Within last year scientist at Yale University and University of Rhode Island have developed a synthetic peptide that is known to transport molecules across the cell membrane and into the cytoplasm of a low pH cell. Donald M. Engelman, a professor from Yale, led the study. The peptide is a called pHLIP (pH low-insertion peptide) and can function as a nanosyringe to deliver drugs to the cell, monitor control genes and provide images of diseased tissue. PHLIP can only insert the head of the peptide into cells in acidic extracellular environments. Cells that are normal are surrounded by extracellular fluid with a pH of 7.4 whereas inflamed, tumorous, or cancerous cells have a low pH surrounding, pH 5.5-6.5, caused by the protons being pumped out of the cell.

The way pHLIP enters the cell is not by means of the usual endocytosis, pore formations, or cell receptor entry; instead the peptide becomes stiff like a needle in low pH areas and pierces through the cell membrane. The polypeptide itself does not go further than the membrane, except the disulfide bond holding onto the molecule is the only part meeting the cytoplasm. The peptide forms an alpha-helix in the lipid bilayer of the cell membrane due to its characteristic of being a globular protein and folding caused by hydrogen bonding. The molecule is the only part of pHLIP that is inserted into the cell. The cytoplasm has a “reducing environment” that causes the disulfide bond to break and release the molecule into the cytoplasm. If the environment of the cell becomes less acidic and back to the normal 7.4 pH than the reverse effect takes place, dislodging the helix and the retraction of the pHLIP back into the extracellular fluid.

The uses for pHLIP are promising. Thus far, it is said to be useful for drug delivery, making fast and efficient by targeting a specific area. Secondly, it can be used for gene control, regulating the reproduction of RNA for bad cells so that the cells are not reproduced and spread throughout a tissue. Also, pHLIP can monitor and provide images of diseased cells so that we are provided with more information about a damaged area or type of damaged cell. Currently researchers are using fluorescent dye to locate areas of bad cells. They hope to insert molecule-like cameras into cells. This would create a new approach to image diagnosis. Examples of areas of low pH that would create the environment to allow penetration of pHLIP include: tumors, infarcts, infections, inflamed areas, stroke afflicted tissue, lesions from atherosclerosis, and damaged tissue form trauma.

Hopes are arising for pHLIP to be a new method of treatment for cancer. Either by drug delivery or through gene control – stopping cancerous cells from spreading. If used for drug delivery the peptide could preserve the good cells from damage by the drugs and target only the cancerous cells. This would allow for a less debilitating treatment than chemotherapy.

REFERENCES:


