What are your specific research interests?

For more than two decades, my primary research interests in biology and biochemistry have been the spontaneous reactions of sugars with amines (Maillard reactions) and the impact of these on organisms. In living systems, reactive sugars and amines must coexist in the same setting, thus Maillard reactions are unavoidable. Since these reactions are non-enzymatic and random, their impact on the tightly controlled and regulated chemistry of life is overwhelmingly negative. In other words, Maillard reactions are one of the entropic challenges that living organisms have to overcome in order to maintain themselves and reproduce.

In what way have these interests changed over the years?

When I first became involved in researching Maillard reactions in biology, the dominant view was that they were irreversible and not much could be done about them. I was one of the first researchers to postulate that Maillard reactions in living systems are in fact controlled, and even reversed, by mechanisms that use energy to control them. These defences are analogous to the multi-layered protective mechanisms of living systems against oxygen toxicity. Both oxygen and sugars are essential for life but also have considerable toxic potential that needs to be controlled. My proposal was not merely a theoretical stance since I was a pioneer in the discovery and characterisation of two enzymes that control and reverse some glucose-mediated Maillard reactions in vivo. Recently, I developed a hypothesis that methylglyoxal (MG) and similar toxic byproducts of metabolism are eliminated from organisms through the combined actions of scavenger compounds and removal of the results adducts via the kidneys.

Can you provide an insight into the levels of MG-scavengers in avian blood? What can humans learn from this avian model?

Birds are endothermic animals with body temperatures 2-3 °C higher than humans. In addition, compared with humans, birds have blood glucose levels that are between two- and fivefold higher. In other words, as assessed by human criteria, all birds are diabetic. However, in spite of blood sugar levels that would be lethal to humans, birds do not experience any diabetic complications. In fact, when compared with mammals of similar size, birds are exceptionally longlived. For instance, while the maximal lifespan of rats is two to three years, that of pigeons is 20-25 years. While the elevated concentration of MG-scavenging amino acids in avian plasma is a fact, it is not clear whether or not this plays a role in the resistance of birds to chronic hyperglycaemia. At present, this hypothesis is yet to be tested. However, should it be shown that elevated levels of MG-scavengers in avian plasma are indeed important, then increasing levels of MG-scavengers in humans is also likely to be beneficial by attenuating, or perhaps even preventing, diabetic complications caused by methylglyoxal.

You believe in creatine’s potential as an MG-scavenger. How do you plan to investigate this agent?

At this time, the most promising dietary MG-scavenger appears to be creatine. There are two reasons for this. First, creatine is an effective MG-scavenger in vitro. Second, supplementation of the diet of type 2 diabetics with creatine results in lower levels of glycated haemoglobin (HbA1c) portending better outcomes with diabetic implications. This finding suggests that creatine supplementation is likely to attenuate the severity of diabetic complications and delay their onset. My plan is to repeat the creatine supplementation studies using larger populations of subjects and optimised supplementation schedules in which intake of creatine will be coordinated with meals. Should the previous report on the efficacy of creatine prove correct, this would indicate that the incidence and prevalence of diabetic complications can be lowered by augmenting diets with creatine either as a supplement or as an added ingredient in foods.

Can you discuss your unique approach?

My philosophy is that in the vast trove of published research there are many treasures hidden in plain sight and, in order to discover, evaluate and fit them into coherent schemes, a researcher needs not only expertise and interest, but also patience, persistence and time. Since time is such a luxury for scientists, a researcher needs not only expertise and interest, but also patience, persistence and time. Since time is such a luxury for scientists, many interesting papers and potentially valuable data are neglected and ignored. Being retired gives me a lot of time. Consequently, over the past three years my approach has proven productive in leading me to formulate hitherto unarticulated questions and propose new hypotheses about Maillard reactions in hyperthermophiles and birds.
Healthy sacrifices

In the context of the ongoing and worsening global obesity and diabetes epidemic, scientists from Deglycation Research highlight the importance of dietary interventions that remove reactive sugars from the human body.

