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Review Article

Twin Molecular Docking for Intra Cellular Electric Field Sensing and Modulation - A Literature Review - A New Concept in Therapeutics

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Abstract

Developmental bioelectricity refers to the regulation of cell, tissue, and organ level patterning and behaviour as the result of endogenous electricity mediated signalling.

Cells and tissues of all types use ion fluxes to communicate electrically. Bioelectric modulation has shown control over complex morphogenesis and remodelling, not just merely setting the individual cell identity.

With the advances in bio-engineering, multifunctional organic molecular devices with electric field sensing and modulation capability have been designed named as Twin bio-molecular intra cellular electro sensing device. The sensor module is derived from Tetraphenylethylene (TPE), which is a two photon fluorophore. The TPE sensor relies on the ultrafast photo-induced electron transfer (PeT) process to allow large changes in the electric field to be detected. The modulator module is an organic photoconductor, made of naphthalimide (NAI), whose resistivity can be tuned by using an ultraviolet optical source.

This Twin bio-molecular intra cellular electro sensing device, through cellular docking can be assessed and modulated to bring about homeostasis.

Keywords: Photoconductivity; Tetraphenylethylene (TPE); Naphthalimide (NAI); Bioelectricity; Fluorophore

Introduction

There are many unexplored domains to understand the physiological aspect of the human body as a pathfinder in diagnosis and treatment. One such domain is Cellular bioelectricity. Bioelectricity refers to the endogenous ion fluxes, transmembrane and transepithelial voltage gradients and electric currents that sustains the living cells and tissues. In physiological bioelectrical activity, when the muscle is in resting condition, the electrical potential is called resting membrane potential [2]. When the muscle is stimulated, electrical changes occur which are collective called action potential.

There are almost 40-50 trillion of cells present in our body. Every cell in human body has a minus voltage on the inside and positive voltage on the outside which is governed by Na-K ions [3]. So, every cell is a modulated set of charged batteries.

This electrical activity is often used for various bio modulations like during embryogenesis [4] and regeneration. It is a one layer of the complex field of signals that impinge upon all cells in vivo and regulates their interactions during pattern formation and maintenance. Resting potential, voltage gradients are more prevalent and essential to life's physiology, ranging from bioenergetics, motion, sensing, nutrient transport, toxin clearance and signalling in homeostatic and disease or injury conditions. These bioelectrical distributions are dynamic, evolving with time and with the microenvironment and even long distant conditions to serve as instructive influences over cell behaviour and large scale patterning during embryogenesis and regeneration. Bioelectric control mechanisms are an important emerging target for advances in regenerative medicine, birth defects, and synthetic bioengineering.

For maintaining homeostasis of body, there should be a balance in bioelectric gradients in body. If there is any variance of transepithelial potential gradients it may leads to pathologic conditions like developmental disturbances, infection, injury, cancer and various pathology.

Till date there are few methods to detect bioelectricity extracellularly like electrocardiogram (ECG), electromyogram (EMG) and electroencephalogram (EEG) [5] are used in medicine for diagnosis of various diseases.

Now for the first time researchers from University of Southern California, Los Angeles [1] have invented a multifunctional twin molecular device, which can do both – record and manipulate cell's bioelectric field.

Mechanism of action

The device is made up of two multifunctional optical organic molecules. The modulator module is an organic photoconductor, made of Naphthalimide (NAI) and the sensor module is derived from Tetraphenylethylene (TPE). The TPE and NAI modules were judiciously chosen for low overlap of their absorption and emission spectra to reduce resonant energy transfer.

TPE (sensor module) which is a two photon (2p) fluorophore that absorbs light energy of a specific wavelength and re-emits light at a longer wavelength. The TPE sensor module relies on the ultrafast photo-induced electron transfer (PET) process by which large changes in the electric field to be detected. Unlike voltage sensitive dyes, PeT molecules show better sensitivity [6,7]. The sensor module (TPE) excited in the near-IR (NIR).

The molecular device is comprised of two covalently coupled molecules: a tetraphenylene (TPE)-based PeT dye connected with naphthalimide (NAI)-based photoconductor [8]. The "senser" module of NAI–TPE-PyS was designed based on TPE but was modified with PyS (Pyridinium inner salt) to create TPE-PyS, representing the donor-spacer- acceptor system, as required by a PeT dye. So,this molecule, named as NAI–TPE-PyS, is comprised of two non-

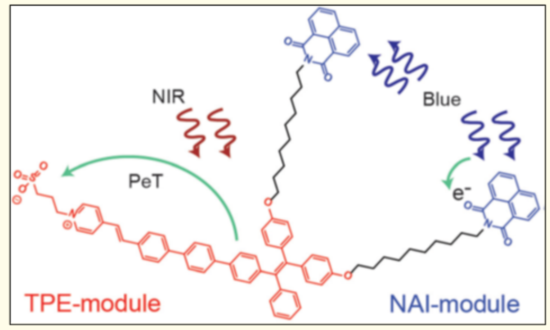

Figure 1: Chemical structure of NAI–TPE-PyS with TPE-module in red and NAI-module in blue.

interacting modules that are connected together by a non-interacting spacer like alkyl chain. The non-interacting alkyl chain does not affect the photophysical properties of the molecules but reduces dexter energy transfer between molecules by physical spacing.

The "modulator" NAI molecule was chosen due to its extensive use as an organic photoconductor and was incorporated without structural modification. The modulator module naphthalimide (NAI), whose resistivity can be tuned using an ultraviolet optical source.

The device is triangular in shape and smaller than virus and similar to diameter of DNA strand. The device would sit partially inside and outside the cell membrane. The sensing module (TPE) would detect the local electric field when activated by near infrared radiation. A voltage sensitive dye is used to sense abnormal electric potential gradients. The modifier molecule (NAI) would alter that electric field when activated by blue light. That's how the device works. The potential of NAI–TPE-PyS as a multifunctional electric field molecular probe is proved theoretically and experimentally.

So, by using this twin molecular device, the cell can be brought back from disease state to health.

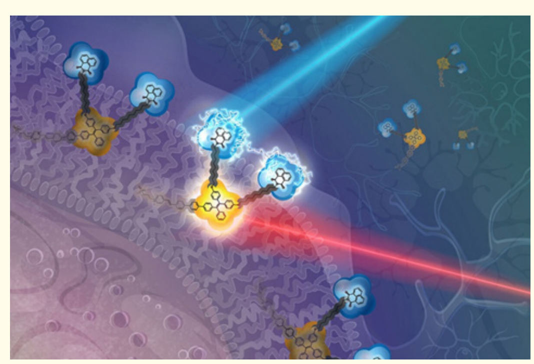

Figure 2

Advantages

The advantages of this molecular device are first of all it is non-invasive, electrical alteration can be documented by high resolution confocal microscope setup and most importantly modulator molecule alters electric field only at single point without damaging nearby cells and tissues [1].

Conclusion

In conclusion, the multifunctional molecular device, NAI–TPE-PyS, has been successfully designed in vitro. The photophysical and optoelectronic properties of NAI–TPE-PyS as a multifunctional electric field molecular probe have been investigated and proved experimentally and theoretically. But further experiments are required to implement this molecular device clinically. In future this twin molecular device could prove to be a valuable tool for understanding the complex bioelectric field of human cells with higher sensitivity and specificity, thereby aiding in better therapeutics.

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