipeptidyl peptidase IV (DPP IV) inhibitor class for the treatment of type 2 diabetes.

F.K. Knop et al.
Incretin-based therapy of type 2 diabetes mellitus.

T. Salvatore et al.

W. Benalla et al.
Antidiabetic medicinal plants as a source of alpha glucosidase inhibitors.
Curr. Diab. Rev. 6, 87-100 (2010)

J. Gerich
DPP-4 inhibitors: what may be the clinical differentiators?

Y. Seino et al.
GIP and GLP-1, the two incretin hormones: Similarities and differences.
J. Diabetes Investig. 1, 8-23 (2010)

B. Ahren
The future of incretin-based therapy: novel avenues - novel targets.
Diabetes Obes. Metab. 13 Suppl 1, 158-166 (2011)

M.J. Davies et al.
Liraglutide - overview of the preclinical and clinical data and its role in the treatment of type 2 diabetes.
Diabetes Obes. Metab. 13, 207-220 (2011)
As with humans, diabetes has become a growing problem with dogs and cats in recent years due to their increasing life expectancy in combination with obesity and lack of exercise.

Despite the steady progress in research, the dramatic spread of diabetes mellitus which is observed throughout the world remains one of the most challenging health problems of the 21st century. Today, diabetes mellitus is one of the main causes of death in most developed countries.
### Peptides and Diabetes

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<tr>
<td>I. Kanazawa</td>
<td>Osteocalcin as a hormone regulating glucose metabolism.</td>
<td>World J. Diabetes 6, 1345-1354 (2015)</td>
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**AMYLIN (IAPP)**

Amylin (human)  
H-7905  
KCNTATCATQLANFLVHSSNNFGAILSTNVGSNTY-NH₂  

Amylin (free acid) (human) NEW  
H-7692  
KCNTATCATQLANFLVHSSNNFGAILSTNVGSNTY

Biotinyl-Amylin (human)  
H-7398  
Biotinyl-KCNTATCATQLANFLVHSSNNFGAILSTNVGSNTY-NH₂

5-FAM-Amylin (human)  
H-7392  
Fluorescein-5-carbonyl-KCNTATCATQLANFLVHSSNNFGAILSTNVGSNTY-NH₂

Amylin (1-13) (human)  
H-5708  
KCNTATCATQLA

Amylin (8-37) (human)  
H-2742  
ATQRLANFLVHSSNNFGAILSTNVGSNTY-NH₂

Acetyl-Amylin (8-37) (human)  
H-2744  
Ac-ATQRLANFLVHSSNNFGAILSTNVGSNTY-NH₂

Amylin (14-20) (human) NEW  
H-8094  
NFLVHSS

Amylin (20-29) (human)  
H-3746  
SNNFGAILSS

Amylin (mouse, rat)  
H-9475  
KCNTATCATQLANFLVHSSNNLGPVLPPTNVGSNTY-NH₂

Biotinyl-Amylin (mouse, rat)  
H-7394  
Biotinyl-KCNTATCATQLANFLVHSSNNLGPVLPPTNVGSNTY-NH₂

5-FAM-Amylin (mouse, rat)  
H-7396  
Fluorescein-5-carbonyl-KCNTATCATQLANFLVHSSNNLGPVLPPTNVGSNTY-NH₂

**C-PEPTIDE**

(Tyr⁹)-C-Peptide (dog)  
H-2914  
YEVEDLQVRDVELAGAPGEGQLOPLALE

C-Peptide (human) NEW  
(Acetate salt)  
H-7722  
EAEDLOQVQVELGGPGAGSLQPLALEGSLQ (Acetate salt)

C-Peptide (human)  
(Trifluoroacetate salt)  
H-2470  
EAEDLOQVQVELGGPGAGSLQPLALEGSLQ (trifluoroacetate salt)

(Tyr⁹)-C-Peptide (human)  
H-4934  
YEAEQVQVELGGPGAGSLQPLALEGSLQ

([D₉]Val¹⁸⁰)-C-Peptide (human)  
H-4242  
EAEDLOQ[D₉]VQ[VQ][D₈]VELGGPGAGSLQ-PLALEGSLQ

Proinsulin C-Peptide (31-63) (porcine)  
H-2142  
RREAENPQAGAVELGGGLQLQALLEGPPKQKR
**EXENDIN**

