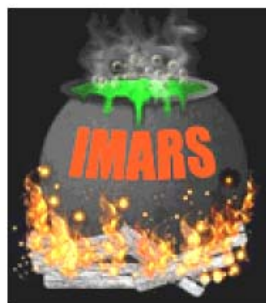


# IMARS Highlights



## Research Commentaries for Members of The International Maillard Reaction Society

A Non-profit Research and Education Organization in Biomedicine and Food Science:  
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## **Editorial comment**

Welcome to the November issue of IMARS Highlights. It gives me great pleasure to bring to your attention highlights in glycation research selected by our contributing editors – this month, John Baynes, Monika Pischetsrieder, Varoujan Yaylayan and Alan Stitt (with Josephine Glenn). I have also added two new features. Firstly, a contribution on what it is like for researchers at all levels working on glycation and being involved with IMARS. In this issue I am very happy to include a contribution by Miss Sahar Waris, a PhD student working on nucleotide glycation, on her views of the IMARS www pages. Secondly, a contribution on the outcome for recipients of IMARS travel awards/support. In this issue, Abdulhakim Elosta and Jamil Abdullah describe the benefits of attending the recent 9<sup>th</sup> Maillard Reaction Symposium, Munich 2007. I hope to make these regular features in IMARS highlights. Feedback from readers on these and other features in this issue are very welcome.

Following the recent success of the Junior Scientist Writing Competition for postgraduate and post-doctoral researchers in Biomedical Sciences and Food Sciences divisions in 2006, I would like to give all potential future authors advance notice that we will be running a further competition in 2008. The winners will be invited to present oral papers at the 10<sup>th</sup> Maillard Reaction Symposium, Australia, 2009, with a contribution to the cost of attending the meeting.

## **Analysis of the Glycated Plasma Proteome – I. Fructosamine glycation**

*John Baynes, University Of South Carolina, Columbia, SC, USA*

In an effort to do what has not been done before, Thomas Metz and colleagues at the Pacific Northwest National Laboratory (PNNL) are developing methods to define the glycated plasma proteome. In this preliminary study (1), they marry classical and modern techniques to define the glycated plasma proteome and identify a library of glycated peptides and proteins in plasma glycated *in vitro*. Glycated proteins and peptides are first isolated from a commercial preparation of glycated plasma by affinity chromatography on a phenylboronate resin, and then analyzed by electron-transfer dissociation mass spectrometry (ETD-LC/MS). Affinity chromatography reduces the complexity of both the protein and peptide mixtures, yielding greater sensitivity for identification of glycated peptides by MS/MS; ETD is an alternative dissociation technique that overcomes a major limitation of collision-induced dissociation (CID) MS during the analysis of labile post-translational modifications; in the case of glycation, the presence of high-abundance ions resulting from multiple neutral losses of water molecules interferes with the identification of peptides required used for sequence determination. Metz and colleagues demonstrate that ETD was 5-times more sensitive effective than CID for identification of glycated peptides from human serum glycated *in vitro*. They also demonstrate that a two-stage sample enrichment procedure yields the best results: first, the isolation of the glycated proteins by affinity chromatography; and then, after proteolytic digestion, the isolation of glycated peptides. Overall, they were able to identify 88 unique peptides from 27, mostly high-abundance, proteins in the glycated plasma preparation. The long-range goal of these studies is to define differences in glycation of plasma proteins between control and diabetic patients and to apply differential proteomic analysis of protein glycation in clinical studies of patients with pre-diabetes and diabetes or at risk for diabetic complications. Immunodepletion of the more abundant plasma proteins should permit increased coverage of low abundance glycated proteins that may serve as biomarkers of developing diabetic complications. The authors have access to an impressive array of sophisticated instrumentation at the PNNL - it will be interesting to see the results of future studies. In the meantime, “Metz TO” might be a good term to add to your monthly library search.

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## **The Amadoriase: Prevention, but no Cure**

*Monika Pischetsrieder, Food Chemistry, Emil-Fischer-Center Erlangen, Germany*

After many years of research in the field, it is still an unsolved task how to control the Maillard reaction during food processing. In many food products, such as milk powder or infant formulas, glycation reactions are unwanted because they don't look or taste right and their physiological consequences are still unclear. However, means to control the Maillard reaction are mostly limited to decreasing the duration or temperature of thermal treatment. The most powerful chemical inhibitor of the Maillard reaction, sodium sulfite, is mostly avoided due to possible adverse side effects.