LINKAGES BETWEEN SOCIETY’S increasing adoption of a Western lifestyle and a consequential increase in levels of obesity – largely observed in developing countries – have been the subject of research all over the world. Dr Benjamin Szwergold of Deglycation Research has been grappling with the underlying causes of these epidemics by learning how lifestyle and diet influence this process and the ways in which possible dietary interventions can address these challenges. In particular, he has been building a body of knowledge about the different ways to remove reactive sugars, such as methylglyoxal (MG), from the human body. His goal is to effectively mitigate these enormous public health challenges through dietary interventions, such as augmenting diets with natural supplements that will remove toxic byproducts of metabolism, and thereby restore some of the health benefits of ‘traditional’ diets.

THE IMPORTANCE OF TRADITIONAL DIETARY ELEMENTS

One of the key challenges in preventing and treating type 2 diabetes is to improve understanding of how changed dietary habits have stimulated the rampant growth of obesity and type 2 diabetes. “Our understanding of the role of diet in obesity and associated conditions is just beginning to evolve, to the point where we may be able to control or reverse this ominous epidemic,” Szwergold observes. He has identified two principle trends. First, increased consumption of refined sugar, flour, oils and meat almost invariably leads to obesity. Second, and less well understood, is the reduction/elimination of certain key dietary components that were found in traditional foods. Researchers have discovered that in societies that have maintained their traditional diets, such as Okinawans and the San Blas Islands residents of Panama, people are not subject to the high levels of obesity and diabetes that are affecting indigenous populations that adapted to Western-style diets, such as those in the Pacific islands.

THE ROLE OF METHYLGLYOXAL AND ITS SCAVENGERS

Szwergold has delved deeply into the major role that sugars, such as MG, contribute to diabetic complications. MG and similar molecules react with nitrogen-containing compounds in a complex process known as Maillard reactions. MG reacts rapidly and randomly with proteins, phospholipids and nucleic acids: “It thereby disrupts normal functions of cells and organs by crosslinking structural macromolecules, interfering with signalling pathways and disrupting the function of DNA,” Szwergold explains. In fact, MG is about 20,000 times more reactive than glucose. Even though its toxicity is predominantly managed by glyoxalase I and glyoxalase II, this control is not perfect. Szwergold has noted that when blood sugar is elevated, such as in diabetes, more MG is produced and the body’s defence system is less efficient. Szwergold therefore proposes that an additional factor in defence against MG toxicity is its removal by dietary MG scavengers.

Research has shown that when the Kuna people of San Blas Islands in Panama, who live on a traditional diet, move to the mainland and start consuming a Western diet, their obesity and diabetes rates increase to match that of their fellow mainland dwellers. Szwergold points out that the Kuna traditional diet contains plantains, native vegetables, seafood and cocoa, which are all known to be rich in MG scavengers. In other cases, the benefits of a Mediterranean diet, and lower obesity levels, can also be correlated to a high consumption of seafood with taurine and arginine, as MG scavengers.

Szwergold has spent many hours trawling through extensive biomedical literature in order to better understand the use of various MG scavengers, to prevent or slow down the development of diabetic complications. For example, he has carefully reviewed research on the use of taurine as a supplement. He concluded that the uniformly positive results seen in animal trials with taurine and inconsistent results seen with the supplement in human studies are due to differences in dosage and timing of the taurine supplements between animal and human trials. As a result, Szwergold has formulated a hypothesis to overcome these problems: “My plan is to optimise the effectiveness of MG scavenger supplements by coordinating their administration with meals, since the postprandial period is the time at which MG concentrations increase significantly and have the most pronounced effect.”
Szwergold and his collaborators are hopeful that, in the future, by augmenting the Western diet with MG-scavengers, it will be possible to not only control, but reverse, type 2 diabetes.