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Extracellular Matrix: A General Overview

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The extracellular matrix (ECM) is a non-cellular component, which is important in providing structural stability to tissues. It consists of proteins, water and polysaccharides. ECM triggers specific processes and signals, which are necessary for differentiation, morphogenesis and homeostasis. Any dysfunction and anomaly in ECM components during the development could result in various disorders (Jarvelainen et al., 2009; Frantz et al., 2010). The cell adhesion to ECM is very crucial for cell migration. This process is mediated via ECM receptors like syndecans, fibronectin, laminin, collagen and integrins (Humphries et al., 2006; Alberts et al., 2007; Schaefer and Schaefer, 2010; Schmidt and Friedl, 2010). ECM is important for communicating with cell-surface receptors, which in turn evoke signal transduction and manage gene transcription. By binding to growth factors, ECM is involved in physiological function and morphological organization (Frantz et al., 2010). ECM is very progressive structural network, which undergoes remodeling regularly that is operated via different matrix degrading enzymes.

The ECM is broadly composed of fibrous proteins and proteoglycans. Fibrous proteins consist of fibronectin, collagen and laminins. Whereas syndecan-4 is the important proteoglycan. Fibronectin is important for guiding cellular coupling. Cellular traction forces can stretch it multiple times. It is mainly involved in management of interstitial ECM (Smith et al., 2007). Due to fibronectins role in cell migration, it is involved in tumor metastasis and cardiovascular diseases during development stage (Tsang et al., 2010; Rozario and DeSimone, 2010). Collagen, which is also interstitial ECM component, maintains tensile strength, manage cell adhesion, support cell migration and chemotaxis (Rozario and DeSimone, 2010). Within the tissue, maximum extracellular interstitial space is covered by proteoglycans. Their function varies from hydration, binding and buffering (Jarvelainen et al., 2009). Syndecans are main proteoglycans and are sub-divided into Syndecan 1-4. To be more specific in its structure, the extracellular domain of syndecan-1 consists of chondroitin sulfate and heparan sulfate glycosaminoglycan side chains. Whereas, syndecan-2, -3 and -4 only contain the heparan sulfate chains, which communicate with fibronectin and growth factors (Multhaupt et al., 2009).

As ECM is considered important in governing cell and tissue behavior, due to major changes in the content and distribution of its components throughout tissue development, differentiation and in reaction to growth factor, cytokine and hormone impact. Various ECM-dependent cellular behaviors are documented in vitro studies. Where as in vivo studies focused on genetic approach. It clearly exhibits that genes encoding ECM components are very important (Carson, 2004). ECM is very important source of cytokines and growth factors, which mostly binds to ECM protein components or polysaccharides. In almost all

cellular responses to ECM needs interaction of cell surface receptors, the factors which aggravate with cell surface receptor interactions. Mucins are known to coordinate these events. Sometimes, Mucins also possess complicated behavior as they restrict cell-cell and Cell-ECM interactions but can also interact with other cell surface receptors such as selectins (Carson, 2004).

Junctional integrity can be compromised due to tissue aging, where number of junctional proteins is reduced. This can be easily observed as gaps in between the epithelial cells (Akintola et al., 2008). Similarly, disproportion of collagen crosslinking can lead to tissue solidification. And as a result, young tissue is less rigid and more elastic compared to aged tissue that is also mechanically frail (Calleja-Agius et al., 2007). This could lead to various age-dependent disorders such as cancer. This is due to abnormal mechanical condition as it affects ECM assembly and alter epithelial functioning (Coppe et al., 2010; Sprenger et al., 2008). Abnormal behaviour of cellular components and loss of tissue functioning leads to diseases like cancer. It results from mutations in genes. A normal tissue is generally less hard than cancerous tissue which is very stiff. Tissue hardening is due to ECM deposition and remodelling by resident fibroblasts and more epithelium contractility (Butcher et al., 2009; Levental et al., 2009).

Surge in ECM breakdown could lead to tissue damage. Proteinases like MMPs and ADAMs, contemplate the abnormal ECM destruction. Specific ADAMs level is abnormally increased in osteoarthritis. Similarly, increases level of MMP1 result in cardiomyopathy (Kim et al., 2000; Bondeson et al., 2008). Due to ECM differential structural and biochemical forms and its specific cell signalling alter general function that is crucial for initial steps of inflammation, for e.g., immune cell migration into inflamed tissues and its differentiation (Sorokin, 2010).

To study the interaction between ECMs biochemical and biophysical characteristics, multiple tissue culture models are developed. To understand the cell adhesion process in cancer, the studies are done on coated tissue culture dishes. They are coated with combinations of mixtures of ECM proteins to get 2D monolayer (Kuschel et al., 2006). To study important features of tissue specific architecture and differentiation, scientists are focusing on reconstituted ECM gels and natural ECM gels. This will indeed highlight the aspect of 3D and ECM remodelling. Inadequacy of mechanical strength and endurance of interstitial ECM in Fibrin made natural biodegradable scaffolds could still be moderate achievement in tissue engineering (Blomback and Bark, 2004; Shaikh et al., 2008). Collagen I gel could be a good natural scaffold substrates but very heterogenous, which can alter the final results (Johnson et al., 2007). Hence denuded ECM scaffold for different tissues is better substitute (Macchiarini et al., 2008). To overcome the drawbacks of natural scaffolds, synthetic matrices are created. They are well composed with proper mechanics and ECM remodelling prospects. Mostly used synthetic matrices are polyethylene glycol hydrogels as they support cell adhesion and growth (Lutolf and Hubbell, 2005). Peptide-based hydrogels such as peptide-amphiphiles easily support stem cell growth and leads to multicellular morphogenesis (Hauser and Zhang, 2010; Sieminski et al., 2008; Ulijn and Smith, 2008). To most used advanced matrices are made from lactic acid polymer, electrospun silk, and PLGA scaffolds. These ECMs are

considered because their remodelling potential can be closely controlled and regulated (Zhang et al., 2009; Frantz et al., 2010).

Overall, ECM plays constructive role in various diseases such as cancer and reproductive processes. It is worth noting the complex management of ECM role and its expression in endocrine and reproductive systems functioning.

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