In the field of biomedicine, several pathways were suggested how AGE formation *in vivo* can be avoided. Although, we are still waiting for the development of a potent AGE inhibitor which is able to reverse or prevent the adverse effects of AGEs in disease, these schemes may also provide useful ideas for the prevention of the Maillard reaction during food processing. One possible target may be the enzymatic cleavage of the Amadori product. Amadoriases, which are expressed for example by fungi, are able to oxidize the Amadori product yielding the free amine, glucosone and hydrogen peroxide<sup>1</sup>. In contrast, mammalian fructosamine 3-kinases catalyze phosphorylation in position 3 of the Amadori product, leading to spontaneous cleavage of the 3-deoxyglucosone from the protein<sup>2</sup>.

A recent study from Fogliano and coworkers added now an interesting aspect to the activity of Amadoriase<sup>3</sup>. Although the enzyme was practically inactive to deglycate proteins and peptides, it was able to prevent Amadori product formation of peptides and smaller proteins, when added during the glycation process. For example, a 44 % reduction in Amadori product formation was observed, when insulin was reacted with glucose in the presence of Amadoriase compared to glycation in the absence of the enzyme. In contrast, the enzyme was practically inactive to cleave the Amadori products of insulin, when added after the glycation step. Admittedly, the application of Amadoriase to prevent Maillard reaction in food is rather limited because of the instability of the enzyme during food processing or storage. Furthermore, the production of hydrogen peroxide and glucosone from the Amadori product is probably asking for trouble. Regardless, the present results are highly interesting, because they are so unexpected and difficult to explain. A possible explanation that glycation leads to a temporary unfolding of the proteins, giving access to the enzyme, was successfully ruled out by the authors.

The only hypothesis I could think of: besides the well characterized oxidative cleavage of the Amadori product, the enzyme may also interact with an earlier intermediate of the Amadori rearrangement - such as the Schiff's base - catalyzing its break down by a mechanism which may be different from the described Amadoriase activity. In this context, it would be interesting to find out if the inhibition of Amadori product formation is also connected to the formation of glucosone and hydrogen peroxide.

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- <sup>2</sup>Delpierre G, Collard F, Fortpied J, van Schaftingen E. Fructosamine 3-kinase is involved in an intracellular deglycation pathway in human erythrocytes *Biochem J* 2002, 365, 801 – 808.
- <sup>3</sup>Capuano E, Fedele F, Mennella C, Visiciano M, Napolitano A, Lanzuise S, Ruocco M, Lorito M, del Castello M, Fogliano V. Studies on the effect of Amadoriase from *Aspergillus fumigatus* on peptide and protein glycation in vitro *J Agric Food Chem* 2007, 55, 4189 – 4195.

*Editor's note:* Ben Szwergold has discussed previously the possible interaction of fructosamine 3-phosphokinase with Schiff's base intermediates (Szwergold,BS, Howell,SK, Beisswenger,PJ: Transglycation - A potential new mechanism for deglycation of Schiff's bases. *Ann.N.Y.Acad.Sci.* 1043:845-864, 2005).

## **Mismanagement of lysosomal degradation - an AGE/RAGE mediated problem in any glia?**

*Josephine Glenn & Alan Stitt, Centre of Vision Science, Queen's University, Belfast, Northern Ireland*

Lysosomes are low pH organelles that, according to cell-type, are responsible for degrading phagocytosed (internalised) material, modified proteins and senescent organelles. Lysosomes contain acid hydrolase enzymes with unique and wide-ranging degradative capability and they are perhaps one of the most significantly altered organelles following exposure to AGE-modified proteins.<sup>1,2</sup> Dysfunction of degradative capacity has been linked to significant diseases such as age related macular degeneration (AMD), chronic kidney disease (CKD) and Alzheimer's disease (AD).<sup>3,4</sup> Recent publications have also highlighted the link between lysosomal and ubiquitin-linked proteasomal systems<sup>5</sup> and the significance of these degradative pathways for those working in the Maillard reaction field was discussed in the July 2007 issue of IMARS highlights by Alejandro Gugliucci (*pgs 5-6*).

