Calcium ions have many uses biology essay

Calcium ions are of vital importance to the human body. Calcium Ions are used throughout human cells for various metabolic functions that include structural roles in the bones cells, as a cofactor for proteins and enzymes, converting electro-physiological signals to chemical signals in neurons and as a intracellular regulator plus many other functions. The focus is on Calcium ions role in the exocytosis of neurotransmitters in neurons as well as its role as in the stimulation of muscle contractions of human cells.

Calcium is the most abundant mineral in the body with the weight of calcium in an average human being 1-2 kilograms. The continual loss of calcium requires a daily intake of around 1000mg per day.(Washington University, 2004). This amount accounts for the over all loss of calcium on day to day living. Although higher amounts may be required if individual is under going growth or pregnancy. 99% of calcium in the body can be found in the skeleton and teeth. The remaining 1% is found in the blood and cytosol of cells and extracellular fluid, with 50% of this as free calcium ions, 40% as cofactors in proteins and enzymes and 10% in compounds with other cellular components. (Washington University, 2004).

The Free calcium ions concentrations are of the most importance to cellular activity. The concentrations of a cells cytosol is at resting is approximately 10^-6M of free calcium ions. Where higher concentrations of 10^-3 M in the extracellular fluid and blood (Washington University, 2004). This creates a concentration gradient between the cells cytosol and the extracellular fluid. As calcium is a larger ion it can not easily diffuse through the cell membrane. This concentration gradient is also regulated by inter-membrane proteins channels and pumps. High concentrations of calcium can also be found in

some membrane bound organelles such as the Endoplasmic Reticulum, Sarcoplasmic Reticulum (in muscle cells) and Mitochondrion in some specialised cells. Calcium binding proteins also maintain the concentration levels by binding to the free calcium ions in the cytosol. This only occurs when the concentration of free calcium in higher than the resting concentrations of the cytosol. This concentration gradient is the key mechanism the cells use to regulate and stimulate cellular processes.

Exocytosis In Neurons

Action Potential

Calcium Ions have a major use in chemical synapses of neurons by converting the electrical signals from the action potential into a chemical signal. This is achieved by the stimulating the exocytosis of neurotransmitters into the synaptic cleft of the two neurons. This highly regulated system of exocytosis is used to convert the electrical signal of the action potential (the transmembrane potential) to a chemical signal in the uses of neurotransmitters as a signalling agent. The first stage of the process is the generation of an action potential on the pre-synaptic neuron.

When the pre-synaptic neuron is stimulated an action potential occurs in the cell membrane creating a depolarisation of the membrane, from its resting state of -70mV to +30mV. Through the change of sodium and potassium ions in and out of the membrane. This chemical gradient creates a transmembrane gradient that can be measured in mV. As sodium is pumped into the cell, through sodium membrane proteins channels, the chemical gradient of sodium inside the cell increases and this also increases the transmembrane potential when the transmembrane gradient reaches

+30mV the threshold is reached and the sodium membrane proteins are deactivated and the potassium channels are activated pumping potassium out of the cells bringing the transmembrane potential back to resting state. This creates a “ wave” of transmembrane potential along the axon of the cell. This increase in the cells transmembrane potential stimulates Voltage-gated calcium channels (VGCCs) in the synaptic knob to open. (Martini and Nath 2009)

Calcium In Exocytosis in Neurons

The VGCCs rely on this transmembrane potential to become active. There are 6 main kinds of voltage-gated calcium channels types T, L, N, P/Q, and R with Type N being found mainly in the brain, spinal cord and peripheral nervous system. (Zamponi, 2005),(Garcia, 2006). Type N has a high voltage activation thus it is found extensively in chemical synapses. When the action potential reaches the synaptic nob where most VGCCs are located and the transmembrane potential is approximately 10-15mV the VGCCs are activated allowing for the transfer of calcium ions from the high concentrations of the extracellular fluid into the cytosol of the pre-synaptic neuron. This creates higher concentrations of calcium ions in the cytosol of the pre-synaptic neuron.

This increase in the concentration of the calcium ions stimulates calcium binding proteins on the surface of the excretory vesicles containing neurotransmitters. There are many various calcium binding proteins used as calcium sensors in regulated exocytosis such as Synaptotagmin and the Soluble N-ethylmaleimide-sensitive Factor Attachment Protein Receptor (SNARE) complex. (Burgoyne and Morgan, 1998) (Yoon and Shin, 2008) .

Synaptotagmin is a highly documented and studied synaptic vesicle membrane protein. (Montes, Fuson, Sutton, Robert. 2006).

