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Metabolomics of the extracellular matrix as diagnostic markers of disease

John M. Whitelock

University of New South Wales, Australia

Abstract

The Extracellular Matrix (ECM) is a dynamic and complex mixture of glycoproteins produced by cells in response to the biological signals present in the surrounding local environment. The end result of this precisely orchestrated process has been referred to as ECM regeneration and has been shown to be altered in many disease states. Proteoglycans (PGs) are a group of ECM molecules that are characterized by their carbohydrate modifications known as glycosaminoglycans (GAGs), and which are linear alternating co-polymers of hexuronic acid and hexoxasamine that are differentially modified with sulfate that provide both molecular weight dispersity and charge heterogeneity. Our fundamental hypothesis is that the protein and carbohydrate structures of PGs change in response to disease and that we can use these changes of structure as a diagnostic of disease. We have shown that a chondroitin sulfate proteogkycan (CSPG), lubricin undergoes alternative splicing and that this might be in response to arthritis. We have also shown that another PG bikunin, which is important in incorporating hyaluronan into the ECM has different CS sulfation patterns in arthritis, which affecr its biological function. Another example from our laboratory focuses in the structure of perlecan, a heparan sulfate (HSPG) that can be decorated with HS, CS or keratan sulfate, which have profound effects on its ability to bind and signal growth factors. We have undertaken a PCR-based, immuno-detection study and have shown that perlecan undergoes alternative splicing that results in forms with different biological functions and forms that are associated with disease.

Biography

Professor John Whitelock graduated with a PhD from the University of Technology, Sydney in 1991, and after completing post-doctoral studies at the University of Alabama, Birmingham and the Commonwealth Scientific Industrial Research Organization (CSIRO) is now the Head of the Graduate School of Biomedical Engineering at the University of New South Wales. His research focuses on the roles of the extracellular matrix and the way tissues and organs are generated during development and how this relates to the regenerative processes seen in disease. He has authored over 200 conference presentations and published over 75 journal articles in international peer-reviewed journals.