AGE accumulation in the lysosomal system is linked to decreased activity of degradative enzymes such as the cathepsins and this also contributes to increased levels of reactive oxygen species and mediators of pro-inflammatory responses. A recent article by Stolzing *et al.*<sup>6</sup> is of interest because it highlights how AGEs affect microglial internalisation and accumulation of AGE modified albumin (AGE-BSA) in the proteasomal and lysosomal systems. Using radio-labelling it was demonstrated that AGEs accumulated in low pH compartments within microglia in concert with an inhibition of intracellular protein turnover. The authors found significant AGE-mediated reductions in activity of the lysosomal/proteasomal systems by 40 % and 20-30 % respectively and that this led to microglial activation.<sup>6</sup> They concluded that AGE-mediated microglial activation responses were linked to increases in nitric oxide and carbonyl stress.<sup>6</sup>

The ability of AGEs to initiate and sustain microglial activation via alteration of the lysosomal/proteasomal system is a significant finding. These specialised, macrophage-like cells phagocytose cellular debris and modulate inflammatory responses and their activation has been implicated in several neurodegenerative disorders such as Alzheimer's, Parkinson's disease and retinopathies<sup>7</sup>. Upregulation of RAGE activity occurs in microglia under diabetic conditions<sup>8</sup> and AGEs or S100B ligands can induce cytokine expression in these cells.<sup>9,10</sup>

The study raises some important questions about how cells process AGE-modified proteins. Traditionally, exogenous AGE-mediated responses are thought to occur via receptor signalling, however, we do not know enough about what happens to these ligands once they are internalised. Recent studies have also demonstrated the importance of intracellular methylglyoxal-modification on protein function<sup>11</sup> and it would be interesting to investigate the ultimate fate of AGE adducts in the cytoplasm. As shown by Stolzing et al., how AGEs impact upon the lysosomal / proteosomal systems can have important pathophysiological consequences.

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*Editor's note:* Readers are referred to the debate on the physiological function of AGE/RAGE - Molecular Nutrition & Food Research 51, 1107 – 1119, 2007 (3 articles).

## Mechanism of furan formation from ascorbic acid

*Varoujan Yaylayan, Department of Food Science and Agricultural Chemistry, Quebec, Canada*

In early 2004, researchers at the U. S. Food and Drug Administration (2004) have identified furan in a number of foods that undergo thermal treatment, specially canned and jarred foods. Furan is a very volatile and colorless liquid and is classified as a possible human carcinogen by International Agency for Research on Cancer (IARC, 1995), it induces tumors and liver toxicity in experimental animals. Although furan had previously been reported in various foods such as coffee, canned meat, baked bread, cooked chicken etc., it was only recently that a more comprehensive study was performed by FDA using larger number of food samples and found furan levels ranging up to approximately 120 ppb. Similar to acrylamide, furan in food could potentially become a serious problem due to its widespread presence in many types of products.

