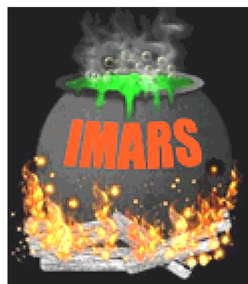


IMARS Highlights

Research Commentaries for Members of The International Maillard Reaction Society

A Non-profit Research and Education Organization in Biomedicine and Food Science: http://imars.case.edu

Volume 1, Number 5 **September 15, 2006**

Editor
Susan Thorpe (USA)

Contributing Editors
John Baynes (USA)
Timo Buetler (CH)
Angelika Bierhaus (DE)
Vincenzo Fogliano (IT)
Alejandro Gugliucci (USA)
Toshio Miyata (JP)
Teruo Miyazawa (JP)
Monika Pischetsrieder (DE)
Caspar Schalkwijk (NL)
Alan Stitt (NI)
Varoujan Yaylayan (CA)
Rosario Zamora (ES)

CONTENTS

What's cooking? Notes from the Editor's Pot………….…………………… *i*

De-AGEing of embryonic stem cells

John Baynes……………………………………………………….…………..….. **1**

The human body is still a black box for food derived AGEs

Monika Pischetsrieder. ……………….………………………..………....…… **2**

Rapid intracellular AGE modification of key cytoplasmic proteins – is mSin3A only the tip of the iceberg?

Alan Stitt ……….……………………………………………….…………….….. **4**

How short chain carboxylic acids are formed during Maillard reactions?

Varoujan Yaylayan ……………………….…………………….………………… **6**

The Maillard proteome

John Baynes ……………………………….…………..…………………...…… **8**

A new role for cysteine in the Maillard reaction

Monika Pischetsrieder…….………………………………..…………...…..... **10**

Advanced glycation – time to enter the great stem cell debate?

Ashay Bhatwadekar and Alan Stitt …………….…………..……………...... **12**

Maillard reaction: Collateral damage

Varoujan Yaylayan ……………………………………….………………… **14**

Corporate Sponsors ………………………………………………………..…. **16**

What's cooking? Notes from the Editor's pot

Accompanying this issue of *IMARS Highlights* is an announcement of a writing competition for articles contributed by graduate students and post-doctoral fellows to encourage their participation in our society journal. This will make *IMARS Highlights* unique in providing an opportunity for students and post-doctoral fellows to present their ideas in a written format. Serendipitously, in this current issue an article was submitted that has been co-authored by graduate student Ashay Bhatwadekar (Queen's University, Belfast, NI) and contributing editor Alan Stitt. Other mentors are certainly encouraged to follow this example and submit articles that have joint authorship with graduate students and post-doctoral fellows.

Once again, two of our contributing editors have identified the same topic for discussion in the journal this time: AGEs in stem cells. Both evaluations point to the under explored potential for intracellular protein modification by the Maillard reaction and non-enzymatic chemistry to affect protein turnover. While these discussions have focused on the proteosomal degradation system, the possibility of impairment of lysosomal degradation also deserves investigation. The role of the Maillard reaction in food chemistry is also constantly expanding and two articles describing new reaction pathways involving amino acids or phenolic compounds are described in this issue as well.

Please remember that IMARS Highlights solicits comments or queries from the membership on any of the current or previous articles. The journal also welcomes contributions in the form of letters, short reports, book reviews and topical reviews from IMARS members. Correspondence can be sent to the editor at the address below.

Susan Thorpe
thorpe@mail.chem.sc.edu

De-AGEing of embryonic stem cells

By John Baynes

Stem cells are considered among the oldest, undifferentiated cells in the body. How is the accumulation of protein damage, including AGE/ALEs, reversed in long-lived embryonic stem cells during differentiation? Using a murine embryonic stem cell (ES) line, Hernebring *et al.* (1) show first that undifferentiated stem cells have a fairly high concentration of protein carbonyls (PC) and AGEs, comparable to levels observed in six-month old (adult) mouse brain and liver. 2D-PAGE and western blot analysis identified several carbonylated proteins in the ES, including cytoskeletal and chaperone proteins, tubulin, actin, HSC70 and HSC90; among these, HSC70 was the only protein identified by a monoclonal anti-CML antibody. Within five days after inducing differentiation of the stem cells, there was a rapid decrease in PCs and CML-protein, 80 and 95% respectively. The authors argue convincingly that this decrease is not the result of synthesis and dilution of the modified proteins because the undifferentiated cells actually have a shorter generation time than the differentiated cells. The loss of modified proteins in differentiated cells was accompanied by a three-fold increase in proteasome activity, consistent with the role of the proteasome in degradation of modified proteins. The relevance of the work was reinforced by parallel experiments showing that PCs and CML proteins are richer in cells in the inner cell mass of mouse blastocysts, but present at lower concentration in differentiated cells in the outer layers. The authors conclude that "elimination of damaged proteins is an integral part of early embryonic development", and perhaps during differentiation, in general. They also argue that the modified proteins are selectively degraded by proteasomes, although the data on this point are less convincing since lysosomal activity is not addressed.

