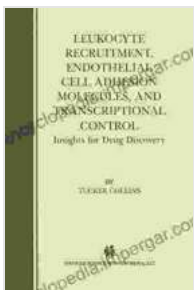


Leukocyte Recruitment, Endothelial Cell Adhesion Molecules, and Transcriptional Regulation: Unlocking the Mechanisms of Inflammation

Inflammation is a complex biological response that plays a crucial role in the body's defense against infection and injury. However, excessive or chronic inflammation can lead to a variety of diseases, including arthritis, atherosclerosis, and cancer.

Leukocyte recruitment, the process by which white blood cells are recruited to sites of inflammation, is a key step in the inflammatory response. This process is mediated by endothelial cell adhesion molecules (ECAMs), which are expressed on the surface of blood vessels. ECAMs bind to specific receptors on leukocytes, allowing them to adhere to the blood vessel wall and migrate into the surrounding tissue.

Transcriptional regulation plays a critical role in the expression of ECAMs. A number of transcription factors have been identified that regulate ECAM expression, including nuclear factor-kappa B (NF- κ B), activator protein-1 (AP-1), and specificity protein-1 (Sp-1).



Leukocyte Recruitment, Endothelial Cell Adhesion Molecules, and Transcriptional Control: Insights for Drug Discovery by Tucker Collins

★★★★☆ 4 out of 5

Language : English

File size : 6144 KB

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Enhanced typesetting : Enabled

Print length : 462 pages
Screen Reader : Supported



Leukocyte recruitment is a multi-step process that involves the following steps:

1. **Margination:** Leukocytes roll along the surface of blood vessels, a process mediated by selectins.
2. **Adhesion:** Leukocytes adhere to the blood vessel wall, a process mediated by ECAMs.
3. **Transmigration:** Leukocytes migrate through the blood vessel wall and into the surrounding tissue.

ECAMs play a critical role in the adhesion step of leukocyte recruitment. They bind to specific receptors on leukocytes, allowing them to adhere to the blood vessel wall. The most important ECAMs are:

- **E-selectin:** E-selectin is expressed on activated endothelial cells. It binds to sialyl Lewis X (sLeX), a carbohydrate antigen expressed on neutrophils and monocytes.
- **P-selectin:** P-selectin is expressed on activated platelets and endothelial cells. It binds to P-selectin glycoprotein ligand-1 (PSGL-1), a carbohydrate antigen expressed on all leukocytes.
- **ICAM-1:** ICAM-1 is expressed on activated endothelial cells. It binds to lymphocyte function-associated antigen-1 (LFA-1) and macrophage-1 antigen (Mac-1), integrins expressed on leukocytes.

- **VCAM-1:** VCAM-1 is expressed on activated endothelial cells. It binds to very late antigen-4 (VLA-4), an integrin expressed on leukocytes.

ECAMs are a family of transmembrane proteins that are expressed on the surface of endothelial cells. They play a critical role in leukocyte recruitment by binding to specific receptors on leukocytes. The most important ECAMs are:

- **E-selectin:** E-selectin is an inducible ECAM that is expressed on activated endothelial cells. It binds to sLeX, a carbohydrate antigen expressed on neutrophils and monocytes.
- **P-selectin:** P-selectin is a constitutively expressed ECAM that is stored in Weibel-Palade bodies. It is released upon activation of endothelial cells and binds to PSGL-1, a carbohydrate antigen expressed on all leukocytes.
- **ICAM-1:** ICAM-1 is an inducible ECAM that is expressed on activated endothelial cells. It binds to LFA-1 and Mac-1, integrins expressed on leukocytes.
- **VCAM-1:** VCAM-1 is an inducible ECAM that is expressed on activated endothelial cells. It binds to VLA-4, an integrin expressed on leukocytes.

The expression of ECAMs is regulated by a number of transcription factors, including NF- κ B, AP-1, and Sp-1.

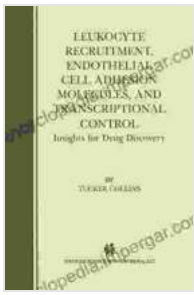
- **NF- κ B:** NF- κ B is a transcription factor that is activated by a variety of stimuli, including cytokines, bacterial products, and oxidative stress.

NF- κ B binds to the promoter region of ECAM genes and activates their transcription.

- **AP-1:** AP-1 is a transcription factor that is activated by a variety of stimuli, including cytokines, growth factors, and phorbol esters. AP-1 binds to the promoter region of ECAM genes and activates their transcription.
- **Sp-1:** Sp-1 is a transcription factor that is expressed in all nucleated cells. Sp-1 binds to the promoter region of ECAM genes and either activates or represses their transcription, depending on the cellular context.

Leukocyte recruitment, endothelial cell adhesion molecules, and transcriptional regulation are key components of the inflammatory response. Understanding the molecular mechanisms of these processes is essential for developing new therapies for inflammatory diseases.

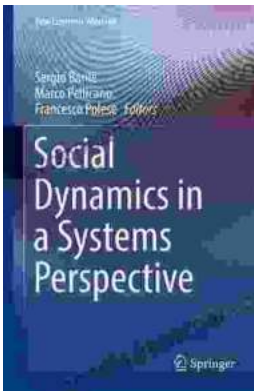
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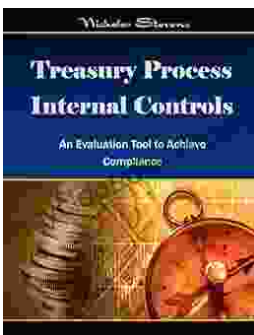
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