Medical Hypotheses (2006) **67**, 572–577

ELSEVIER

medical hypotheses

http://intl.elsevierhealth.com/journals/mehy

Physics models of centriole replication

Kang Cheng *, Changhua Zou

Science Research, 205 Hana Road, Edison, NJ 08817, USA

Received 26 February 2006; accepted 28 February 2006

Summary Our previous pre-clinic experimental results have showed that the epithelialization can be enhanced by the externally applied rectangular pulsed electrical current stimulation (RPECS). The results are clinically significant for patients, especially for those difficult patients whose skin wounds need long periods to heal. However, the results also raise questions: How does the RPECS accelerate the epithelium cell proliferation? To answer these questions, we have previously developed several models for animal cells, in a view of physics, to explain mechanisms of mitosis and cytokinesis at a cellular level, and separation of nucleotide sequences and the unwinding of a double helix during DNA replication at a bio-molecular level.

In this paper, we further model the mechanism of centriole replication during a natural and normal mitosis and cytokinesis to explore the mechanism of epithelialization enhanced with the externally applied RPECS at a bio-molecular level. Our models suggest: (1) Centriole replication is an information flowing. The direction of the information flowing is from centrioles to centrioles based on a cylindrical template of 9×3 protein microtubules (MTs) pattern. (2) A spontaneous and strong electromagnetic field (EMF) force is a pushing force that separates a mother and a daughter centrioles in centrosomes or in cells, while a pulling force of interacting fibers and pericentriolar materials delivers new babies. The newly born babies inherit the pattern information from their mother(s) and grow using microtubule fragments that come through the centrosome pores. A daughter centriole is always born and grows along stronger EMF. The EMF mostly determines centrioles positions and plays key role in centriole replication.

We also hypothesize that the normal centriole replication could not been disturbed in centrosome in the epithelium cells by our RPECS, because the centrioles have two non-conducting envelope (cell and centrosome membranes), that protect the normal duplication. The induced electric field by externally applied RPECS could be mild compared with the spontaneous and natural electric field of the centrioles. Therefore, the centriole replication during the epithelium cellular proliferation may be directly, as well as indirectly (e.g., somatic reflex) accelerated by the RPECS.

Introduction

The idea to use externally imposed electrical stimulation to enhance skin wound healing probably came from the knowledge that there is an injury current around a fresh wound, which could play a role in skin wound healing [1]. As early as 1860s, the founder of the science of bioelectricity, Du Bois–Reymond, discovered that an injured bleeding finger is electrically positive compared with an uninjured finger [2]. To our knowledge, the first modern application of electric current stimulation to a pre-clinic skin wound healing was reported in 1962 [3]. From that time on, electrical current stimulation has been frequently used in both

* Corresponding author. Tel.: +732 248 0790.
E-mail address: kangcheng.1@netzero.net (K. Cheng).

0306-9877/$ - see front matter
doi:10.1016/j.mehy.2006.02.041

pre-clinic and clinic investigations of cutaneous regeneration.

In our previous pre-clinic investigation of epithelialization enhanced with the externally applied rectangular pulsed electrical current stimulation (RPECS) and conforming electrodes, we observed, at a tissue level, that wounds treated with RPECS were healed about 15% faster than the control wounds [4]. The pre-clinical experimental results impelled us to measure in vitro conductivity [5] and in vivo 3D distributions of electric fields [6] on/in pig skin with RPECS. Our measured data indicate the externally applied electric field (EF) is about three times as strong on the skin surface under the electrode edges, where the bacteria could mostly invade the skin wound, as that in the skin. The results of our observation suggest that not only the epithelialization but also the infection/anti-infection could be related to the cell proliferation and the externally applied EF.

However, the results also raise questions: How does the RPECS accelerate the epithelium cell proliferation? What are the relationships between the cellular proliferation and the spontaneous electromagnetic field (EMF)? What could be the driving force for the proliferation, in wild types of cells? To answer these questions, we have developed several models, in a view of physics, to explain mechanisms of mitosis and cytokinesis at a cellular level [7,8], and separation of nucleotide sequences and the unwinding of a double helix during DNA replication at a bio-molecular level [9].

In this investigation, with assistance of a model of RPECS for skin wound healing [10] and a model for mitosis and cytokinesis [7], we continue our exploration on centriole replication in wild types of animal cells in a perspective of physics. We believe centriole replication is one key procedure during the epithelium cell proliferation.

In the research field of centriole replication, centrioles structures with cells from fibroblasts and stimulated lymphocyte were studied in 1970s [11] and the reproduction of centrosomes was investigated in 1980s [12]. Centrosome organization and centriole architecture and their sensitivity to divalent cations were investigated in early of 1990s [13]. For most animal cells, centrosomes are thought to ensure spindle bipolarity and thus correct chromosome segregation during mitosis [14]. Recently, centrioles and centrosomes positioned and duplicated in eucaryotes were observed and models were provided to depict the mechanism of centrosome positioning from physiological or biological perspective [15—17]. However, those models have likely focused on centrosome positioning, rather than a comprehensive explanation of overall centrioles replication. We have not found any model in a view of physics to explain the mechanisms of this process, to answer the question: What is the kind or the source of the separating (pushing) force? And how does the force depart the centrioles and duplicate centrioles?

In this paper, based on our previous models and published biological data, we are the first to develop an original model to approach the mechanism of centriole replication using the concept of inner spontaneous EF [7,18] in a view of physics. Then considering an externally applied EF, such as RPECS, to influence the natural and normal replication, we propose a hypothesis for the mechanisms of the overall centriole replication to explain the epithelium regeneration acceleration by RPECS based our previous pre-clinic experimental results [4].

Model development of centriole replication

Experimental data show a centrosome is usually composed of two centrioles at proximately right angle. Each centriole is a cylindrical organelle organized with nine groups of three microtubules (MTs) [11,13]. MTs nucleating at the mother centriole were observed [19] and MTs are found to have functions to move cellular components [20].

In addition, experimental investigation have showed: at a activated state, at a certain point in G1 of a cell life cycle, the mother and daughter centrioles begin to departure from each other. During S phase, baby centrioles begin to grow near their mothers and MT always nucleate at a mother centriole [19].

We analyze those experimental data and provide our explanation: at a rest state, a mother centriole has much more positive charge than that of a daughter centriole has, a mother is almost saturated with positive charges, and a daughter is not. But, the EF interaction (pushing force), between a pair of centrioles is too weak to overcome the maximum resistance, including static friction. At the activated state, the daughter is saturated with positive charges too. When a pair of mother and daughter centrioles have enough positive charges, the interactive repulsing (pushing) EF force is strong enough to overcome the maximum resistance including the both static and dynamic friction (or viscosity), and to separate the pair of mother and daughter centrioles. We believe that biochemical or biophysical events provoke the spontaneous and strong interactive EMF, which is approximately a quasi-static EF [7,8].