To my knowledge, there are no other reports on levels of AGE/ALEs in fetal or adult stem cells or ova, but these initial studies are certain to stimulate greater interest. One implication of the work is that the increase in PCs and AGEs in older cells may actually be the result of a decrease in proteasomal activity. Decreased proteasomal activity might be an equally important factor in the accumulation of AGE/ALEs in tissues during aging and in disease. Could the decline in the rate of degradation of AGE/ALE-proteins be more important than an increase in their rate of production in aging and disease? Understanding the mechanism of recognition and handling of AGE/ALEs by stem cells may suggest some novel approaches for reversing the increase in AGE/ALEs in other tissues in aging and disease.

Reference

1. Hernebring M, Brolen G, Aguilaniu H, Semb H, Nystrom T (2006) Elimination of damaged protein during differentiation of embryonic stem cells. *Proc Natl Acad Sci* 103:7700-7705.

The human body is still a black box for food derived AGEs

By Monika Pischetsreider

Numerous in vitro studies point towards beneficial, but also harmful effects of food derived Maillard products. However, the fate of Maillard products after their consumption is still largely unknown. The recovery of defined Maillard products in urine and feces ranges between almost 100 % for pyrraline and less than 5 % for fructosyl-lysine in humans (1,2). These results indicate that the postprandial composition of Maillard products in plasma may vary largely from their composition in the processed food. In this context, several pathways must be taken into consideration: First, the resorption of the Maillard products may be incomplete. This assumption was recently supported by a study of Grunwald et al. (3): only low transepithelial flux of CML and fructosyl-lysine was observed in a monolayer of Caco-2 (human colon adenocarcinoma) cells in vitro. Both Maillard products also showed only low affinity towards the H(+)-peptide co-transporter PEPT1 or to carriers of natural amino acids indicating that a considerable portion of the Maillard products passes from the small intestine to the colon. In the colon, they likely interact with the gut microbiota. In a recent review it was pointed out that the interaction of Maillard products with colonic bacteria is multifaceted (4).

A second consideration, suggested many years ago by Erbersdobler and others, is that Maillard products can be efficiently degraded and transformed by bacterial metabolism. Microbiotic degradation would explain the low recovery of some glycation products in urine and feces as well as preventing their biological activity in vivo. On the other hand, transformation products of unknown chemical nature and biological activity could be absorbed in the colon and add to the Maillard pool in vivo. Further, the interaction between Maillard products and gut bacteria is also a two-way street: a preliminary study indicates that glycated proteins can also change the composition of the gut microbiota thus interfering indirectly with the metabolism of other nutrients.

Finally another recent publication by Prior et al. calls attention to a third pathway which has been neglected for a long time (5): in this study, the presence of metabolites of 5-(hydroxymethyl)-2-furfural (HMF) were screened in human urine after the consumption of dried plum juice, which is rich in HMF. It was shown that HMF is very rapidly transformed into 5-hydroxymethyl-2-furoic acid and other minor conjugates which were excreted in the urine. Thus, metabolism by phase I and II enzymes, an efficient detoxification mechanism for xenobiotics in vivo, can make a large contribution to the low recovery of Maillard products in human blood. On the other hand, there are several examples known, most prominently acrylamide, where phase I metabolism becomes a toxifying mechanism by transforming rather inert molecules in mutagens.

Thus it has to be appreciated that our understanding of the various transformation and degradation processes after the consumption of Maillard products is rather anecdotal than complete. However, there are more and more studies in progress which will give provide insights into the intricate network of mechanisms regulating the fate ingested Maillard products.

References

1. Förster A, Henle T (2003) Glycation in food and metabolic transit of dietary AGEs (advanced glycation end-products): studies on the urinary excretion of pyrraline. *Biochem Soc Trans* 31: 1383 – 1385.

