Nobel prize in Physiology / Medicine -2013

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The Eukaryotic cell has a very dynamic machinery that performs specialised functions in the system. This cell has highly organised compartments that perform various cellular activities. One of the central activities of the cell is Protein Synthesis that is essential for the function and survival of the cell. More than 20,000 known protein-coding genes are present in the human genome. A cell at any given point of time produces numerous proteins. Each protein that is synthesised in the cell needs to be transported to its target compartment within the cell or to other cells.

The protein synthesis takes place in the rough endoplasmic reticulum with the help of ribosomes. The protein that is synthesised is then transported to the golgi apparatus, where it is subject to chemical modifications like glycosylation and phosphorylation. From the golgi apparatus, the mature protein is packed and transported to its destination. Given the large amount of proteins being synthesised in the cell, it was a puzzle how the protein reached its destination. This transport has to be highly precise in spite of the complexities of diverse number of proteins being synthesised and diverse number of target destinations. The destination could be both within the cell (eg: nucleus, endoplasmic reticulum, etc) or can be to other cells (eg: delivery of hormones, cytokines, neurotransmitters etc).

This year Nobel Prize in Physiology or Medicine was awarded to Dr.Randy Schekman, Dr.James Rothman and Dr.Thomas Südhof: the three scientists who gave insights into how this delivery of the synthesised protein takes place with utmost accuracy. They discovered the key role played by a specialised compartment of the cell called as vesicles, which organised the transport system both within and between the cells. The vesicle is a small membrane bound organelle that is of three types (Figure-1)

(i) Cop II coated vesicles that transport proteins from Endo Plasmic Reticulum to the Golgi Apparatus.

(ii) Cop I coated vesicles that do a reverse transport from Golgi Apparatus to the Endo Plasmic Reticulum.

(iii) Clathrin coated vesicles that transport the proteins from the Golgi Apparatus to the Lysosome or Plasma Membrane. The Clathrin coated vesicles are the most common type of vesicles that are involved in protein transport between the cells.

The specificity of the transport system is achieved by means of specific receptors present on the membrane of the vesicles. This receptor has specific ligands in the target cell/organelle and the interaction between the vesicular receptor and the ligand determines the specificity of the transport.

Dr. Randy Schekman identified genes that are involved in vesicular fusion in the yeast. His group defined a set of *sec* genes in the yeast by developing temperature sensitive mutants of these genes. The organism that was mutant to the *sec* genes had accumulation of proteins in the cell. Further, a set of 23 sec genes were identified that were involved in the vesicular fusion with different organelles of the cell[1,2].

Dr.James Rothman identified the specific vesicular membrane receptor that was essential for the fusion of the vesicle to the target organelle. His team first discovered a protein called as N-ethylmaleimide Sensitive Factor (NSF) that is a key receptor involved in vesicular fusion. His group further characterized Soluble NSF Attachment Protein (SNAP) in the vesicles and their receptor called SNAP Receptor (SNARE) that determine the specificity of the vesicular fusion with the target[3,4].

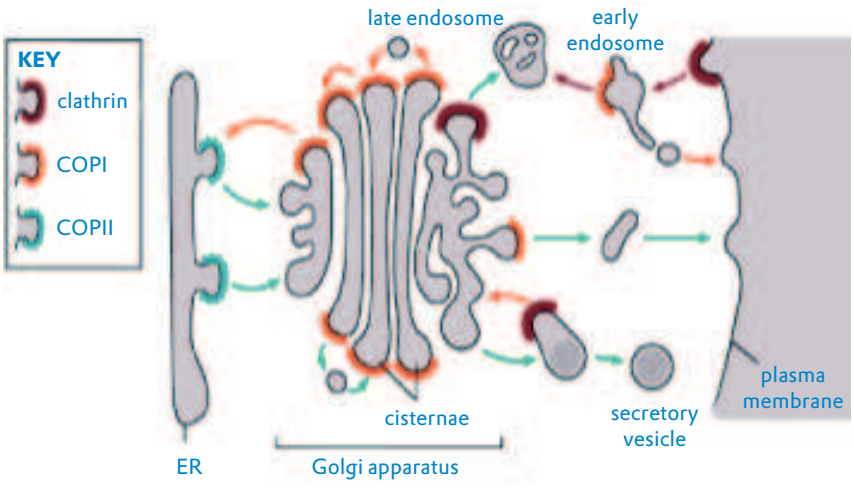

Fig 1: Types of Vesicles in an Eukaryotic Cell

Dr.Thomas Südhof gave insights into the control of vesicular fusion. Using Neuron cell as a model his team identified specific proteins called as synaptotagmin-1 that interacts both with the Phoshpholipid bilayer and Ca2+ ions. It is known that Ca2+ ion concentration was critical in determining the neuronal signal.

Identification of the synaptotagmin-1 molecule described that the release of the vesicular package was mediated by synaptotagmin-1 molecule in response to Ca2+ concentration thus controlling the timing of the vesicular fusion[5,6].

About the Nobel Laureates
(Adapted from the press release of The Nobel Assembly at Karolinska Institute)

James E. Rothman was born 1950 in Haverhill, Massachusetts, USA. He received his PhD from Harvard Medical School in 1976, was a postdoctoral fellow at Massachusetts Institute of Technology, and moved in 1978 to Stanford University in California, where he started his research on the vesicles of the cell. Rothman has also worked at Princeton University, Memorial Sloan-Kettering Cancer Institute and Columbia University. In 2008, he joined the faculty of Yale University in New Haven, Connecticut, USA, where he is currently Professor and Chairman in the Department of Cell Biology.

Randy W. Schekman was born 1948 in St Paul, Minnesota, USA, studied at the University of California in Los Angeles and at Stanford University, where he obtained his PhD in 1974 under the supervision of Arthur Kornberg (Nobel Prize 1959) and in the same department that Rothman joined a few years later. In 1976, Schekman joined the faculty of the University of California at Berkeley, where he is currently Professor in the Department of Molecular and Cell biology. Schekman is also an investigator of Howard Hughes Medical Institute.

Thomas C. Südhof was born in 1955 in Göttingen, Germany. He studied at the Georg- August-Universität in Göttingen, where he received an MD in 1982 and a Doctorate in neurochemistry the same year. In 1983, he moved to the University of Texas Southwestern Medical Center in Dallas, Texas, USA, as a postdoctoral fellow with Michael Brown and Joseph Goldstein (who shared the 1985 Nobel Prize in Physiology or Medicine). Südhof became an investigator of Howard Hughes Medical Institute in 1991 and was appointed Professor of Molecular and Cellular Physiology at Stanford University in 2008.

References

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Answer to : **Diagose the Condition**

This ECG shows wide QRS complex with ventricular rate of around 85/min. The P waves are seen just after QRS complex. But in the long strip of lead II, fifth and seventh QRS complexes are narrow and were preceded by a normal P wave. There is a slight difference in the morphology in such a way that fifth complex is narrower than seventh complex. Fifth beat is called a CAPTURE BEAT and seventh beat is a FUSION BEAT.

This is a classical ACCELERATED IDIOVENTRICUALR RHYTHM. AIVR is a reperfusion arrhythmia common after acute MI. AIVR needs no specific treatment and it usually resolves spontaneously.

-**Dr.M.Chokkalingam,** Consultant Cardiology, CSSH