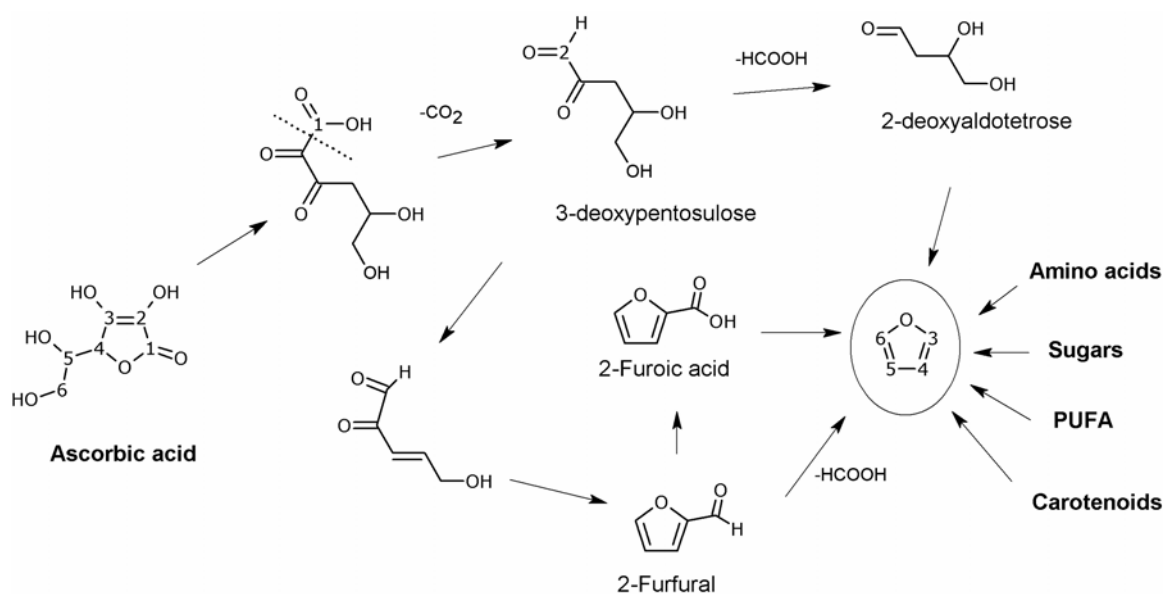


Figure 1

Although there are numerous precursors of furan in food such as amino acids, sugars, carotenoids and PUFA, ascorbic acid has been identified as a major source of furan. Modeled after furan formation from <sup>13</sup>C-labelled sugars, Perez Locas and Yaylayan (2004) proposed several pathways of furan formation from ascorbic acid. A recent publication by Limacher et al., (2007) using <sup>13</sup>C-labelled ascorbic acid, have conformed the major pathways of furan formation from ascorbic acid under roasting and cooking conditions (See Figure 1). Based on their analysis, ascorbic acid undergoes hydrolytic ring opening followed by dehydration to generate 3-deoxyxypentosulose (see Figure 1). This intermediate can undergo decarboxylation

to lose C-1 of ascorbic acid followed by hydrolytic  $\beta$ -dicarbonyl cleavage or  $\alpha$ -dicarbonyl cleavage to lose C-2 of ascorbic acid as formic acid. The resulting aldotetrose can cyclize and dehydrate to generate a furan ring containing C-2 to C-6 carbon atoms of ascorbic acid. Other precursors include 2-furoic acid and 2-furfural that can be converted into furan through either decarboxylation as in the case of 2-furoic acid or oxidative cleavage of the aldehyde group as in the case of 2-furaldehyde.

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## Proteomic Analysis of the Glycated Proteins

*John Baynes, University Of South Carolina, Columbia, SC, USA*

Mass spectrometric analysis of glycated proteins in biological samples is complicated by the presence of large quantities of unglycated proteins and by heterogeneous modification of the glycated protein. Affinity adsorption, coupled to MALDI-TOF MS, provides a method both for enrichment of glycated proteins and for measurement of total glycated species. The challenge is to develop a high-capacity affinity chip! Gontarev *et al.* (1) describe a novel approach to analysis of glycated proteins using a phenylboronic acid (PBA)-agarose affinity resin on a MALDI chip. The basic technique involves etching of an aluminum surface to promote adsorption of a melted agarose gel, then direct MALDI-TOF analysis of glycated protein bound in the agarose matrix. The authors demonstrate that the technique works in several modes: by off-line binding of glycated protein to PBA-agarose by column chromatography, then addition of the resin to an agarose gel on the chip; by adsorption of glycated proteins to a PBA-agarose gel on the chip; and even by derivatization of the agarose gel with PBA *in situ* (on the chip), followed by adsorption of glycated proteins. Salt effects are minimized by using volatile triethanolamine acetate buffer, analytical sensitivity is improved by the thickness of the three-dimensional agarose matrix, and the method requires minimal sample handling, such as elution of bound proteins from an affinity column and application to the MALDI plate. The technique was evaluated by analysis of serum albumin and a standard protein mixture, both glycated *in vitro*. Strong signals at the appropriate molecular weights were obtained for the glycated proteins; the background from unglycated proteins was removed during washing steps. While this method is still at an early stage in development and will require some fine-tuning and standardization for analysis of biological samples, it provides a significant increase in sensitivity, compared to conventional SELDI techniques. It is also readily adaptable for high-throughput applications and shows promise for routine analysis of glycated proteins in plasma and tissue samples.

