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Quantum biology in regenerative medicine

Abstract

This review explores the potential of Quantum Biology in the understanding of the activation of hVSEL stem cells using a QiLaser™. There is a focus on the quantum mechanics of the interaction of modulated laser light from the QiLaser™ on the hVSEL stem cell surface antigen CXCR4-EPI-X4 complex. Understanding cell biology and the action of the QiLaser™ at the quantum level may allow significant advances in physiology, pathology and treatment.

Keywords: CXCR4-EPI-X4, quantum biology, QiLaser™, regenerative medicine, Very Small Embryonic Like (VSEL) stem cells

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Introduction

Not only does God play dice but... he sometimes throws them where they cannot be seen.

Stephen Hawking

When I was at Cambridge University in the late 1970's the human cell was usually represented as a two-dimensional square containing a circle representing the nucleus, a dot for the nucleolus and various squiggles representing the different organelles within the cytoplasm. This was great for me as a student because reproducing such a concept in examination conditions meant that a First Class mark was very possible! Even when I looked down a microscope at living blood cells, they seemed fairly static and two dimensional. Looking back, these were very simplistic times in terms of the true understanding of the structure and function of the human cell.

More recently, it is now possible to begin to describe some of the function of living cells at the quantum level using concepts from quantum physics such as quantum coherence,[1] quantum tunnelling,[2] quantum entanglement[3] and superposition.[4] The application of such concepts to the living cell promises a new level of understanding in cell biology.[5] Current concepts in quantum mammalian biology have been used to explore the function of the retina,[6] the sense of smell[7] and even insights into the pathophysiology of depression and other psychiatric disorders.[8] It is possible that quantum biology will allow the description and manipulation of mammalian biology and pathology in the future which could also lead to new and innovative approaches to treatment.[9]

Stem cells in regenerative medicine

Regenerative medicine is a growing field of study based around the use of various types of stem cells to treat tissue and organ disease.[10] Regenerative medicine has a long history with the first bone marrow stem cell transplant for a blood disorder in 1956.[11] There are currently several stem cell types being investigated as possible routes towards regenerative medicine and these include Mesenchymal Stem Cells (MSC),[12] Embryonic Stem Cells (ESC),[13] Induced Pluripotent Stem Cells (iPSC)[14] and pluripotent human Very Small Embryonic Like stem cells (hVSEL).[15] Each of these stem cells has pros and cons when used in regenerative medicine but hVSEL stem cells have potentially the most promise for the following reasons:

1. They are pluripotent and can therefore be used to create and repair all tissue types in the body.
2. They can be obtained from the peripheral blood by a simple venepuncture and the processing of the hVSEL stem cells in Platelet Rich Plasma (PRP) is quick, cheap and easy.
3. hVSEL stem cells can be returned to the patient either directly to the site in which they are required (e.g. a joint) or intravenously.

Some workers suggest that hVSEL stem cells are biologically inactive in normal physiology[16] but other workers suggest that hVSEL stem cell numbers are increased in certain pathologies.[17,18]

QiLaser activation of hVSEL stem cells

It has been clearly demonstrated that a patented modulated red laser (known as the QiLaser™ and previously known as the SONG modulated laser) can be used to upregulate surface antigens (notably CXCR4) on hVSEL stem cells obtained from PRP.[19] These QiLaser™ hVSEL stem cells and MSC have been shown to be effective in the treatment of end stage heart failure with 80% of patients who received treatment were able to be removed from the heart transplant list.[20] Other workers have shown the importance of the CXCR4 surface antigen and ligand in the treatment of ischaemic heart disease.[21] The fact that the QiLaser™ was able to upregulate CXCR4 surface antigens, and other surface antigens on hVSEL stem cells, led to the exploration of possible quantum biology mechanisms for this unique action.

The modulated QiLaser™

The QiLaser™ produces modulated (5mW, 670 nm) red laser light. The modulation of the laser light cancels the central wavelength band of the laser output using non-fringing destructive interference. The remaining upper and lower wavelength bands in the modulated laser light form a beat frequency pattern of space nodes representing the remaining visible light. This is a complex waveform which results from modulation of the wave form pattern which in turn produces a rapid pulse repetition frequency repeating at a sub-femtosecond rate. This destructive interference and sparseness of the nodes reduces the flare at the surface of the laser-tissue or cell interface. The resultant QiLaser™ modulated light is adjusted using optical phase conjugation to achieve a power of 1 mW output for 3 minutes.