Synaptotagmin is a membrane bound protein found on the membranes of vesicles found at the synapses of neurons. It mediates the stimulus of increased calcium concentrations and mediates the fusion with the neurons synaptic membrane and the vesicle. A total of 16 alleles of the Synaptotagmin gene have been found in humans. With some types of synaptotagmin has been discovered to have low affinity to the calcium ion, others have high sensitivity to calcium ions showing high specificity to the presence of high calcium concentrations. (Yoshihara & Montana, 2004) Synaptotagmin 1 has been documented as the major protein in the synaptotagmin protein family to regulate the exocytosis in neural cells by acting as the primary sensor to calcium ions. It operates by acting on the pre-synaptic membrane in particular the SNARE complex.

The SNARE complex consists of synaptobrevin, syntaxin and SNAP-25 as the core SNARE proteins. Synaptobrevin acts as the v-SNARE being attached to the vesicle membrane while syntaxin and SNAP-25 are the t-SNAREs on the target (pre-synaptic) membrane. These proteins when stimulated have intertwining sections that form “ zippers” from the free N terminus of the protein to the C terminus in the membrane bound section. This greatly lowers the energy required for membrane fusion as shown in Figure .....

This use of synaptotagmin as a calcium ion sensor and the SNARE complex in membrane fusion greatly decreases the speed of the over all reaction of exocytosis from what could take minutes to perform only take 60 Î¼s from

calcium channel opening to neurotransmitter release.(Burgoyne and Morgan, 1998). For this speed in reaction time to occur the pre-packaged vesicles are situated in close proximity to the synaptic membrane. So the synaptotagmin sensors can bind quickly to the free calcium ions and stimulate the SNARE complex.

Lowering Calcium Concentration in Cells

As concentrations of calcium ions is raised from 10^-6M to 10^-3M by the influx of extracellular calcium ions, the high concentrations of calcium ions in the pre-synaptic cytosol will continually stimulate the release of neurotransmitters by the pre-synaptic neuron. This concentration of intracellular calcium is then lower through a variety of cellular mechanisms. Some calcium is lost in the process of exocytosis, concentrations are also lowered by binding to the free calcium ions to the calcium binding proteins. Calcium is also transported into the endoplasmic reticulum and mitochondria of the cell. These techniques are used to lower the cells free calcium ion concentration enabling the cell to prepare for the next action potential.

Neurotoxins

These series of events that lead to the exocytosis of neurotransmitters through the use of free calcium ions can have problems occur, particularly in the occurrence of toxins in the body. Some major toxins that affect the control of calcium concentration in the cytosol of neurons affect the VACCs such as Ï‰-CtxGVIA found in toxins from predatory marine Cone Snails, Ï‰-agatoxins found in venom from spiders such as the funnel-web spider Agelenopsis Aperta. (Uchitel, 1997). Other toxins such a botulism an exotoxin produced by the bacteria Clostridium botulinum has been shown to

block the SNARE proteins from operating effectively by binding to the SNAP-25 and Synataxin and cleaving the “ Zipper” tails of the proteins. These toxins actively inhibits the exocytosis of neurotransmitters and prevent the role of calcium to fully perform its biological function.

Skeletal Muscle Contraction

Muscle Cell Anatomy

Muscles are a collection of specialised cells that contract and relax to control over all movements of the body. The skeletal muscle cells are elongated cells that contain vital specialised organelles such as Myofibrils and Sarcoplasmic Reticulum. Skeletal muscle cells also contain multiple Nucleus’s and a high number of mitochondria. The Myofibrils are long protein filaments that are made of units called Sarcomeres , made of around 10, 000 units repeated end to end. (Martini and Nath, 2009) These Sarcomeres are made of two types of protein filaments, Thick filaments consisting of Myosin and thin filaments consisting of Actin, Troponin and Tropomyosin. (Sanger, Wang, Fan, White, Sange, 2010). These filaments are arranged in a structure as shown in figure.....

The Myofibrils are encased in the Sarcoplasmin Reticulum (SR) . The SR is similar in structure to the endoplasmic reticulum in the it is made of a Phospholipid bilayer. The SR contains low concentrations of free calcium ions, it fuses and forms expanded chambers called Terminal Cisternae, these contain high concentrations of calcium ions up to 1000 times higher than in the SR. A calcium binding protein called Calsequestrin is found in the Terminal Cisternae of the SR these proteins have a high capacity to bind to free calcium ions but low affinity to the calcium thus it is used as a storage

protein. This allows for the concentration of calcium to be maintained by the calcium pumps in the Sarcoplasmic membrane. (Park, Wu, Dunker, Kang. 2003)