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**C-PEPTIDE (CONTINUED)**

**Proinsulin C-Peptide (55–89) (human)**

H-1800
RGREAELQVGQLVAGPSQGLQPLA-LGSGLQKR

**Tyr-Proinsulin C-Peptide (55–89) (human)**

H-2465
YRGREAELQVGQLVAGPSQGLQPLA-LGSGLQKR

**C-Peptide 1 (rat)**

H-6136
EVEDPQVQPELGPGAGDLQTLAL-EVARQ

**C-Peptide 2 (rat)**

H-6122
EVEDPQVQLELGPGAGDLQTLAL-EVARQ

**EXENDIN**

**Exenatide** *(Exendin-4)*

H-8730
HGEFTSDLKQMEEEAVRL-FIEWLKNQGGPSSGAPPNS-NH₂

**Acetyl-Exenatide**

H-7488
Ac-HGEFTSDLKQMEEEAVRL-FIEWLKNQGGPSSGAPPNS-NH₂

**(D-Asn²⁸)**-Exenatide

H-8192
HGEFTSDLKQMEEEAVRL-FIEWLKNQGGPSSGAPPNS-NH₂

**(Asp²⁸)**-Exenatide

H-7496
HGEFTSDLKQMEEEAVRL-KFIEWLKNQGGPSSGAPPNS-NH₂

**(D-Asp²⁸)**-Exenatide

H-8184
HGEFTSDLKQMEEEAVRL-KFIEWLKNQGGPSSGAPPNS-NH₂

**β**-(Des-Gly²⁸)-Exenatide

H-7486
HGEFTSDLKQMEEEAVRL-FIEWLKNQGGPSSGAPPNS-NH₂

**Endo-38a-Pro-Exenatide**

H-7492
HGEFTSDLKQMEEEAVRL-FIEWLKNQGGPSSGAPPNS-NH₂

**(D-His¹)**-Exenatide

H-7494
HGEFTSDLKQMEEEAVRL-FIEWLKNQGGPSSGAPPNS-NH₂

**(Met(O)¹⁴)**-Exenatide *(Exendin-4 sulfoxide)*

H-7498
HGEFTSDLKQMEEEAVRL-FIEWLKNQGGPSSGAPPNS-NH₂

**Glu³**-Exenatide *(2–39)* NEW

H-7544
HGEFTSDLKQMEEEAVRL-FIEWLKNQGGPSSGAPPNS-NH₂

**Exendin-3**

H-8735
HSDGFTSDLKQMEEEAVRL-FIEWLKNQGGPSSGAPPNS-NH₂

**Exendin-4 (1–8)**

H-6454
HGEFTFTS-NH₂

**Exendin-4 (3–39)**

H-3864
HGEFTSDLKQMEEEAVRL-FIEWLKNQGGPSSGAPPNS-NH₂
GLUCAGON, GRPP, OXYNTOMODULIN

**Glucagon (1-29) (human, rat, porcine)**

- **(human, rat, porcine)**
  - H-6790
  - HSQGTFSDSKYLDSRRAQD-FVQWLMT

- **(human, rat, porcine) (Acetate salt)** NEW
  - H-7754
  - HSQGTFSDSKYLDSRRAQD-FVQWLMT (Acetate salt)

- **([13C6]Leu14)-Glucagon (1-29) (human, rat, porcine)** NEW
  - H-7236
  - HSQGTFSDSKY[13C6]LDSRRAQD-FVQWLMT

**Biotinyl-Glucagon (1-29) (human, rat, porcine)**

- **(human, rat, porcine)**
  - H-8258
  - HSEGFTSDSKYLDSRRAEDFVQWLMT

**Bio-Γ-Glucagon (1-29) (human, rat, porcine)**

- **(human, rat, porcine)**
  - H-8258
  - HSEGFTSDSKYLDSRRAEDFVQWLMT

**Lixisenatide**

- **((Des-Pro³⁸)-Exendin-4(-Lys)₆ amide)**
  - H-7426
  - HGEGTFTSDSKQMEEEAVRL-FIEWLKNMGPGAPPSKKKKNH₂

**Exendin (9-39)**

- **H-8740**
  - DLSDKQMEEEAVRLFIEWLKNMGPGASPPS-NH₂

**Exendin (CONTINUED)**

**Gastric Inhibitory Polypeptide (human)**

- **(Glucose-Dependent Insulinotropic Polypeptide (human), GIP (human))**
  - H-5645
  - YAEGTFISDYIAMDHIQDFVNLWLAQKGGKNDWKHNITQ

- **(D-Ala²)-Gastric Inhibitory Polypeptide (human) NEW**
  - H-7586
  - YaEGTFISDYIAMDHIQDFVNLWLAQKGGKNDWKHNITQ

