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Glucose Regulation Physiology Editing Sample

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Before[1]:

Aiming to develop a fast and inexpensive method for commercial insulin purification, in 1923, Charles Kimball and John Murlin precipitated a pancreatic fraction that, after evaporation and reconstitution in water, had a robust hyperglycemic effect when injected into rabbits and dogs [3]. Because the fraction was incapable of decreasing blood glucose, Kimball and Murlin hypothesized that the hyperglycemic effect resulted from a secreted factor, one that antagonizes insulin's hypoglycemic effect. The factor was named 'the glucose agonist', *or "glucagon" [3]. Over the subsequent decades, substantial research efforts were directed toward unravelling the molecular underpinnings of glucose regulation by the two opposing pancreatic hormones (as reviewed in [4,5]). Among the numerous major discoveries made in this regard was the finding that the hyperglycemic effect of glucagon resides in its ability to act in the liver to stimulate glycogenolysis and gluconeogenesis [[6], [7], [8], [9], [10], [11], [12]] despite its seemingly paradoxical ability to stimulate insulin secretion in humans reported by Ellis Samols in 1965 [13]. In the early 1950's, Earl Sutherland and Christian de Duve demonstrated that pancreatic glucagon production was abolished when the function of islet α-cells was compromised by treatment with either cobalt or synthalin A but was preserved upon alloxan-induced impairment of the exocrine pancreatic acinar and islet β-cells [14,15]. Subsequent histological studies by Claes Hellerstrom and Bo Hellman divided α-cells into α_1-and α_2-subtypes, but it was not until the early 1960s that convincing evidence was provided that α_2-cells were the source of glucagon [16]. This conclusion was based on suppression of α_2-cell numbers in rats and guinea pigs by administration of exogenous glucagon [17,18] plus the strong staining in α_2-cells for tryptophan, which is an amino acid present in glucagon. Later, α_1-cells were shown by Bo Hellman and Ake Lernmark to be the source of an inhibitor of insulin secretion [19]. This was eventually established as somatostatin.*

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After:

In 1923, Charles Kimball and John Murlin set out to develop a fast and inexpensive method to purify commercial insulin, so they precipitated a pancreatic fraction. When it was evaporated and reconstituted in water, the pancreatic fraction had a robust hyperglycemic effect upon experimental rabbits and dogs.[3] Kimball and Murlin hypothesized that the fraction failed to decrease blood glucose because of a secreted factor that opposes insulin's hypoglycemic effect. They called the factor 'the glucose agonist', or "glucagon".[3] Over the subsequent decades, researchers directed substantial efforts toward unravelling the physiology of glucose regulation governed by the two opposing pancreatic hormones. [4,5] One of the major discoveries was that glucagon exerts its hyperglycemic effect by acting in the liver to stimulate the breakdown of glycogen and the synthesis of glucose.[6,7,8,9,10,11,12] This occurs despite being at odds with the finding that glucagon also stimulates insulin secretion in humans, as reported by Ellis Samols[13] in 1965. In the early 1950s, Earl Sutherland and Christian de Duve showed that when islet α-cells were damaged by either cobalt or synthalin A treatment, the pancreas stopped producing glucagon. But when the acinar- and islet β-cells of the pancreas were damaged with alloxan, the pancreas continued producing glucagon.[14,15] Claes Hellerstrom and Bo Hellman later divided α-cells into α_1-and α_2-subtypes, and in the early 1960s, researchers found convincing evidence that α_2-cells were the source of glucagon.[16] Researchers concluded this because they found that when they administered exogenous glucagon in rats and guinea pigs, it suppressed the numbers of α_2-cells in these subjects.[17,18] This coupled with the finding that α_2-cells strongly stain for tryptophan, an amino acid present in glucagon. Later, Bo Hellman and Ake Lernmark showed that α_1-cells were the source of a molecule that inhibits insulin secretion.[19] This came to be known as somatostatin.

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References

1. Müller TD, Finan B, Bloom SR, et al. Glucagon-like peptide 1 (GLP-1). *Mol Metab*. 2019;30:72-130. doi:10.1016/j.molmet.2019.09.010.

Note: *References 3-19 omitted for portfolio purposes.*