11. Metalloproteins

We are in general familiar with making proteins and although their formation is not straightforward it is well understood. However, we now also know that metals such as iron, manganese, copper, calcium, nickel etc. play a very important role in the functioning of the cell and work as a part of the proteins. What is interesting is that only a very small amount of metal, just a few atoms, added to a protein consisting of many thousands of atoms is sufficient to perform very critical catalytic functions. However, the formation of metalloproteins is much more intricate than the formation of proteins and it shows how ingenious and clever the cell's design is. As we know genes provide information about the coding of proteins by defining the sequence of amino acids, but there is nothing in genes about adding metals, so the cell must find a way around this. First, proteins which will work with metals are produced, and next metal atoms are added to these proteins.

The protein must be designed in such a way that it must have a suitable binding site which will accept a metal ion. Therefore, the acceptance of metal by a protein must be coded in DNA.

However, the acquisition of metals and linking them with the right proteins is not that simple.

The problem is that different metals have different affinity/attraction to make a link with a protein. Metal with a strong affinity would kick out a metal with weak affinity which is already linked to the protein. Metals with weak affinities are magnesium, calcium and manganese and metals with strong affinities are nickel, copper and zinc.

Normally several of these metals would be present in the cell's cytoplasm and they would compete to link to the proteins. We have to understand that a protein can accept different metals.

Somehow, and this is the clever thing, the cell 'knows' about these affinities and tries to prevent competitive metals linking to the wrong protein. To solve the problem, the cell first puts competing metals in different locations in the cell, then a special protein links to the required metal and folds in such a way that the 'weak' metal is inside the protein and cannot be kicked out by the 'strong' metal.

Another clever solution adopted by the cell is to restrict the number of metal atoms within the cytoplasm so that 'weak' metals do not compete with other metals for a limited pool of proteins, but rather each protein competes with other proteins for a limited pool of metal atoms. But how does the cell discern the different metals and control their effective intracellular concentrations? The cell's membrane has a sophisticated system to control the transport of materials in and out of the cell. Special proteins called metal transporters transfer metals through the membrane. Most importantly, metal transporters have binding sites which bind only the correct metal atoms. The metal transporters make sure that when there is a surplus of metal atoms which cannot find the right proteins they are exported from the cell, otherwise these strong atoms would displace weak atoms during further processing.

To help with the insertion of metal atoms into the proteins there are special helpers which bind the metal when it is transported into the cell, take them to the right protein and make sure that it is correctly fitted.

To control metal handling by the cell there are metal sensors for each metal used. There are seven groups of sensors controlling about eleven different metals. They make sure that there are just enough metal atoms needed by the proteins. In case there is a shortage of specific metal atoms, the metal sensor sends a signal to the genes to start making more metal transporters.

The handling of metals by the cell is achieved by a very well designed system. It starts with DNA which codes not only metal specific proteins but also metal specific transporters, chaperons, carrier proteins and sensors. This system operates as a sophisticated mechanism controlling the import and export of metals, initiating the building of transporters and influencing cell metabolism. There is no need to emphasize that this system can only operate as a whole unit and could not have evolved in separate parts via small improvements.

It is estimated that about 30 percent of all types of proteins are metalloproteins. They play a critical role in cell metabolism. The most well known metalloprotein is hemoglobin, carrying oxygen in the red blood cells of almost all vertebrates. Important cell functions which are controlled by metalloproteins are the splitting of water into oxygen and hydrogen and the fixing of atmospheric nitrogen.