- **(Pro³)-Gastric Inhibitory Polypeptide (human) NEW**
  - H-7584
  - YAPGTFISDYIAMDHIQDFVNLWLAQKGGKNDWKHNITQ

**Gastric Inhibitory Polypeptide (6-30) amide (human)**

- **H-6102**
  - FISDYIAMDHIQDFVNLWLAQK-NH₂

**Gastric Inhibitory Polypeptide (porcine)**

- **(Glucose-Dependent Insulinotropic Polypeptide (porcine), GIP (porcine))**
  - H-3824
  - YAEGTFISDYIAMDHIQDFVNLWLAQK-NH₂

**Gastric Inhibitory Polypeptide (1-30) amide (porcine)**

- **(Glucose-Dependent Insulinotropic Polypeptide (porcine), GIP (porcine))**
  - H-3824
  - YAEGTFISDYIAMDHIQDFVNLWLAQK-NH₂

**Gastric Inhibitory Polypeptide (3-42) (human)**

- **H-6614**
  - EGTFISDYIAMDHIQDFVNLWLAQK-GKKNDWKHNITQ

**Exendin (9-39)**

- **H-8740**
  - DLSDKQMEEEAVRLFIEWLKNMGPGASPPS-NH₂

**Lixisenatide**

- **((Des-Pro³⁸)-Exendin-4(-Lys)₆ amide)**
  - H-7426
  - HGEGTFTSDSKQMEEEAVRL-FIEWLKNMGPGAPPSKKKKNH₂
GLUCAGON-LIKE PEPTIDES

GLP-1 (1-36) amide (human, bovine, guinea pig, mouse, rat)
H-6025
HDEFERHAEGTFSDVSSYLEGQAAKEFIAWLVKGR-NH₂

GLP-1 (1-37) (human, bovine, guinea pig, mouse, rat)
H-5552
HDEFERHAEGTFSDVSSYLEGQAAKEFI-AWLVKGRG

GLP-1 (7-36) amide (chicken, common turkey)
H-5824
HAEGTYTSDITSYLEGQAAKEFI-AWLVPN-GR-NH₂

GLP-1 (7-36) amide (human, bovine, guinea pig, mouse, rat)
H-6795
HAEGTFSDVSSYLEGQAAKEFI-AWLVKGR

GLP-1 (7-36)-Lys(biotinyl) amide (human, bovine, guinea pig, mouse, rat)
H-5956
HAEGTFSDVSSYLEGQAAKEFI-AWLVKGRK(biotinyl)-NH₂

GLP-1 (7-36)-Lys(6-FAM) amide (human, bovine, guinea pig, mouse, rat)
H-5954
HAEGTFSDVSSYLEGQAAKEFI-AWLVKGRK(fluorescein-6-carboxyl)-NH₂

GLP-1 (19-29) amide (human, rat, porcine)
H-2758
AQDFVQWLMNT

GLP-1 (1-36) amide (human, bovine, guinea pig, mouse, rat) NEW
H-8262
HSQGTFTSDYKLDSSRAQDFVQWLMT-NH₂

GLP-1 (1-37) (human, rat, porcine) NEW
H-8266
HSQGTFTSDYKLDSSRAQDFVQWLMT

(GLu²⁰)-Glucagon (1-29) (human, rat, porcine)
H-8262
HSQGTFTSDYKLDSSRAQDFVQWLMT-NH₂

(Glu²⁴)-Glucagon (1-29) (human, rat, porcine)
H-8266
HSQGTFTSDYKLDSSRAQDFVQWLMT

(Des-Thr⁵)-Glucagon (human, rat, porcine)
H-6156
HSQGTFTSDYKLDSSRAQDFVQWLMT

(Des-Thr⁷)-Glucagon (human, rat, porcine)
H-6158
HSQGTFTSDYKLDSSRAQDFVQWLMT

(Met(O)₂⁷)-Glucagon (1-29) (human, rat, porcine)
H-6148
HSQGTFTSDYKLDSSRAQDFVQWLMT

(GLu²⁰)-Glucagon (1-29) (human, rat, porcine) NEW
H-8262
HSQGTFTSDYKLDSSRAQDFVQWLMT-NH₂

(GLu²⁴)-Glucagon (1-29) (human, rat, porcine)
H-8266
HSQGTFTSDYKLDSSRAQDFVQWLMT

(Des-His¹,Glu⁹)-Glucagon (1-29) amide (human, rat, porcine)
H-2754
SQGTFTSEYKLDSSRAQDFVQWLMT-NH₂

