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Evolution of gradient concept for the application of regenerative medicine

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Abstract

It has been recognized that tissue engineering and regenerative medicine (TERM) offers the next generation technology for whole organ and tissue transplantation for diseased, failed or malfunctioned organs. Biomaterials might be the one of the important factors to apply the complete bio-organ using TERM techniques. Around 30 years ago, the primitive concept of "Gradient Surface" had been introduced to improve the biocompatibility for biomaterials. However, the gradient concept of surface property is changing now numerous kinds of physicochemical properties very recently. In this review, the importance of the concept of gradient, the historical evolution of experimental methodology for the manufacturing of gradient surface during last over ~30 years in my research group and finally perspective as enabling technologies for the TERM area are summarized.

Jel Classifications: Tissue Engineering and Regenerative Medicine

Keywords: Gradient; Surface modification; Physicochemical treatment; Tissue engineering; Regenerative medicine

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1. Introduction

It has been recognized that tissue engineering and regenerative medicine (TERM) offers the next generation technology for whole organ and tissue transplantation for diseased, failed or malfunctioned organs [1]. Millions of patients are suffered by end-stage organ failure or tissue loss annually. Recent advances in TERM using stem cell science and technology have shown a great potential for the clinical trial and research of next generations medications. Science and technology of regenerative medicine might change the paradigm of the nature of medicine [1–4].

Very recently, four stem cell products have been launched in Korean market after the approval from Korea Food and Drug Administration including world first autologous bone marrow derived stem cell (BMSC) for the treatment of myocardial infarction on 2012, world first autologous adipose derived stem cell (ADSC) for the treatment of Crohn's disease, world first allogenic umbilical cord derived stem cell (UBMSC) for the treatment of chondyle defect on 2012 and BMSC for the treatment of amyotrophic lateral sclerosis (ALS) on 2014 [4]. Similarly, several tissue engineered products introduced in market as artificial skin using biomaterials scaffold and autologous or allogenic keratinocyte. Also over one–two hundred clinical trial phase I–III with broad range of medical area are in progress through the world. Even though this step might be an infant step for the development of TERM compare with conventional medication treatment, they show good sign for the future for the application of stem cell and TERM therapy [1].

To accomplish a successful treatment or therapy by regenerative medicinal technique, triad components such as (i) cells which are harvested and dissociated from the donor tissue including nerve, liver, pancreas, cartilage and bone as well as embryonic stem, adult stem or precursor cell, (ii) biomaterials as scaffold substrates which cells are attached and cultured resulting in the implantation at the desired site of the functioning tissue and (iii) growth factors (cytokines) which are promoting and/or preventing cell adhesion, proliferation, migration and differentiation by up-regulating or down-regulating the synthesis of protein, growth factors and receptors must be needed [5,6].

Among these triad components, biomaterials might be the one of the important factors to apply the complete bio-organ using TERM techniques. It has been widely recognized that the behavior of the adhesion and proliferation of anchorage-dependent cells and tissue on scaffold biomaterials depend on the surface characteristics such as wettability (hydrophilicity/hydrophobicity or surface free energy), chemistry, charge, roughness, and rigidity. In order to improve the biocompatibility, we have been carried out the surface modification including the fabrication of gradient surface [7–37].

In this review, the importance of the concept of gradient, the historical evolution of experimental methodology for the manufacturing of gradient surface during last over ~30 years in my research group and finally perspective as enabling technologies for the TERM area are summarized. Readers can find many review and feature articles reported elsewhere.

2. The important of the concept of gradient

The meaning of gradient includes some properties changed gradually with physical, chemical, concentrational and so on of one, two or three dimension. One of the most significant examples very recently is that the embryonic development follows chemical gradient as vitamin E and/or pH concentration [9]. Lander calls this kind of gradient for developmental biology it as “Morphogen Gradient” [38]. Also whole our human body keeps gradients in cellular–extracellular architecture to satisfy spatially diverse functional needs.

Fig. 1 shows the schematic diagram of the phagocytosis action of white blood cell toward foreign body. Once some inflammation has been occurred at the injury site, the cytokine related with inflammation is produced. Patrolled neutrophils start to locomote at speeds of 200–300 μm/h along the gradient of cytokine concentration (chemogradient) toward source of infection through the extracellular matrix. Sometimes it called

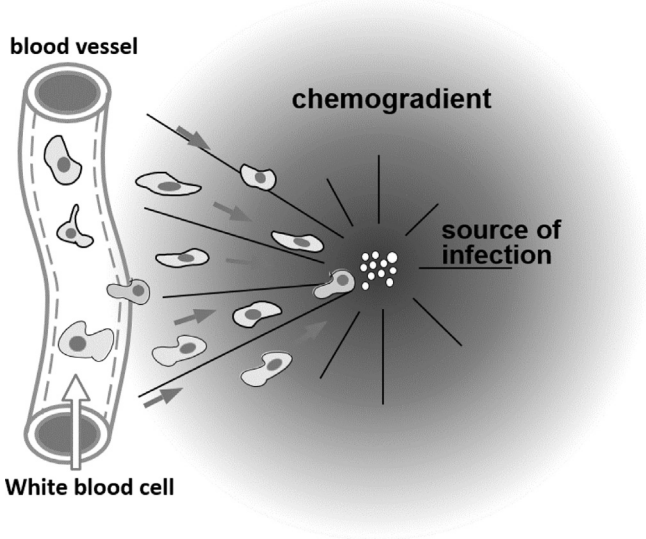

Fig. 1. Schematic diagram of the phagocytosis action of white blood cell toward foreign body.