Stimulation Of Skeletal Muscle Cell

As the neurons releases the neurotransmitters into the synaptic cleft a post synaptic cell is stimulated to perform a specific function according to the type of neurotransmitter used. One highly important neurotransmitter is Acetylcholine. This neurotransmitter is released by motor neurons. Acetylcholine binds to specific receptors on Sarcolemma (muscle cell membrane containing Phospholipid bilayer, proteins and polysaccharides). Acetylcholine stimulates the Nicotinic Acetylcholine receptors on the Sarcolemma, altering the membrane to become more permeable to sodium ions creating an action potential on the Sarcolemma of the muscle cell. This action potential has the same effect on the Sarcolemma as on the neurons cell membrane creating a sodium/potassium based transmembrane potential. The action potential travels along the Sarcolemma and into the Transverse (T) tubules. The T tubules are narrow tubes that are a continuous membrane that act as passage way into the cells body. The T tubules are filled with extracellular fluid, this enables the action potentials to enter in to the cells. (Martini and Nath , 2009)

Calcium Release

The need for T tubules are quite simple, when a muscle fibre contracts all of the functioning units must be stimulated simultaneously this can only be done by the action potential being able to reach the inner most Myofibrils of the muscle cell, the T tubules allow for this to occur. This action potential

does not stimulate the VGCCs in the T tubules membrane to let calcium ions in from the extracellular fluid unlike in neurons, the action potential acts upon a different set of proteins found in the SR. The Action potential stimulates Sarco-, Endoplasmic Reticulum Ca2+ ATPase (SERCA) pumps in the Sarcoplasmic Reticulum and also the releases of calcium ions bound to the Calsequestrin proteins. The SERCA pumps releases calcium from inside the Cisternae to the Sarcomeres. This flow of calcium against the gradient through the SERCA pumps produces ATP molecules from ADP and Inorganic Phosphate.(Gilchrist, Palahniuk, Bose. 1997). This increase in the concentration of calcium stimulates the contraction on the muscle cells by interacting with calcium binding proteins in the Sarcomeres.

The calcium ions entering the Sarcomeres binds to the calcium binding protein complex Troponin found on the thin filaments. The Troponin complex proteins consists of 3 subunits, Troponin C (TnC), Troponin I (TnI) and Troponin T (TnT). TnT binds to the Tropomyosin which in turn binds to the Actin protein. This makes up the structure of the thin filament. The main role of Troponin is to inhibit the binding of the thick filaments , Myosin heads, to the thin filaments , the Actin. The Troponin is the regulator of the muscle contraction and the calcium is the key. When there is no muscle stimulation the presence of free calcium ions is low and the Troponin is not stimulated, this locks the Tropomyosin into the position over the active sites of Actin, by the TnI subunit, not allowing for the contraction of the filaments. (Farah, Reimach, 1995). When the stimulation occurs and the influx of calcium ions into the Sarcomere occurs the TnC subunit binds to the free calcium and removes the TnI subunit from Tropomyosin. Tropomyosin then is removed

from the active site of the Actin protein allowing for the binding of Myosin heads to the active site of Actin.

Myosin and Contraction

The Myosin protein consists of globular heads that contain an enzymatic active site and a

binding active site as well as a coiled tail consisting of multiple Î±-helix structures. (Harrington, Rodger. 1984). Thousands of these Myosin proteins are bound together to form the thick filament of the Sarcomere. The enzymatic active site binds to Mg2+ ATP and hydrolyses it to ADP and Inorganic Phosphate (Pi). This break down of the ATP molecule also energises the Myosin heads and sets it in the “ cocked” position. The Myosin heads can not proceed from this position when the Actin active sites are not available to bind to. (Martini and Nath, 2009)

In the presence of Calcium the active sites are available to bind to the Myosin heads form a cross bridge with the Actin active site. When the cross bridge is established the the stored energy in Myosin heads from being set in the “ cocked” position in released pulling the thick filament towards the M line (Shown in Figure 2) of the Sarcomere. This occurs over multiple Myosin heads so when one head is being cocked another is in the cross bridge position allowing for the gripping of the thin filaments by the thick filaments. As all Sarcomeres operate in unison this forms the contraction of the Myofibrils and the muscle cell.(Martini and Nath, 2009)

Lowering Calcium Concentration in Cells

This contraction of the Myofibrils will continue to occur while Acetylcholine is being released from the motor neuron. When the muscle cell ceases to be stimulated the level of calcium in the Sarcomeres is lowered. This occurs by the same protein that was stimulated to pump the calcium ions into the Sarcomeres during contraction, the SERCA pumps. The SERCA pumps are reversible in their role as calcium ion pumps. By pumping the calcium against the gradient of calcium from inside the Sarcomeres to into the Cisternae the SERCA pumps require the energy from ATP molecules. (Gilchrist, Palahniuk, Bose. 1997). This pumping recreates the concentration gradient in the Cisternae and recycles the calcium used in the contraction of the muscle.

Hypercaltermia