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Biological Atlas Of Insulin Resistance

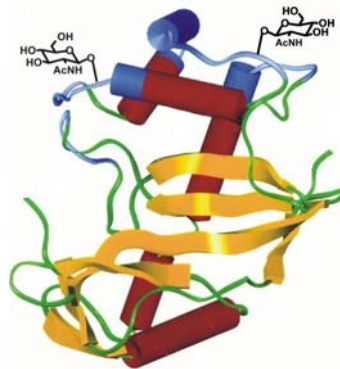
FAQs and Facts about Glycoproteomics

What is glycoproteomics?

Glycoproteomics is the study of glycoproteins, which are proteins that are covalently modified with glycans. There is increasing acceptance of the importance of glycosylation in cell-cell and cell-matrix recognition and as a potential modulator of protein function.

How does it differ from general proteomics?

Most proteomic studies focus on the identification of proteins through sequencing of a small number of their peptides. Glycoproteomics is technically more challenging as it requires a specific subset of peptides to be identified – the glycosylated peptides. Only through mapping the specific sites of glycosylation can the glycosylation be defined. An additional challenge is that the glycosylation is often sub-stoichiometric and heterogeneous.



Where does glycosylation occur within a cell?

There are two main types of glycosylation: complex and simple. The majority of cell-surface and secreted glycoproteins carry complex glycans that are biosynthesised in the ER and Golgi by a great variety of membrane bound glycosidases and glycosyltransferases. Simple glycosylation is found on cytosolic and nuclear proteins, and results from the addition of a single sugar residue by a soluble glycosyltransferase. Complex glycosylation

normally remains static whereas simple glycosylation is dynamic. Both types of glycosylation are important but the current focus of the BAIR Glycoproteomics team is on simple glycosylation.

What exactly is simple glycosylation?

It is called O-GlcNAc glycosylation and results from the attachment of N-acetylglucosamine (GlcNAc) to the hydroxyl group of serine or threonine.

Is simple glycosylation simple to analyse? Why?

No it is very difficult. The three main reasons are: (i) low abundance; (ii) O-GlcNAc is labile and can be readily lost; (iii) analytical methods do not always discriminate between O-GlcNAc and phosphorylation

So, it is important to look at phosphorylation in parallel with simple glycosylation?

Yes. It is particularly relevant as proteins that are targets for phosphorylation are usually also targets for O-GlcNAc addition – indeed the two modifications can compete for the same site on the protein.

Why is O-GlcNAc thought to be important in diabetes?

Evidence suggests that O-GlcNAc is a nutrient sensor. When the levels of glucose increase, more glucose is channelled down the hexosamine biosynthetic pathway ending up with increased levels of UDP-GlcNAc, the donor for O-GlcNAc. Higher levels of UDP-GlcNAc subsequently lead to target proteins becoming glycosylated instead of phosphorylated. It is becoming apparent that the interplay between phosphate addition and O-GlcNAc addition is important in insulin resistance, as many of the proteins implicated in resistance are potential targets for O-GlcNAc modification.