(Des-Thr⁵)-Glucagon (human, rat, porcine)
H-6156
HSQGTFTSDYKLDSSRAQDFVQWLMT

(Des-Thr⁷)-Glucagon (human, rat, porcine)
H-6158
HSQGTFTSDYKLDSSRAQDFVQWLMT

Met(O)₂⁷)-Glucagon (1-29) (human, rat, porcine)
H-6148
HSQGTFTSDYKLDSSRAQDFVQWLMT

(GLu²⁰)-Glucagon (1-29) (human, rat, porcine) NEW
H-8262
HSQGTFTSDYKLDSSRAQDFVQWLMT-NH₂

(GLu²⁴)-Glucagon (1-29) (human, rat, porcine)
H-8266
HSQGTFTSDYKLDSSRAQDFVQWLMT

(Des-His¹,Glu⁹)-Glucagon (1-29) amide (human, rat, porcine)
H-2754
SQGTFTSEYKLDSSRAQDFVQWLMT-NH₂

(Des-Thr⁵)-Glucagon (human, rat, porcine)
H-6156
HSQGTFTSDYKLDSSRAQDFVQWLMT

(Des-Thr⁷)-Glucagon (human, rat, porcine)
H-6158
HSQGTFTSDYKLDSSRAQDFVQWLMT

Met(O)₂⁷)-Glucagon (1-29) (human, rat, porcine)
H-6148
HSQGTFTSDYKLDSSRAQDFVQWLMT

(GLu²⁰)-Glucagon (1-29) (human, rat, porcine) NEW
H-8262
HSQGTFTSDYKLDSSRAQDFVQWLMT-NH₂

(GLu²⁴)-Glucagon (1-29) (human, rat, porcine)
H-8266
HSQGTFTSDYKLDSSRAQDFVQWLMT

(Des-His¹,Glu⁹)-Glucagon (1-29) amide (human, rat, porcine)
H-2754
SQGTFTSEYKLDSSRAQDFVQWLMT-NH₂

(Des-Thr⁵)-Glucagon (human, rat, porcine)
H-6156
HSQGTFTSDYKLDSSRAQDFVQWLMT

(Des-Thr⁷)-Glucagon (human, rat, porcine)
H-6158
HSQGTFTSDYKLDSSRAQDFVQWLMT

Met(O)₂⁷)-Glucagon (1-29) (human, rat, porcine)
H-6148
HSQGTFTSDYKLDSSRAQDFVQWLMT

(GLu²⁰)-Glucagon (1-29) (human, rat, porcine) NEW
H-8262
HSQGTFTSDYKLDSSRAQDFVQWLMT-NH₂

(GLu²⁴)-Glucagon (1-29) (human, rat, porcine)
H-8266
HSQGTFTSDYKLDSSRAQDFVQWLMT

(Des-His¹,Glu⁹)-Glucagon (1-29) amide (human, rat, porcine)
H-2754
SQGTFTSEYKLDSSRAQDFVQWLMT-NH₂

(Des-Thr⁵)-Glucagon (human, rat, porcine)
H-6156
HSQGTFTSDYKLDSSRAQDFVQWLMT

(Des-Thr⁷)-Glucagon (human, rat, porcine)
H-6158
HSQGTFTSDYKLDSSRAQDFVQWLMT

Met(O)₂⁷)-Glucagon (1-29) (human, rat, porcine)
H-6148
HSQGTFTSDYKLDSSRAQDFVQWLMT

(Glu²⁰)-Glucagon (1-29) (human, rat, porcine) NEW
H-8262
HSQGTFTSDYKLDSSRAQDFVQWLMT-NH₂

(GLu²⁴)-Glucagon (1-29) (human, rat, porcine)
H-8266
HSQGTFTSDYKLDSSRAQDFVQWLMT

(Des-His¹,Glu⁹)-Glucagon (1-29) amide (human, rat, porcine)
H-2754
SQGTFTSEYKLDSSRAQDFVQWLMT-NH₂

(Des-Thr⁵)-Glucagon (human, rat, porcine)
H-6156
HSQGTFTSDYKLDSSRAQDFVQWLMT

(Des-Thr⁷)-Glucagon (human, rat, porcine)
H-6158
HSQGTFTSDYKLDSSRAQDFVQWLMT

Met(O)₂⁷)-Glucagon (1-29) (human, rat, porcine)
H-6148
HSQGTFTSDYKLDSSRAQDFVQWLMT

