READING GUIDE

PART 1: THE PENTOSE PHOSPHATE PATHWAY

Objectives

1. Diagram and describe the pentose phosphate pathway and its role in other metabolic pathways
2. Describe a cause of hemolytic anemia as it relates to the pentose phosphate pathway
3. Describe how the pentose phosphate pathway is important in the synthesis of nitric oxide

PENTOSE PHOSPHATE PATHWAY

Big picture (Fig. 13.2)

What are the primary two products of the pentose phosphate pathway?

Why is this pathway sometimes referred to as the oxidative pentose phosphate (OPP) pathway?

Is there another way to make ribose 5-phosphate other than the oxidative decarboxylation of glucose 6-phosphate?

Spend a little time thinking about the stoichiometry of these reactions. How do you make C6 and C_3 compounds from C_5 compounds (and vice-versa) and come out even in the end?

What is the key regulated step in pentose phosphate pathway starting with glucose 6-phosphate?

What is the ratio of NADPH to NADP+ under most metabolic conditions in the cell?

When does the cell take advantage of just the reversible non-oxidative reactions of the PPP?

NADPH AND SOME OF ITS ROLES IN THE CELL

Big picture (Fig. 13.4)

What is the difference in molecular structure between NADPH and NADH?

What, generally speaking, is the difference in how these two reducing agents are used by the cell?

Regeneration of reduced glutathione by NADPH (Fig. 13.5,6)

Oxygen free radicals, which come in the various types described in Fig. 13.5, are very reactive molecules and can readily damage DNA, proteins, and lipids. They are thought to be involved in many pathogenic processes including aging. The cell has several mechanisms for deactivating oxygen free radicals and one important one involves glutathione.

What is the function of glutathione peroxidase?

What is glutathione and what is its role in controlling oxygen free radical production?

How does NADPH play a role in the conversion of hydrogen peroxide to water? What enzyme is involved?

Hydroxylation by monooxygenase (cytochrome Page 450) enzymes using NADPH (Fig. 13.7)

Monooxygenases use molecular oxygen to add hydroxyl groups to molecules. This is a very important reaction and there are many different types of monooxygenases.

What is one of the primary functions of monooxygenase enzymes in mitochondria?

What do the monooxygenase enzymes in the endoplasmic reticulum catalyze?

What is the prosthetic group in the monooxygenase (you can know this from P450 in its name)?

How do the electrons from NADPH reach the active site of the monooxygenase (think about the other cofactors involved)?

Oxygen-dependent cellular weapon using NADPH (Fig. 13.8)

Some cells, particularly neutrophils, have the ability to kill foreign cells, like bacteria, using superoxide anion and hypochlorous acid (HOCl); a very efficient mechanism for ridding the body of foreign invaders.

How does NADPH contribute to the production of super oxide anion?

How myeloperoxidase further toxify the phagosome and augment the damaging effect of superoxide anion?

Nitric oxide synthesis (Fig. 13.9)

You should be seeing a pattern by now. The enzymes utilizing NADPH are largely a group of enzymes that can manipulate molecular oxygen, reducing it to reactive intermediates for addition as hydroxyl or other oxygen moieties on substrates. In some cases, it is the reactive oxygen species themselves that are produced and used (like with NADPH oxidase). NADPH is also very important for its role in substituting oxygen on arginine and releasing nitric oxide.

What cofactors are used by nitric oxide synthase (NOS)?

What is the basic signaling pathway that NO works through?

What are the various function of NO?

Glucose 6-phosphate dehydrogenase (G6DH) deficiency
(Fig. 13.12,13)

How common is G6DH deficiency and how homogeneous is it?

Is the disease uniformly detrimental?

What kinds of situations exacerbate a G6DH condition?

Why are red cells hardest hit by G6DH deficiencies? What happens to the red cell? And what the connection with protein denaturation? (Fig. 13.10,11)

Summary (Fig. 13.14)

PART 2

GLYCOSAMINOGLYCANS, PROTEOGLYCANS, AND GLYCOPROTEINS

Objectives

1. Diagram the basic features of glycosaminoglycans (GAGs) and proteoglycans and describe the basis of diseases that result from defects in the degradation pathway of GAGs
2. Describe the synthesis of glycoproteins and the importance of modifying protein with sugar

What is a glycosaminoglycan (GAG)? (Fig. 14.1)

What are the sugars typically found in GAGs? (Fig. 14.2)

What is the function of GAGs and how does their structure?

What is the most abundant GAG in the body? (Fig. 14.4)

Which GAG is not sulfated?

Which gag is the only one not secreted when it is made? What cells make this GAG and what is its function?

What's the difference between a GAG and a proteoglycan? (Fig. 14.5,7)

How are GAGs attached to their protein core? (Fig. 14.6,11)

SYNTHESIS OF GAGS (Fig. 14.8)

GAGs are linear chains of sugar molecules that are elongated by glycosyltransferases much like glycogen is synthesized. Given that GAGs are secreted, where do you think these glycosyltransferases are located within the cell?

Where does the amino group come from in the amino sugars? How about the acetyl group?

How are the sugars activated so they can be used by the glycosyltransferases? Fig. 14.10

How is glucuronic acid made and incorporated into a GAG? How about iduronic acid?

Sulfotransferases add sulfate groups to the sugars in GAGs. What is the donor molecular from which the sulfate group is transferred? When are the sugars in GAGs sulfated?

DEGRADATION OF GAGS

Where are GAGs degraded and how do they get to this cellular location?

What enzymes are involved in degradation of GAGs?

What are some of the mucopolysaccharidoses and what are their symptoms? (Fig. 14.12)

GLYCOPROTEINS

Big picture (Fig. 14.13)

Glycoproteins are different than proteoglycans in that the amount of sugar in glycoproteins is less (usually much less) than proteoglycans, and the sugar polymers are not necessarily linear or composed of repeating acidic and amino sugars. Any protein with carbohydrate attached becomes a glycoprotein.

What are some of the functions of the carbohydrate moieties on glycoproteins?

What kind of proteins are typically glycosylated?

How are the carbohydrates attached to glycoproteins?

Are there differences between O-linked and N-linked oligosaccharides on glycoproteins? (Fig. 14.14)

Where does glycosylation begin and how does the protein to be glycosylated get there? (Fig. 14.15)

What are the carbohydrate chains on glycoproteins built from?

What is the basic process by which N-linked glycosylation takes place? How is it different from O-linked glycosylation? (Fig. 14.16)

What is the targeting signal that sends newly synthesized glycoproteins (like acid hydrolases) to the lysosome? What happens if this signaling pathway is defective? (Fig. 14.17)

What is I-cell disease?

How are glycoproteins degraded?

Summary (Fig. 14.18)