2. Erbersdobler H, Faist V (2001) Metabolic transit of Amadori products. *Nahrung* 45 : 177 – 181.

3. Grunwald S, Krause R, Bruch M, Henle T, Brandsch M (2006) Transepithelial flux of early and advanced glycation compounds across Caco-2 cell monolayers and their interaction with intestinal amino acids and peptide transport systems. *Br J Nutr* 95: 1221 – 1228.

4. Tuohy K, Hinton D, Davies S, Crabbe J, Gibson G, Ames J (2006) Metabolism of Maillard reaction products by the human gut microbiota – implication for health *Mol Nutr Food Res*: 50 e-pub ahead.

5. Prior R, Wu X, Gu L (2006) Identification and urinary excretion of metabolites of 5-(hydroxymethyl)-2-furfural in human subjects following consumption of dried plums or dried plum juice. *J Agric Food Chem* 54: 3744 – 3749.

Rapid intracellular AGE modification of key cytoplasmic proteins – is mSin3A only the tip of the iceberg?

By Alan Stitt

Maillard reactions between reducing sugars and the free amino groups on macromolecules is an inevitable consequence of glucose metabolism and nearly all body proteins carry some "burden" of chemically attached carbohydrate. This has added significance for diabetic patients in which advanced glycation endproducts (AGEs) accumulate at supra-normal levels in intracellular and extracellular microenvironments.

Evidence suggests that one pathway to AGEs is via increased flux through glycolysis. This metabolic switch occurs in many cells during hyperglycaemic conditions and can lead to enhanced formation of the dicarbonyl methylglyoxal (MGO) derived from dihydroxyacetone and glyceraldehyde-3-phosphates. MGO is elevated in plasma and cells from diabetic patients, diabetic animal models and cells exposed to high glucose conditions where it may participate in very rapid formation of AGEs such as arginine-hydroimidazolone, N^{ε}-(carboxyethyl)lysine (CEL) and argpyrimidine.

In many cells, MGO is efficiently metabolised to lactate by the glyoxalase system which consists of the enzymes glyoxalase-I and –II together with reduced glutathione as a required co-factor (1). However, when there is increased flux through glycolytic pathways MGO levels can overwhelm this protection system and AGEs begin to accumulate. Until recently it was largely unknown what proteins became modified by MGO and how adduct formation affects functionality.

A publication in the journal *Cell* by Yao and colleagues (2) has demonstrated that retinal Muller macroglia grown in high glucose accumulate MGO and that this serves to AGE-modify the cytoplasmic protein mSin3A. This leads to increased association of mSin3A and the transcription factor Sp3 with O-linked N-acetylglucosamine (O-GlcNAc) transferase. Through an array of complex experimental protocols they also established that MGO-modification of mSin3A ultimately leads to reduced suppression of the glucose-response element on the angiopoeitin-2 promoter (2). The net result is an increased expression of angiopoeitin-2, a potent vasoactive peptide that has been linked to retinal capillary damage during diabetes (3). MGO-mediated responses were prevented if the Muller cells were engineered to over-express glyoxalase-1 (2).

This study shows that MGO is more than a short-lived metabolite that is elevated in diabetes. MGO-mediated AGE-modification of proteins can have a profound influence on cell function and this dicarbonyl could influence a wide range of macromolecules wherever it comes in contact with them. The findings of Yao at al. certainly suggest that mSin3A could be the tip of the iceberg. A global proteomic analysis of AGE-modified proteins is probably warranted to identify the so-called "Maillardome". A full and detailed analysis of which AGEs form on which proteins and how these modifications may alter functions such as enzymatic activity, structural integrity and cell signalling could go a long way towards our understanding of the pathogenicity of the Maillard reaction in biological systems.

References

1. Thornalley PJ. (2003) Glyoxalase I--structure, function and a critical role in the enzymatic defence against glycation. Biochem Soc Trans 31:1343-8.