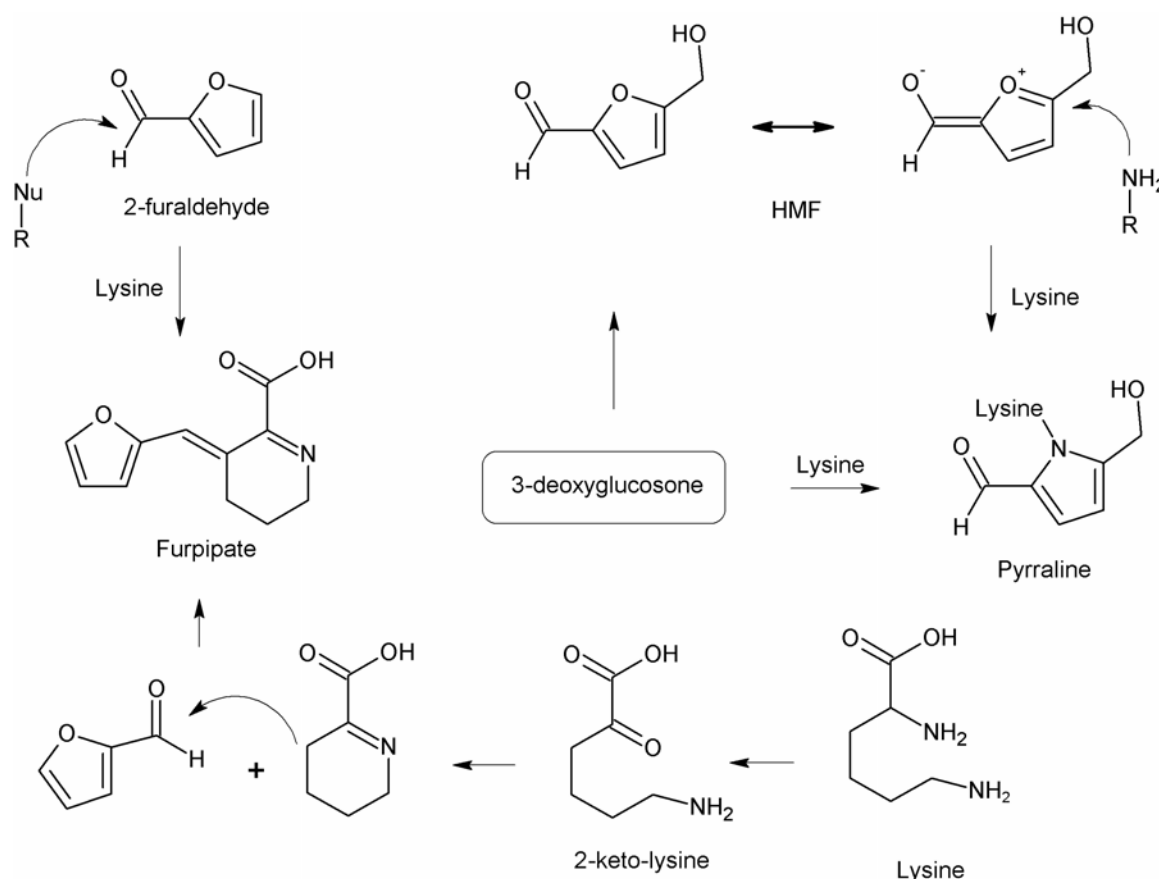
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Gontarev S, Shmanai V, Frey SK, Kvach M, Schweigert FJ (2007) Application of phenylboronic acid modified hydrogel affinity chips for high-throughput mass spectrometric analysis of glycated proteins. *Rapid Commun Mass Spectrom* 21:1-6.

