Editorial

Gene Transfer by Electric Fields

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Gene therapy is a very promising technique for a large number of diseases (including, in addition to inherited disorders, cancer and viral infections). However, up to now, gene therapy has only poorly been used in clinics for the treatments of diseases having no other possible cure. The main drawbacks of the gene therapy techniques are due to their limited efficiency and/or lack of safety. Among these techniques, electroporation appears as one of the most promising. This physical method, based on the local application of electric fields at the cells and tissues level, leads to a transient change of membrane permeability to low and non-permeant molecules [1]. Due to its safety, efficiency, low cost and easy way of use, electroporation has rapidly developed into different medical applications. A procedure, called electrochemotherapy [2], is nowadays used in clinics for the treatment of cancers [3]. A European project (ESOPE, European Standard Operating Procedures of electrochemotherapy) has allowed to define the standard operating procedures (cytotoxic drugs, pulse parameters, pulse generators) [4, 5]. In addition to chemotherapeutic drugs, large molecules such as plasmid DNA can be introduced into cells using electroporation, a process called gene electrotransfer or electrogenetherapy in the context of clinics [6]. During the last 30 years, considerable progresses have been made both in the comprehension of the underlying mechanisms and the development of electrodes and pulses generators. Gene electrotransfer can nowadays be successfully performed on many tissues. The first phase I clinical trial has been conducted in patients with metastatic melanoma and several clinical studies for DNA vaccination have been monitored or are currently ongoing (http://clinicaltrials.gov). In spite of the widespread use of gene electrotransfer and its noticeable applications in medical care, the mechanisms that govern DNA delivery into cells and tissues remain to be fully elucidated. A full understanding of the processes involved in cells and tissues permeabilization and electrotransfer of molecules will allow gene electrotransfer to be optimized and safely employed for disease treatment.

Following the First World Congress on Electroporation and Pulsed Electric Fields in Biology, Medicine and Food & Environmental Technologies held in Portorož, Slovenia, 6th to 10th, 2015, we (Prof Damijan Miklavcic, the host of the Congress and the main organiser, and Dr Marie-Pierre Rols) invited and selected outstanding researchers to contribute to the present Special Issue.

The review “Gene electrotransfer: a mechanistic perspective” by Rosazza and collaborators is a very comprehensive review of gene electrotransfer from the mechanistic perspective. According to the reviewers “this is really a seminal piece of work, which covers the entire gene electrotransfer concept, from practical application, theory, mechanistic insight and research models. The review without any doubt will be of great interest not only to those dealing with the electroporation but also to those interested in gene delivery or gene therapy in general”.

Gene electrotransfer into the skin is of particular interest for the development of medical applications. However, it is limited due to poor understanding of the underlying mechanisms governing DNA electrotransfer within human tissue. Studies are being carried out in rodent models as their skin varies from human skin. The next article entitled “Gene Electrotransfer in 3D Reconstructed Human Dermal Tissue”, by Madi and collaborators describes a tissue-engineering approach to study gene electrotransfer mechanisms in a human tissue context.

The next one “Visualization of Non-Specific Antitumor Effectiveness and Vascular Effects of Gene Electro-Transfer to Tumors” by Kamensek and collaborators reports the use of a noninvasive bioluminescence technology to explore the phenomena associated with gene electrotransfer to tumors by a real time monitoring of the transfection efficiency as well as cell death following the treatment. This method could be helpful when designing improved and more effective cancer gene therapy, in order to accelerate the transfer of the technology into clinical trials.

Lastly article entitled “Thermal Assisted *In Vivo* Gene Electrotransfer” by Donate and collaborators aims to minimize potential tissue damage and/or discomfort. The approach has explored the combination of electrotransfer with heat. While further optimization can be performed to enhance expression and optimize delivery, this approach provides the basis for a novel method and instrument that may greatly enhance the impact of the potential translation of gene electrotransfer.

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Altogether, these studies will in the next future allow electroporation to be a method of choice in gene therapy. This will also require, as already done for electrochemotherapy, to define the standard operating procedures (design of plasmids, pulse parameters, pulse generators).

We hope that this special issue will benefit not only to the researchers and physicians already using the so-called electroporation technique, but also to the other ones working in the field of gene therapy.

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