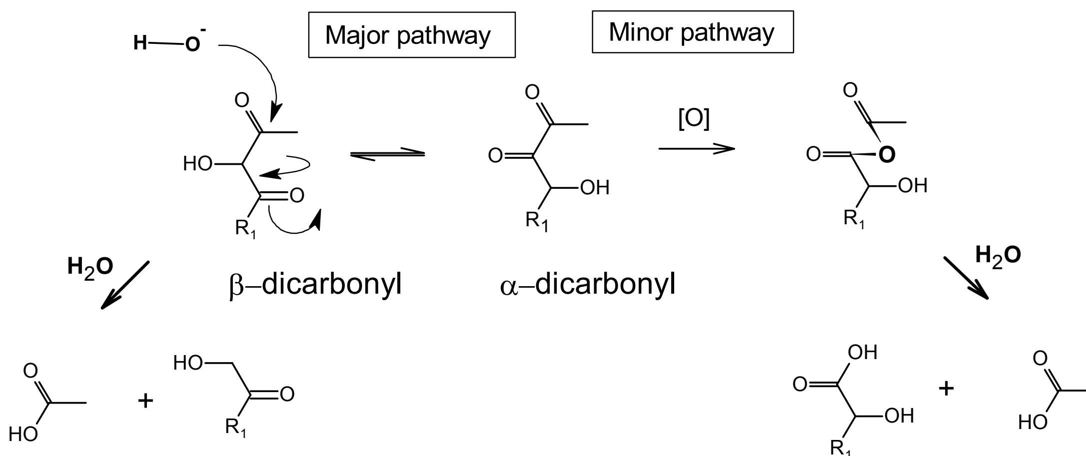
2. Yao D, Taguchi T, Matsumura T, Pestell R, Edelstein D, Giardino I, Suske G, Ahmed N, Thornalley PJ, Sarthy VP, Hammes HP, Brownlee M (2006). Methylglyoxal modification of mSin3A links glycolysis to angiopoietin-2 transcription. *Cell* 24::275-86.

3. Hammes HP, Lin J, Wagner P, Feng Y, Vom Hagen F, Krzizok T, Renner O, Breier G, Brownlee M, Deutsch U (2004) Angiopoietin-2 causes pericyte dropout in the normal retina: evidence for involvement in diabetic retinopathy. *Diabetes* 53:1104-10

HOW SHORT CHAIN CARBOXYLIC ACIDS ARE FORMED DURING MAILLARD REACTIONS ?

by Varoujan Yaylayan

The mechanism of formation of short chain carboxylic acids from sugar degradation products during Maillard reaction has been a subject of speculation since Hodge proposed his famous Scheme describing various aspects of the reaction. Two recent contributions (1,2) from Nestlé Research center have identified two distinct pathways of formation of such acids. A major pathway involving isomerization of the reactive α-dicarbonyl intermediates into β-dicarbonyl form, followed by hydrolytic β-dicarbonyl cleavage as shown below. For example, 1-deoxy-glucosone can undergo such cleavage and produce acetic acid plus a keto sugar. Studies using ^{13}C-labelling have indicated that acetic acid can arise from C-1/C-2, C-3/C-4 and C-5/C-6 carbon units of glucose.



Alternatively, α-dicarbonyl intermediates can directly undergo an oxidative α-dicarbonyl cleavage (Minor pathway) as shown above. In this proposed mechanism molecular oxygen is incorporated at any of the carbonyl carbons of the dicarbonyl moiety, followed by a single electron transfer, Baeyer-Villiger type rearrangement and finally hydrolysis to produce two carboxylic acid fragments. Terminal aldehydes of many hydoxylated sugar fragments can also undergo oxidation by molecular oxygen into their corresponding carboxylic acids and can be detected as volatile lactones (3).

References

1. Davidek T, Devaud S, Robert F and Blank I (2006) Sugar fragmentation in the Maillard reaction cascade: isotope labeling studies on the formation of acetic acid by a hydrolytic beta-dicarbonyl cleavage mechanism. *J Agric. Food Chem.* 54: 6667-6676.

2. Davidek T, Robert F, Devaud S, Vera, FA and Blank I (2006) Sugar fragmentation in the Maillard reaction cascade: formation of short-chain carboxylic acids by a new oxidative alpha-dicarbonyl cleavage pathway. *J Agric. Food Chem.* 54: 6677-6684.

3. Yaylayan VA, Haffenden LB, Chu LF, Wnorowski A (2005) Oxidative pyrolysis and postpyrolytic derivatization techniques for the total analysis of Maillard model systems: Investigation of control parameters of Maillard reaction pathways. *Ann. N.Y. Acad. Sci.* 1043: 41-54.

