11.3J: The Acute Phase Response

Skills to Develop

1. Briefly describe the mechanism behind the acute phase response.
2. State the functions of the following acute phase proteins:
   a. C-reactive protein
   b. mannose-binding lectin

We will now take a closer look at the acute phase response. The acute phase response is an innate body defense seen during acute illnesses and involves the increased production of certain blood proteins termed acute phase proteins.

Activated macrophages and other leukocytes release inflammatory cytokines such as tumor necrosis factor-alpha (TNF-alpha), interleukin-1 (IL-1), and interleukin-6 (IL-6) when their pattern-recognition receptors (PRRs) bind pathogen associated molecular patterns or PAMPs - molecular components associated with microorganisms but not found as a part of eukaryotic cells. These include bacterial molecules such as peptidoglycan, teichoic acids, lipopolysaccharide, mannans, flagellin, pilin, and bacterial DNA. There are also pattern-recognition molecules for viral double-stranded RNA (dsRNA) and fungal cell walls components such as lipoteichoic acids, glycolipids, mannans, and zymosan.

These cytokines travel through the blood and stimulate hepatocytes in the liver to synthesize and secrete acute phase proteins. This response provides an early defense and enables the body to recognize foreign substances early on in the infection process prior to the full activation and implementation of the immune responses. Two important acute phase proteins are C-reactive protein and mannose-binding protein. They function as soluble pattern-recognition receptors.

1. C-reactive protein (CRP) binds to the phosphorylcholine portion of teichoic acids and lipopolysaccharides of bacterial and fungal cell walls. It also binds to the phosphocholine found on the surface of damaged or dead human cells. It functions as an opsonin, sticking the microorganism to phagocytes, and activates the classical complement pathway by binding C1q, the first component in the pathway.
2. Mannan-binding lectin (MBL) - also known as mannan-binding protein or MBP - binds to mannose-rich glycans (short carbohydrate chains with the sugar mannose or fructose as the terminal sugar). These are common in microbial glycoproteins and glycolipids but rare in those of humans. It functions as an opsonin, sticking the microorganism to phagocytes, and activates the lectin pathway.

Products of the complement pathways, in turn, promote inflammation, attach microbes to phagocytes, cause to MAC cytolysis, and chemotactically attract phagocytes to the infected area.

Summary

1. The acute phase response is an innate body defense seen during acute illnesses and involves the increased production of certain blood proteins termed acute phase proteins.
2. Inflammatory cytokines produced during innate immunity travel through the blood and stimulate hepatocytes in the liver to synthesize and secrete acute phase proteins.
3. Two important acute phase proteins are C-reactive protein and mannose-binding protein, both functioning as soluble pattern-recognition receptors.
4. C-reactive protein (CRP) binds to certain PAMPs bacterial and fungal cell walls as well as to phosphocholine found on the surface of damaged or dead human cells.
5. CRP functions as an opsonin, sticking the microorganism to phagocytes, and activates the classical complement pathway by binding C1q, the first component in the pathway.
6. Mannan-binding lectin (MBL) - also known as mannan-binding protein or MBP - binds to mannose-rich glycans on microbial cell walls.
7. MBL functions as an opsonin, sticking the microorganism to phagocytes, and activates the lectin pathway.

Contributors

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