(GLu²⁰)-Glucagon (1-29) (human, rat, porcine) NEW
H-8262
HSQGTFTSDYKLDSSRAQDFVQWLMT-NH₂

(GLu²⁴)-Glucagon (1-29) (human, rat, porcine)
H-8266
HSQGTFTSDYKLDSSRAQDFVQWLMT

(Des-His¹,Glu⁹)-Glucagon (1-29) amide (human, rat, porcine)
H-2754
SQGTFTSEYKLDSSRAQDFVQWLMT-NH₂

(Des-Thr⁵)-Glucagon (human, rat, porcine)
H-6156
HSQGTFTSDYKLDSSRAQDFVQWLMT

(Des-Thr⁷)-Glucagon (human, rat, porcine)
H-6158
HSQGTFTSDYKLDSSRAQDFVQWLMT

Met(O)₂⁷)-Glucagon (1-29) (human, rat, porcine)
H-6148
HSQGTFTSDYKLDSSRAQDFVQWLMT
GLUCAGON-LIKE PEPTIDES (CONTINUED)

(Ser⁸)-GLP-1 (7-36) amide (human, bovine, guinea pig, mouse, rat)
H-4592
HSEGTFTSDVSSYLEGQAAKEFIAWLVK-GR-NH₂

GLP-1 (7-37) (human, bovine, guinea pig, mouse, rat)
(Acetate salt)
H-9560
HAEGTFTSDVSSYLEGQAAKEFIAWLVK-GRG

GLP-1 (7-37) (human, bovine, guinea pig, mouse, rat)
(Trifluoroacetate salt)
H-5102
HAEGTFTSDVSSYLEGQAAKEFIAWLVK-GRG

GLP-1 (9-36) amide (human, bovine, guinea pig, mouse, porcine, rat)
H-4012
EGTFTSDVSSYLEGQAAKEFIAWLVKGR-NH₂

Liraglutide*
(Acetate salt) NEW
(HN2211, (Lys(y-Glu-palmitoyl)²⁶,Arg³⁴)-GLP-1 (7-37))
H-8148
HAEGTFTSDVSSYLEGQAAKEFIAWLVKGR-

Liraglutide*
(Trifluoroacetate salt)
(HN2211, (Lys(y-Glu-palmitoyl)²⁶,Arg³⁴)-GLP-1 (7-37))
H-6724
HAEGTFTSDVSSYLEGQAAKEFIAWLVKGR-

Semaglutide* NEW
(NN9535, (Aib², Lys(y-Glu-AEEAc-AEEAc-
-17-carboxy-heptadecanoyl)²⁶,Arg³⁴)-GLP-1 (7-37))
H-7894
H-Aib-

GLP-2 (1-33) (human)
(Trifluoroacetate salt)
H-5662
HADGSFSDEMNTILDNLAARDFIN-

GLP-2 (1-34) (human)
H-4766
HADGSFSDEMNTILDNLAARDFIN-

GLP-2 (rat)
H-5002
HADGSFSDEMNTLDNLATRDFIN-

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INSULIN, INSULIN-LIKE GROWTH FACTOR (IGF)

H-Asn-Pro-Glu-Tyr(PO$_3$H$_2$)-OH
H-2706
NPepY

rec IGF-I (human)
H-5555

IGF-I Analog
H-1356
CYAAPLKPAKSC
(Disulfide bond)

IGF-I (1-3)
H-2468
GPE

IGF-I (24-41)
H-3098
YFNKPTGYGSSRRAPQT

IGF-I (30-41)
H-7460
GYGSSRRAPQT

rec IGF-II (1-67) (human)
H-7020
AYRPSETLCGELVDTLQFCGDRGFRYFS-RPASRVSRRSRGIVEECFRSCDLALLE-TCATPAKSE

IGF-II (33-40)
H-7250
SRVSRRSR

Lys-Lys-IRS-1 (891-902) (dephosphorylated) (human)
H-6178
KKKSPGEYVNEFG

Insulin B (22-25)
H-6005
RGFF

RELATED PRODUCTS: DPP IV SUBSTRATES AND INHIBITORS

H-Gly-Pro-AMC · HBr
I-1225
GP-AMC · HBr

H-Gly-Pro-4MβNA
J-1210
GP-MNA

H-Gly-Pro-βNA
K-1335
GP-βNA

H-Gly-Pro-pNA · HCl
L-1880
GP-pNA · HCl

H-Gly-Pro-pNA · p-tosylate
L-1295
GP-pNA · p-tosylate

Diprotin A
H-3825
IPI

Diprotin B
H-5290
VPL
Peptides and Diabetes

**RELATED PRODUCTS: PEPTIDES**

- **Adropin (34-76) (human, mouse, rat)**
  H-6686
  CHSRSADVSDLSESSPNSSPGPCPE-KAPPQKPSPHEGYLQQP

