

Topic: EURIA Glucagon, RB 310

In 1923 Kimball and Murlin described a hyperglycaemic component in a pancreatic extract which they named glucagon¹, the primary structure of glucagon was published in 1957².

Glucagon is mainly tested for in cases of suspected glucagonoma. In addition, glucagon is an important parameter to measure in relation to the development of different drugs intended for treatment of diabetes type 1 and 2. In the development or functional assessment of a drug, determination of the glucagon/insulin ratio is important. Many drug candidates are derived from incretins such as glucagon-like peptide 1 (GLP-1) and gastric inhibitory polypeptide (GIP). Hence, glucagon is a useful parameter for the Pharma/CRO working in projects within diabetes.

Chemical structure

Glucagon is a 29 amino acid linear peptide hormone, liberated in the cells of the islets of Langerhans. The structure is well conserved in mammals and has been characterized for several mammals such as camel, rat, pig, cow, rabbit and human. The guinea pig is a major exception³, as the difference is entirely related to the C-terminal domain of the peptide⁴. Regarding structure one should also consider the related peptides glicentin and oxyntomodulin, both primarily secreted in the gut.

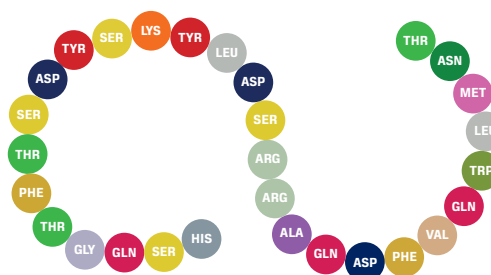


Figure 1. Primary structure of human glucagon.

All three peptides are products of the glucagon gene located on chromosome 2q36, 37⁵. Glucagon differs from the two other peptides with its truncated C-terminal. Otherwise the primary structure is identical. Oxyntomodulin is also highly preserved among different mammalian species.

Glucagon

HSQGTFTSDY SKYLD SRRAQ **DFVQW LMNT**
Q L K L V

HUMAN, ALL TESTED MAMMALS

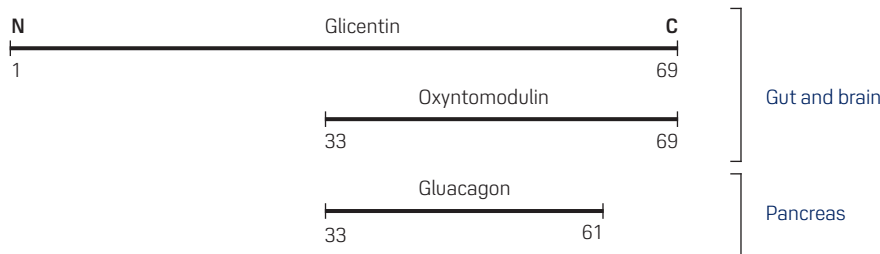
GUINEA PIG

Oxyntomodulin

HSQGTFTSDYSKYLDSRRAQDFVQWLMNTKRNRRNNIA
HSQGTFTSDYSKYLDSRRAQDFVQWLMNTKRN**K**NNIA

HUMAN, MOUSE, RAT

BOVINE, DOG, PORCINE



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Assay characteristics

There are two main characteristics that need to be met with a good glucagon assay, specificity and sensitivity. Specificity is important as there are several "glucagon related" peptides in the circulation that are produced in other organs; their secretion is stimulated differently, and may act differently. It is therefore essential to employ antisera that are specific for unique parts of glucagon, not cross reacting with glicentin, oxyntomodulin or GLP. The EURIA Glucagon assay show very good cross reactivity data and is very specific for glucagon.

- Normal level of glucagon in plasma after 12 hours fasting: <60 pmol/L
- The lowest detectable concentration in the assay is 3 pmol/L
- EURIA Glucagon assay standard preparation has been correlated with the WHO preparation 69/194 showing almost complete agreement, $R^2 = 0,9979$

Cross reactions:

Compound	Cross reactivity
Glucagon, pancreatic, human	100%
Gut GII	<0.1%
Secretin	<0.02%
Cholecystokinin -39	<0.02%
Vasoactive intestinal peptide	<0.02%
Gastric inhibitory peptide	<0.02%
GLP1	<0.1%
Oxyntomodulin	<0.1%

The EURIA glucagon assay is the only approved Glucagon IVD test in Japan.

References

1. **Kimball C.P. and Murlin J.R.** Aqueous extracts of pancreas: Reactions of insulin III. Some precipitation. *J. Biol. Chem.* 1923, 58:337-346.
2. **Bromer W.W. et al.** The Amino Acid Sequence of Glucagon. V. Location of Amide Groups, Acid Degradation Studies and Summary of Sequential Evidence. *J. Am. Chem. Soc.*, 1957: 79; , 2807–2810
3. **Sundby F.** Species variations in the primary structure of glucagon. *Metabolism - Clinical and Experimental* 1976: 25, *Supplement*;1319–1321
4. **Huang CG, et al.** Guinea pig glucagon differs from other mammalian glucagons. *Diabetes.* 1986;35:508-12.
5. **Bell G.I. et al.** Hamster preproglucagon contains the sequence of glucagon and two related peptides. *Nature* 1983; 302: 716-718.

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Doc. No: E-128-GB00, April 2015

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