## Further reaction of 2- furaldehyde with lysine

V. Yaylayan, *Department of Food Science and Agricultural Chemistry, Quebec, Canada*

Although furan derivatives such as 2-furaldehyde and hydroxymethylfurfural (HMF) are formed in relatively high amounts from sugars in food, their further reactions with amino acids are not well studied. HMF could be considered an indicator for hexoses and 2-furaldehyde for pentoses and ascorbic acid. There is indication in the literature that HMF or its precursor the 3-deoxyglucosone can interact with nucleophiles and form N-analogs of HMF such as pyrrole (see the Figure). In a recent publication, Murata et al. (2007) have identified a colored lysine adduct of 2-furaldehyde formed through aldol condensation between a modification of lysine and the carbonyl group of 2-furaldehyde. This is an unexpected reaction due to the deactivation of the aldehyde through conjugation with the aromatic ring.



The authors provide convincing spectroscopic evidence for its structure and they name the product as furpilate (see the figure).

Although the authors do not propose any mechanism of formation, this condensation most likely involves formation of 2-keto-lysine through transamination reaction followed by cyclization to form the tetrahydropyridine intermediate. This imine intermediate is capable of undergoing aldol condensation to produce furpipate.

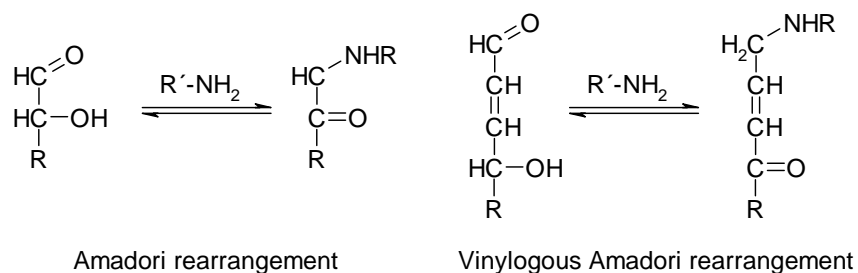
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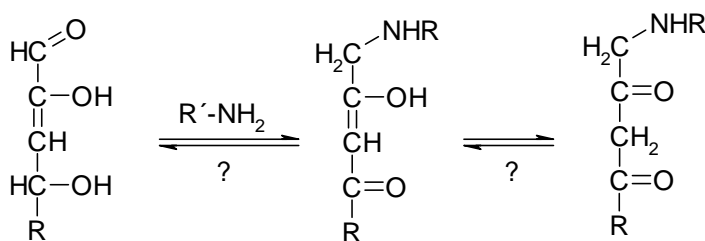
## Vinylogous Amadori rearrangement: a novel degradation pathway of sugars?

Monika Pischetsrieder, Food Chemistry, Emil-Fischer-Center Erlangen, Germany

The Amadori rearrangement is a fundamental step in the course of the Maillard reaction. In a recent study, Yaylayan and Locas pointed out the importance of the vinylogous Amadori rearrangement<sup>1</sup>: Analogous to the reaction of  $\alpha$ -hydroxy aldehydes to give  $\alpha$ -aminoketones,  $\alpha,\beta$ -unsaturated  $\gamma$ -hydroxy aldehydes lead to the formation of  $\alpha,\beta$ -unsaturated  $\gamma$ -amino ketones (scheme 1). The simplest systems, where vinylogous Amadori rearrangement can take place, are 4-hydroxy-2-alkenals. 4-Hydroxy-2-alkenals are formed during lipid oxidation and are susceptible to nucleophilic attack of amines either by Michael addition or by Schiff Base formation. The latter reaction will then allow vinylogous Amadori rearrangement. The authors further showed that 4-hydroxy-2-alkenals may also be formed by  $\beta$ -elimination of 2-deoxysugars.



At this point it is noteworthy that other sugars, such as glucose may also undergo  $\beta$ -elimination leading to 2,4-dihydroxy-2-alkenals, which could also undergo vinylogous Amadori arrangement (scheme 2). Interestingly, the resulting dicarbonyl intermediates or products thereof have not been identified so far.



Hypothetical mechanism of a vinylogous Amadori arrangement of sugars

As a consequence, it would now be interesting to find out, if these compounds have so far only be overlooked (like the Lederer deoxyosone), or if in “regular sugars” other reaction pathways are more favored.

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<sup>1</sup> Yaylayan V, Locas C. Vinylogous Amadori rearrangement: implications in food and biological systems. Mol Nutr Food Res 2007, 51, 437 – 444.

