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Perspective

# Heparan Sulfate Proteoglycans as Potential Biomarkers in Diseased State

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## DESCRIPTION

Heparan Sulfate Proteoglycans (HSPGs) are complex molecules found on the cell surface and within the extracellular matrix, playing pivotal roles in various biological processes. Comprising a core protein and long chains of heparan sulfate, these proteoglycans are involved in critical cellular functions, including cell signaling, adhesion, and the regulation of growth factors. HSPGs exhibit promising potential as biomarkers in various medical contexts. These complex molecules composed of a core protein and heparan sulfate chains, play crucial roles in cellular functions and the extracellular matrix. Their involvement in cell signaling, adhesion, and regulation of growth factors makes them valuable candidates for biomarker exploration.

HSPGs are ubiquitously present on the cell surface and in the extracellular matrix, forming an essential part of the glycocalyx-A carbohydrate rich layer on the cell surface. In the extracellular matrix, HSPGs contribute to the structural integrity and organization of tissues. They interact with other matrix components, providing support and stability. Alterations in HSPG expression or structure are associated with several diseases, including cancer, neurodegenerative disorders, and cardiovascular diseases. Understanding these associations provides insights into disease mechanisms and potential therapeutic targets.

### Types of HSPGs as biomarkers

- Syndecans are a family of transmembrane HSPGs with four members (Syndecan-1 to Syndecan-4). They are involved in cell signaling, adhesion, and inflammation. Altered expression of syndecans has been associated with cancer progression, making them potential biomarkers in cancer diagnosis and prognosis.
- Glypicans are anchored to the cell surface *via* glycosylphosphatidylinositol (GPI) and play roles in signaling pathways, including those related to growth factors. Aberrant glypican expression has been implicated in various cancers, suggesting their potential as cancer biomarkers.
- Perlecan is a large, multi-domain HSPG found in the extracellular matrix. It contributes to matrix structure and cell signaling. Changes in perlecan expression have been linked to cardiovascular diseases, making it a candidate biomarker for such conditions.
- Heparanase is an enzyme that degrades heparan sulfate chains. Elevated levels of heparanase have been observed in cancer and inflammation, suggesting its potential as a biomarker for these conditions.
- Another small leucine-rich proteoglycan with heparan sulfate chains, biglycan is involved in tissue repair and inflammation. It has been implicated in cardiovascular diseases, making it a potential biomarker in this context.

### HSPGs biomarkers for specific diseases

**Cancer:** Altered expression of syndecans and glypicans has been observed in various types of cancer. These HSPGs are involved in cell signaling, adhesion, and growth factor interactions. Their dysregulation is associated with cancer progression, invasion, and metastasis. Therefore, they are being investigated as potential biomarkers for cancer diagnosis and prognosis.

**Cardiovascular diseases:** Perlecan, found in the extracellular matrix, and biglycan, a small leucine-rich proteoglycan, have been implicated in cardiovascular diseases. Changes in their expression levels are associated with conditions such as atherosclerosis and cardiac remodeling. These HSPGs are under scrutiny as potential biomarkers for cardiovascular diseases.

**Inflammatory disorders:** Elevated levels of heparanase, an enzyme that degrades heparan sulfate chains, have been linked to inflammatory conditions. Heparanase is associated with tissue inflammation and remodeling. Monitoring heparanase levels is being explored as a potential biomarker for inflammatory disorders.

**Neurodegenerative diseases:** HSPGs, particularly syndecans and glypicans, play roles in the nervous system and have been implicated in neurodegenerative diseases. Aberrant expression or

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processing of these molecules is being investigated as potential biomarkers for conditions such as Alzheimer's and Parkinson's diseases.

**Renal diseases:** In renal diseases, alterations in syndecan expression have been observed. Syndecans are involved in renal development, and their dysregulation is associated with conditions like diabetic nephropathy. Syndecans are being explored as potential biomarkers for renal diseases.

**Glycosaminoglycan disorders:** Diseases characterized by abnormal glycosaminoglycan metabolism, such as mucopolysaccharidoses, involve HSPGs. Monitoring changes in specific HSPGs may serve as biomarkers for these rare genetic disorders.

## CONCLUSION

In conclusion, Heparan Sulfate Proteoglycans (HSPGs) stand at the intersection of intricate cellular processes, playing pivotal roles in cell signaling, adhesion, growth factor regulation, and extracellular matrix integrity. Their involvement in critical physiological functions, coupled with observed alterations in disease states, has spurred research into their potential as biomarkers. Standardized assays, a deeper understanding of their roles in specific diseases, and the development of targeted therapeutic interventions are ongoing areas of investigation.