



Review

Role of Extracellular Matrix in Development and Cancer Progression

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Abstract: The immense diversity of extracellular matrix (ECM) proteins confers distinct biochemical and biophysical properties that influence cell phenotype. The ECM is highly dynamic as it is constantly deposited, remodelled, and degraded during development until maturity to maintain tissue homeostasis. The ECM's composition and organization are spatiotemporally regulated to control cell behaviour and differentiation, but dysregulation of ECM dynamics leads to the development of diseases such as cancer. The chemical cues presented by the ECM have been appreciated as key drivers for both development and cancer progression. However, the mechanical forces present due to the ECM have been largely ignored but recently recognized to play critical roles in disease progression and malignant cell behaviour. Here, we review the ways in which biophysical forces of the microenvironment influence biochemical regulation and cell phenotype during key stages of human development and cancer progression.

Keywords: tumour microenvironment; cancer progression; extracellular matrix; matrix remodelling; fibrosis

1. Introduction

The extracellular matrix (ECM) is most commonly defined as the non-cellular component of tissue that provides both biochemical and essential structural support for its cellular constituents. Rather than serving simply as an intercellular filling, the ECM is a physiologically active component of living tissue, responsible for cell–cell communication, cell adhesion, and cell proliferation [1]. Fundamentally, the ECM is composed of an interlocking mesh of water, minerals, proteoglycans, and fibrous proteins secreted by resident cells. However, every organ has a unique composition of these elements to serve a particular tissue-specific purpose [1,2]. Indeed, this unique composition arises through dynamic biophysical and biochemical feedback between cellular components and their evolving microenvironment during tissue development [3,4]. For any specific tissue, components of the ECM are created and arranged by resident cells in accordance with the needs of the tissue. The production of essential fibrous proteins, such as collagen, elastin, and laminin are controlled by the ECM and adapt during various stages of embryonic development and disease progression. As a highly dynamic structure, the ECM is constantly undergoing a remodelling process, by which components are degraded and modified, facilitated primarily by ECM proteinases [5,6]. The balance between degradation and secretion of ECM, orchestrated by ECM-modifying cells, is responsible for tensional homeostasis and the properties of each organ, such as elasticity and compressive/tensile strength.

In vitro, most animal cells are known to only maintain viability when adhered to a substrate [7]. In this regard, cells rely heavily on their sense of touch to survive by protruding, adhering, and spatially interacting with the surrounding ECM. Various cellular growth factor receptors and adhesion

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