## **Benefits of expressing your RAGE: New evidence for neuroprotective effects of RAGE-ligand binding**

*Alan W. Stitt, Centre of Vision Science, Queen's University, Belfast, Northern Ireland*

The receptor for advanced glycation endproducts (RAGE) is a member of the immunoglobulin superfamily of cell surface molecules and is present in multiple tissues such as endothelium, smooth muscle and neurons.<sup>1</sup> RAGE is a promiscuous receptor and binds many ligands including AGEs,  $\beta$ -amyloid, S100B and high-mobility group box (HMGB1). In terms of AGEs, which will interest most IMARS members, it acts as a receptor for several AGE ligands, including CML and methylglyoxal-derived AGEs.<sup>2</sup> There is a strong correlation between type of AGEs and their binding affinity with RAGE. For example, ribose-derived AGEs have higher binding affinity over glucose- and fructose-derived AGEs; a response that could be related to the free amine content.<sup>3</sup> It is well established that RAGE ligand binding provokes a pro-inflammatory response, leading to NF- $\kappa$ B activation, oxidative stress, and expression of various adhesion molecules and cytokines which varies according to the cell-type involved.<sup>4</sup>

A recent publication by Pichiule et al. adds to our understanding of RAGE pathobiology.<sup>5</sup> Using a murine model of acute cerebral ischaemia (stroke) in combination with systemic hypoxia, the authors demonstrated that RAGE was up-regulated and, remarkably, protected against neuronal cell death.<sup>5</sup> This was demonstrated by increased infarct size when the cerebral ischaemia-hypoxia (IH) approach was performed on RAGE knockout mice. The RAGE up-regulation and neuroprotective response was also reproduced using primary neurons in vitro and shown to be linked to receptor activation by low concentrations of exogenous S100B. By contrast, high concentrations of S100B induced neuronal death.

Pichiule *et al.* provide experimental evidence that RAGE activation by low concentrations of S100B could play a protective role in the CNS during acute injury.<sup>5</sup> At first glance, these findings seem to be at odds with the established dogma; that RAGE signalling has deleterious consequences for cells and tissues. Indeed, RAGE knockout animals have been shown to be protected from many diabetes and inflammation-linked conditions, including cardiac ischaemia-reperfusion injury and peripheral nerve damage.<sup>6,7</sup> More research is needed in this area, but it seems clear that a hitherto unrecognised spatio-temporal relationship exists between ligand availability and RAGE activation.

Hypoxia induced by non-perfusion of tissues is a central element of many diseases where hypoxia-inducible factor-1 $\alpha$  (HIF-1 $\alpha$ ) transcribes expression of cytokines and growth factors that drive inappropriate angiogenic and/or pro-inflammatory responses. Hypoxia of rapidly growing tumours that outstrip their vascular supply and ischaemic retinopathies are just two situations in which the current findings could be important. The RAGE promoter has regions that show potential for binding the transcription factor HIF-1 $\alpha$ . Pichiule *et al.* conditionally knocked-down HIF-1 $\alpha$  in mice exposed to the IH regime and established that the previously observed RAGE up-regulation was prevented.<sup>5</sup> This finding indicates that RAGE can be induced in hypoxic neurons (and possibly other cell-types) leading to enhanced receptor signalling by various ligands present in a particular tissue.

RAGE is upregulated in short-term diabetic retinopathy (when overt hypoxia is not present) and inhibition of this receptor can protect against selective early lesions.<sup>8</sup> It has never been shown if hypoxia up-regulates RAGE in the retina but if it occurs, this could serve to enhance receptor activation. Furthermore, the absence of oxygen enhances HIF-1 $\alpha$ -dependent expression of glycolytic enzymes in the conversion of ce-lls to a predominantly glycolytic metabolic state (the Pasteur Effect)<sup>9</sup> leading to increased dicarbonyl production and concomitant AGE formation. Perhaps hypoxia and hyperglycaemic, as occurs in long-term diabetic retinopathy, could operate in a cumulative fashion to activate RAGE with impact on neuronal cell function.

The findings of Pichiule *et al.* are novel and intriguing and should prompt further research that can establish the potential for RAGE and its ligands to mediate cell protection or damage in diverse tissues.