The biology of the CXCR4 surface antigen

The CXCR4 antigen is involved in cell adhesion and is found in a wide range of cells including hVSEL stem cells in PRP.[19] The CXCR4 surface antigen has an endogenous peptide inhibitor known as EPI-X4.[22] The EPI-X4 antagonist is a naturally occurring peptide derived from the fragmentation of albumin and it binds to the CXCR4 surface antigen *via* the N-terminal residues causing an inhibition of G-protein signalling.[23] Several EPI-X4 derivatives have been reported and IC50 values confirm that the N-terminal residues of EPI-X4 are critical for binding to CXCR4.[24] The binding of EPI-X to CXCR4 is achieved through 3 salt bridges and 1 hydrogen bond.[25] The distance between the residues in the salt bridges is 400 picometers (pm).[26]

The EPI-X4 antagonist to CXCR4 is formed from fragmented albumin in the acidic conditions of embryonic gastrulation[27] and dysregulates the CXCR4 expressed by hVSEL stem cells. This in turn maintains hVSEL stem cell quiescence.[28] The observations discussed above suggest the hypothesis that the QiLaser™ penetrates the minor pocket of CXCR4 degrading the salt bridges and hydrogen bonds resulting in the release of the EPI-X4 antagonist and the reactivation of CXCR4.

Quantum mechanics of the hydrogen bond

There is a complex relationship between the modulated laser light generated by the QiLaser™ and the quantized energy levels of hVSEL stem cells. This interaction results in QiLaser™-induced turbulence. The key features of this interaction can be proposed by the hypothesis that the hydrogen bonds have a reduced Hilbert Space in the two diabatic states, which are D-H,A- and D-,H-A. The D-H,A- represents the electronic state of the A- ion of a D-A bond in the absence of an acceptor. The equilibrium of the two states relies on the transfer of a proton from donor to acceptor and back again.

The Hamiltonian function for the two diabatic states depends on the D-H bond length (r) ,the donor-acceptor separation (R) and the angle ϕ which is the deviation from linearity. The resultant Hamiltonian function is:

$$H = \begin{pmatrix} V_D(r) & \Delta_{DA}(R,\phi) \\ \Delta_{DA}(R,\phi) & V_A(r^*) \end{pmatrix}$$

In the Hamiltonian function above $V_D(r)$ and $V_A(r^*)$ represent the Morse potential for the system

And $r^* = \sqrt{R^2 + r^2 - 2rRcos\phi}$ is the length of the A-H bond.

The diabatic states are coupled *via* the off-angle matrix element:

$$\Delta_{DA}(R,\phi) = C\cos\phi\,\frac{R - r\cos\phi}{r^*}$$

Where R , r^* and ϕ are defined above and C represents a scalar which will vary with the chemical identity of the hydrogen bond donor and acceptor atoms.

The system being described has two interacting diabatic states D-H and H-A which are anharmonic. This means that a simple single harmonic potential cannot apply to this system and that the Morse potential will more accurately determine each diabatic state independently. In each case j=D and A represents the donor D-H bond and acceptor H-A bond. The Morse potential is:

$$V_j(r) = D_j\left[e^{-2a_j(r-ro_j)} - 2e^{-a_j(r-ro_j)}\right]$$

Where D_j is the binding energy, ro_j and a_j are constants representing the equilibrium bond length and the decay constant respectively. D_D and D_A are the proton affinity of the donor and acceptor.

The energy of the stationary, interacting diabatic states as described above can be calculated by using the time-independent Schrödinger equation:

$$H\left|\Psi(x)\right\rangle = E\left|\Psi(x)\right\rangle$$

Where E is the energy of the system and Ψ is the wave function.

There is an energy barrier between the donor and the acceptor which reduces as the donor-acceptor distance decreases. At low energy levels hydrogen is strongly bound to the donor. The hydrogen is therefore more likely to be bound on the donor side of the energy barrier and is delocalised when the length is approximately 20-30 pm.[29] As R decreases, and the energy barrier become close to the zero-point energy level for the system, the hydrogen will be found centrally but it remains delocalized. Temperature increase will weaken the hydrogen bonds and increase thermal motion. The length and strength of the hydrogen bond is therefore both temperature and pressure sensitive. Hydrogen bonds are weak, and their internal energy is directly proportional to the bond strength. The equilibrium bond distance is controlled by a combination of quantum mechanics and thermodynamics.

The effect of the QiLaser™ on hydrogen bonds and salt bridges in CXCR4/EPI-X4 binding

The delocalization of the hydrogen atom, on either side of the energy potential curve of weak bonds, is either at the ground state E_0 or at the first excited state E_1. If the hydrogen atom is energized from E_1 to E_2 then it will be more strongly bound to the donor atom. The energy required for the change from E_1 to E_2 is 1.9 eV.