The Maillard proteome

By John Baynes

One of the major questions facing Maillard researchers today is whether AGE modifications of tissue proteins are really significant. We have argued for many years that there are preferred (important?) target proteins that are modified at specific sites, which amplifies the significance of trace modifications detected by chemical analysis. At least three studies have led to identification of discrete AGE-modified proteins by western blot analysis (1-3). These studies are surprising because they seem to suggest hyper-selectivity in AGE modification of cellular proteins – only a single protein was identified in each report: basic fibroblast growth factor in bovine aortic endothelial cells (1), heat shock protein 27 in rat glomerular mesangial cells (2), and corepressor mSin3A in rat retinal Müller cells (3). To my knowledge, only four reports present evidence for a broader range of modification of tissue proteins by AGEs. Poggioli *et al.* (4) identified about 100 AGE-positive proteins in a western blot analysis of human peripheral blood lymphocytes, seven of which were more were highly modified in cells from older (86-91 yr) vs. younger (20-25 yr) subjects; however, none of the AGE-modified proteins were identified. More recently, using a polyclonal anti-AGE antibody, Langer *et al.* (5) identified AGE-proteins in oligodendrocytes and neuroblastoma cells in culture; eight proteins were identified, three of them in both cell types. The majority of these proteins were high abundance proteins, such as actin, tubulin, enolase, and translation factors. Rosca *et al.* (6) used an anti-methylglyoxal-imidazole-AGE monoclonal antibody to analyze mitochondrial proteins. They identified several methylglyoxal-AGE-modified mitochondrial proteins from the kidney cortex of diabetic rats, mostly proteins involved in oxidative phosphorylation and fatty acid oxidation. For several of these proteins, they were modified to a greater extent in renal cortical mitochondria of diabetic rats, and the increase in modification was reversed by treatment with aminoguanidine.

The most significant difference among these studies is the range of protein targets identified – from one (1,2,3) or a few (5,6) in the earlier studies, up to 100 (4). In part, the differences are dependent on the antibodies: monoclonal vs. polyclonal and/or anti-pan-AGE vs. anti-specific-AGE. Regardless, the evidence for the scope and impact of AGE modifications on proteins is beginning to accumulate. One issue that has not been addressed in any of these studies is the extent of AGE modification of any of the target proteins. This remains an important, but unresolved issue. Are AGEs trace modifications, readily detected by sensitive immunoblotting techniques, but unlikely to exert a wide-ranging effect on metabolism? Are AGEs found on high abundance proteins just because these proteins are more readily detectabe? Or are some proteins hot spots for accumulating AGE modifications and, if so, is a significant fraction of these protein molecules modified by AGEs? Quantitative proteomics can provide answers to these questions, but has yet to be applied broadly to the study of AGE modification of proteins.

References

1. Giardino I, Edelstein D, Brownlee M (1994) Nonenzymatic glycosylation *in vitro* and in bovine endothelial cells alters basic fibroblast growth factor activity. *J Clin Invest* 94:110-117.

2. Padival AK, Crabb JW, Nagaraj RH (2003) Methylglyoxal modifies heat shock protein 27 in glomerular mesangial cells. *FEBS Lett* 551:113-118.

3. Yao D, Taguchi T, Matsumura T, Pestell R, Edelstein D, Giardino I, Suske G, Ahmed N, Thornalley PJ, Sarthy VP, Hammes H-P, Brownlee M (2006) Methylglyoxal modification of mSin3A links glycolysis to angiopoietin-2 transcription. *Cell* 124:275-286.

4. Poggioli S, Bakala H, Friguet B (2002) Age-related increases of protein glycation in peripheral blood lymphocytes is restricted to preferential target proteins (2002) *Exper Gerontol* 37:1207-1215.

5. Langer AK, Poon HF, Münch G, Lynn BC, Arendt T, Butterfield DA (2006) Identification of AGE-modified proteins in SH-SY5Y and OLN-93 cells. *Neurotox Res* 9:255-268.

6. Rosca MG, Mustata TG, Kinter MT, Ozdemir AM, Kern TS, Szweda LI, Brownlee M, Monnier VM, Weiss MF (2005) Glycation of mitochondrial proteins from diabetic rat kidney is associated with excess superoxide production. *Am J Physiol Renal Physiol* 289:F420-F430.