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## Views of glycation researchers: IMARS www pages

Going through the webpage of the '**International Maillard Reaction Society**' was indeed an informative experience for a researcher like myself, who is a student working in the field of nucleotide glycation. The weblink relating to 'Maillard reaction education' provided detailed information, right from the historical development, to the chemistry and biological aspects of this interesting reaction mechanism.

The structures and properties of the various glycation adducts generated during the course of this reaction have been touched upon in a well-coordinated manner. The significance of the Maillard Reaction in the etiology of diseases like diabetes and cancer is very well documented, to provide all the necessary and relevant information. The role of the glyoxylase system as an anti-glycation defense is really interesting, specifically how the cancer cells escape the apoptotic machinery to achieve a multi drug resistant state. The active and passive mechanisms of defense that organisms have against glycation further highlights the deleterious effects of this reaction on the biological organisms and how they have evolved to cope up against it.

In the future I look forward to reading more on the challenges staring the researchers of this field and hope to see more literature on nucleotide glycation which is one topic that is slowly gaining significance, in realisation of the fact that any defect of the genetic machinery is difficult or rather impossible to correct.

*Miss Sahar Waris*, PhD student working on "Nucleotide and DNA Glycation" with Professor B.N.Waris, Chemistry Section, Women's College, A.M.U., Aligarh, INDIA and Professor Paul J. Thornalley, Protein Damage and Systems Biology Research Group, Warwick Medical School, University of Warwick, University Hospital, Coventry, U.K.

## **IMARS Travel Grant Awardee – report on participation in the 9<sup>th</sup> Maillard Reaction Symposium, Munich 2007**

We are two PhD students working full time in the glycation field as part of a group of seven researchers led by Dr Nessar Ahmed at the School of Biology, Chemistry and Health Science, Manchester Metropolitan University, UK. The research in our group is focussed in a number of areas including glycation of growth factors and their importance in diabetic wound healing, the toxic effects of high glucose and AGEs on cells and the therapeutic potential of pharmacological and natural products with anti-glycation and antioxidant properties. We would like to thank the International Maillard Reaction Society for their travel grants enabling us to attend The 9th International Symposium on the Maillard Reaction held in Munich, 2007. There was a poster session during the conference and our group presented a total of three posters. We hope to attend and deliver an oral presentation at the next conference.

We were really delighted when our abstracts were accepted allowing us to attend a major international conference on the Maillard reaction for the first time. This was a great opportunity for us to meet scientific researchers from all over the world and to actually put faces to the published papers we had studied. The travel awards were welcomed because our laboratory has limited funding and the offer of two travel grants was generous as it enabled two new researchers to attend this important conference.

The meeting had a very enthusiastic note from the beginning to the end and included keynote speakers, oral and poster presentations. The presentations were divided into two themes covering Maillard reaction in foods and in biomedical science and in general were of a very high standard. The presentations not only increased our understanding of the Maillard reaction and its growing importance in disease processes but also gave us fresh ideas for our own research being conducted in our own laboratory at MMU. We discussed our ideas with each other, with our supervisor and with other delegates during coffee breaks, lunch, dinners and during social sessions. We met distinguished researchers and communicated with them during the poster sessions, taking the benefit of their presence and their advice regarding future work.

We had a great five days in Munich. The conference was really well organised and a credit to the Local Organizing Committee. We enjoyed the social program and made plenty of new friends from all over the world. Since returning from the conference, we feel more motivated towards our work and the conference has really stimulated our interest.

Finally, thanks again for giving us this chance that will last in our memories for a long time.  
Thank you

*Abdulkhikm Elostu and Jamil Abdullah* (School of Biology, Chemistry and Health Science  
Manchester Metropolitan University, Oxford Road, Manchester M1 5GD, United Kingdom).

## Highlights of the glycation literature September – October 2007

*Proceedings of the Appetizer Workshop, Cost Action 927 – International Maillard Reaction Society Meeting, Naples, Italy, May 24<sup>th</sup> May 2006.*

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	<b>INTERNATIONAL MAILLARD REACTION SOCIETY</b>	
	Blstein Building 303 Cornell Road, Room 5127 Cleveland, Ohio 44106. USA.	Phone: 216-368-6613 Fax: 216-368-1357 E-mail: <a href="mailto:imars@case.edu">imars@case.edu</a>

		
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