Standard laser light is quasi-monochromatic with a small wavelength spread around the central wavelength this is known as the spectral width.[30] Standard laser light is highly directional and emitted as a narrow beam.[31] In contrast the QiLaser™ is further focused by both constructive and destructive interference patterns which may enhance laser penetration and reduce 'scattering' effects. In the CXCR4-EPI-X4 complex on the surface of a hVSEL stem cell the receptor (a hydrogen atom) responds to excitation from the QiLaser™ resulting in a transmitter of an amalgam of single atoms, each of which produces its own energy wave.

The reaction at the receiver requires a single atom excitation at the transmitter. The QiLaser™ produces modulated red laser light meaning that each transmitter atom produces red light. This modulated red laser light will react with any E_1 energy hydrogen atom. If the intensity of the modulated red laser light increases, then more single laser atoms become excited but the receiver hydrogen atoms remain at $E_{1\ to}\ E_2$. The modulated red laser light produced by the QiLaser™ will react with atoms in the general *in vitro* environment which is likely to induce an insignificant thermal effect. More importantly, the modulated red laser light produced by the QiLaser™ will penetrate the minor pocket of CXCR4 and supply precisely the energy required to interact with the hydrogen bonds and salt bridges within the minor pocket of CXCR4. Every atom at the source of the modulated red laser light in the QiLaser™ will supply 1.9 eV to every E_1 hydrogen atom and excite it to the E_2 state. This results in two diabatic stationary states:

$$H\left|\Psi_{(0)}\right\rangle = E_{(0)}\left|\Psi_{(0)}\right\rangle$$

$$H\left|\Psi_{(1)}\right\rangle = E_{(1)}\left|\Psi_{(1)}\right\rangle$$

On exposure to the red modulated laser light from the QiLaser™ a third destabilizing state is produced:

$$H\left|\Psi_{(2)}\right\rangle = E_{(2)}\left|\Psi_{(2)}\right\rangle$$

This third destabilizing state results in a change of the two-state equilibrium of both the hydrogen bonds and salt bridges. Using the hypothesis that only the hydrogen atoms are immediately affected, and the donor-acceptor length remains at R then the following elements of the Hamiltonian are the most likely perturbation variants: r , r^* and ϕ

since the Hamiltonian which describes the two interacting diabatic states is:

$$H = \begin{pmatrix} V_D(r) & \Delta_{DA}(R,\phi) \\ \Delta_{DA}(R,\phi) & V_A(r^*) \end{pmatrix}$$

The most significant change will be an increase in ϕ resulting from the hydrogen atom energy delivered by the QiLaser™. The strongest bonds will occur when ϕ is zero. Any increase in ϕ will result in an increase in r and r^* which will weaken the strength of the hydrogen bond. The modulated red laser light produced by the QiLaser™ continuously penetrates the minor pocket of CXCR4 which weakens the stability of hydrogen bonds and the electrostatic bonding of salt bridges. This effect will spread *via* a swapping of thermal energy which increases the local temperature within the binding pocket. When this turbulent environment breaks a hydrogen bond the zero-point energy of that bond is released which leads to further destabilization energy and a subsequent further increase in temperature. This process continues until sufficient bonds are broken to release EPI-X4 from CXCR4. Further work is needed in this complex field, but this initial hypothesis provides a good foundation for further experimental investigations.

Conclusion

The QiLaser™ stimulates the proliferation of hVSEL stem cells *in vitro* and this stimulation can be understood by considering energy exchange at the quantum level. It is clear that the response of hVSEL stem cells to the QiLaser™ is a quantum effect which can be clearly described at the quantum level. This provides further evidence to the fact that quantum mechanics can describe biological processes and how quantum effects may be used to either initiate or even control biological processes. Quantum mechanics are nevertheless complex involving conceptually difficult concepts such as the exclusion principle, spin, entanglement and polarization. It is a reasonable assumption that all of these effects are continuously inaction in the atoms and molecules which constitute human cells. This type of analysis will lead to fundamental questions, and new levels of understanding, in cell biology, optical physics and quantum mechanics. The current work focusses on the CXCR4 antigen found on hVSEL stem cells but it is highly likely that the QiLaser™ may have similar effects on other cells and tissues, to further define the mode of action of modulated laser light on human cells and tissues. The powerful combination of cell biology and quantum mechanics may enable great progress in the detailed understanding of normal physiology, in a complex understanding of the mechanisms of pathology and in the development of ground-breaking therapeutics.

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Conflicts of interest

Author have no conflict of interest.

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