- **(Pyr¹)-Apelin-13 (human, bovine, mouse, rat)**
  H-4568
  <ERPRLSHKGPMF

- **Calcitonin (8-32) (salmon I)**
  H-5502
  VLGKLSQELHKLQTYPRTNTGSTP-NH₂

- **Acetyl-(Asn¹⁰,Tyr³²)-Calcitonin (8-32) (salmon I)**
  (AC187)
  H-4922
  Ac-VLGKLSQELHKLQTYPRTNTGSNTY-NH₂

- **Acetyl-(Asn¹⁰,Tyr³²)-Calcitonin (8-32) (salmon I)**
  (AC187)
  H-4922
  Ac-VLGKLSQELHKLQTYPRTNTGSNTY-NH₂

- **Acetyl-(Asn¹⁰,Tyr³²)-Calcitonin (8-32) (salmon I)**
  (AC187)
  H-4922
  Ac-VLGKLSQELHKLQTYPRTNTGSNTY-NH₂

- **Endotrophin (mouse)**
  H-7382
  TEPLFLTIDICKLSRDAGTCVDFKLL-WHYDLESKSCRFRWYGCGGNNRFH-SQEEECEKMCSPELTV
  (Disulfide bonds, air oxidized)

- **Galanin (1-13)-Mastoparan (Galparan)**
  H-4188
  GWTLNSAGYLLGPNLKAALAKKIL-NH₂

- **Osteocalcin (1-49) (human)**
  H-4912
  YLYQWLGAPVYPDPQL-Gla-PRR-Gla-VC-Gla-LNPDCDELADHGFEAYRFFYGVP
  (Disulfide bond)

- **Galanin (1-13)-Mastoparan (Galparan)**
  H-4188
  GWTLNSAGYLLGPNLKAALAKKIL-NH₂

- **Osteocalcin (1-49) (human)**
  H-4912
  YLYQWLGAPVYPDPQL-Gla-PRR-Gla-VC-Gla-LNPDCDELADHGFEAYRFFYGVP
  (Disulfide bond)

- **Pancreastatin (33-48) (human)**
  H-6506
  EEEEEAVVPQGLFRG-NH₂

- **Phylloseptin-L2**
  H-6704
  FLSLPHVISALSSL-NH₂

- **(Lys¹⁸)-Pseudin-2**
  H-6588
  GLNALKKVFGIHEAIKINHNVQ

- **TRH (Protirelin)**
  H-4915
  <EHP-NH₂

- **(His(3-Me)²)-TRH**
  H-7652
  <EH(3-Me)P-NH₂

- **Pseudin-2**
  H-6586
  GLNALKKVFGIHEAIKINHNVQ

- **N-terminally decarboxylated Osteocalcin (1-49) (human)**
  H-7534
  YLYQWLGAPVYPDPLEPRREVCELNP-DCDELADHGFEAYRFFYGVP
  (Disulfide bond)

- **Xenin 25**
  H-8860
  MLTKFETKSARVGLSFHPKRPWIL
**GENERIC APIs**

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<td>Exenatide Acetate</td>
<td>4044219</td>
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<td>Lixisenatide*</td>
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<td>Glucagon</td>
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**CLINALFA® BASIC**

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<td>U-1270</td>
<td>&lt;ERPRLSHKGPMPF</td>
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<td>U-1160</td>
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<td>GLP-1 (7-36) amide Acetate</td>
<td>U-1190</td>
<td>HAEGLTFTSVSYLEGQAAKEFIAWLVK-GR-NH₂</td>
</tr>
</tbody>
</table>

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Colored transmission electron micrograph (TEM) of a section through two cells of the hormone-secreting islet of Langerhans in the pancreas (the membrane separating the two cells is not seen). At far left and lower right are parts of the nuclei of these cells. The cells contain membrane-bound secretory granules (circular). These contain a dense granular core of hormone (green) separated from the surrounding membrane by a clear space (yellow). The islets of Langerhans secrete insulin and glucagon hormones into the blood, which control blood sugar levels. Magnification: x8700 when printed 10cm wide.

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