Research Says Sugar Coated Proteins Seal in a Memory of Diabetes

June 28 2007

Researchers at the University of Warwick's Warwick Medical School have uncovered a process that locks the body's metabolism in a diabetic state after only relatively limited exposure to high glucose levels.

Researchers were already aware that there seems to be a point of no return in the onset of diabetes. This was apparent in the Diabetes Complications and Control Trial (DCCT) in the 1990s when Type 1 diabetic patients were either placed on standard or intensive treatment regimens to normalize their glucose levels. Because complications were so profoundly reduced in patients with tight glucose control, all the remaining DCCT patients were switched early onto intensive therapy. However a follow-up study found that several years after switching to intensive therapy the patients who started the trial on only the standard treatment regimen continued to have more complications than those who received intensive therapy throughout the trial.

Research since has speculated that exposure to high glucose levels quickly creates a metabolic memory in which diabetes persists long after glucose levels have been corrected. Research to date suggested that oxidation played a role but the exact mechanism was unknown.

The Warwick research team, led by Dr Antonio Ceriello, have now proven that the damage seems to be done in a process called glycation when early on in a period of high glucose levels glucose sugar molecules are able to bind to proteins in the mitochondria of cells (the parts of cells governing the production and regulation of energy). This persists even if

glucose levels later fall to normal. This inhibits and distorts the mitochondria's normal function and results in an overabundance of the production of free radicals (or Reactive Oxygen Species – ROS) which cause oxidation and thus continued diabetic complications.

The Warwick Medical School researchers proved their hypothesis by taking tissue and exposing it to 2 weeks of high levels of glucose, followed by one week of normal glucose – however for half the tissue they also applied several antioxidants at the end of the two weeks of high glucose. The tissue without antioxidants levels of glucose stress remained high but where antioxidants had been applied there was a dramatic fall in the incidence of free radicals and there was also a significant drop in 5 of the 6 key markers for high glucose stress.

The Warwick Medical School research confirms the need for very early tight control of glucose levels to avoid diabetic complication and that that control must be supplemented with the use of antioxidant agents to mitigate the progression of complications.

However long term use of antioxidants can in itself produce health problems so in a further research published this month the Warwick Medical School team have tested the use of the AT-1 receptor blocker Telmisartan and found it can be used in exactly the same way to suppress the build up of free radicals without the side affects that long term use of antioxidants would cause.

Dr Ceriello is now beginning to look at how to move beyond simply suppressing the problematic production of free radicals and actually finding ways of reversing the glycation process itself thus erasing the harmful "metabolic memory".

Source: University of Warwick