A new role for cysteine in the Maillard reaction

By Monika Pischetsreider

For a long time, it was undisputed that lysine and arginine are the most important amino acids engaged in glycation processes: amino acid analysis of glycated proteins after protein hydrolysis consistently show a pronounced decrease in lysine and arginine with a smaller decrease in histidine. A recent publication by Ota et al. now provides more evidence that cysteine may be an overlooked contributor in the Maillard reaction (1). In this study, the Amadori product of maltose and glycine, 1-deoxymaltulosylglycine, was heated with cysteine and the main reaction product was isolated. The new product was identified as 7,8a-dihydroxy-4a-methyl-8-(α-D-glucopyranosyloxy)hexahydro-5-oxa-4-thia-1-azanaphthalene-2-carboxylic acid (Figure 1), which is an adduct of cysteine with the 1-deoxyosone of maltose: the thiol group of cysteine forms a S,O-acetal with the C2-carbonyl group and the amino group a hemiaminal with the C3-carbonyl group.

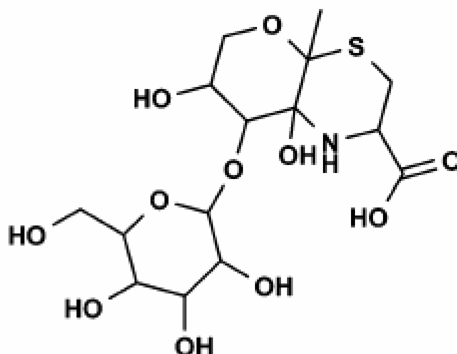


Figure 1. Major reaction product formed between 1-deoxymaltulosylglycine and cysteine. Structure taken from (1).

This structure explains why the cysteine is only reversibly bound and the product releases isomaltol and acetylfuran in acidic solution. This paper fits very well in the context of two earlier studies: Based on ^{1}H-NMR analyses of reaction mixtures of Nα-acetylcysteine and methylglyoxal, a rapid and reversible formation of the hemithioacetal was postulated (2). Furthermore, Münch et al. used dipeptide SPOT libraries to evaluate the reactivity of all amino acids in the Maillard reaction (3). In this study a combinatorial dipeptide library with blocked N-termini were synthesized on paper sheets and incubated with [^{14}C]glucose. Strong radioactivity was detected only in the spots containing lysine or cysteine, and low radioactivity in the spots containing histidine. These results indicate that cysteine readily reacts with sugars and dicarbonyl compounds. The reversible nature of these adducts may explain why the reactivity has not been detected by amino acid analysis of glycated proteins. However, the cysteine conjugates may considerably influence technological and physiological properties of the glycated proteins. Furthermore, the cysteine adducts could serve as a carrier and depot of reactive carbonyl compounds which could slowly release carbonyl independently of the time and location of their formation.

References

1. Ota M, Kohmura M, Kawaguchi H (2006) Characterization of a new Maillard type reaction product generated by heating 1-deoxymaltulosyl-glycine in the presence of cysteine *J Agric Food Chem* 54: 5127 – 5131.

2. Lo T, Westwood M, McLellan A, Selwood T, Thornalley P (1994) Binding and modification of proteins by methylglyoxal under physiological conditions *J Biol Chem* 269: 32299 – 32305.

3. Münch G, Schicktanz D, Behme A, Gerlach M, Riederer P, Palm D, Schinzel R (1999) Amino acid specificity of glycation and protein-AGE crosslinking reactivitied determined with a dipeptide SPOT library *Nature Biotech* 17: 1006 – 1010.

Advanced glycation – time to enter the great stem cell debate?

By Ashay Bhatwadekar and Alan Stitt

It is well appreciated by IMARS members that advanced glycation end products (AGEs) accumulating in cells and tissues could play an important pathogenic role in disease initiation and progression. The role of these adducts in progenitor and stem cells has received comparatively little attention although recent reports have indicated that AGEs can influence the remodelling of cardiac fibroblasts, liver fibrogenesis and transdifferentiation of epithelial cells into myofibroblasts (1-3). AGEs also decrease differentiation of mesenchymal stem cells into adipose tissues, cartilage and bone (1). Adding to our knowledge of a role for AGEs in progenitor and stems cell are novel observations reported in a recent exciting article by Hernebring et al. that reports elimination of AGE adducts during embryonic stem (ES) cell differentiation (4).

In their studies Hernebring et al. have shown enhanced levels of AGEs and precursor carbonyls in undifferentiated ES cells – to levels that were on a par to those observed in brain and liver of mature mice. AGE-modification occurred mainly in the chaperone and cytoskeletal proteins but, interestingly, the level of such modifications dropped dramatically during ES cell differentiation. Parallel i*n vivo* studies also confirmed this elimination of protein damage as cells progressed along different developmental pathways and became more specialised. This "cytoplasmic housekeeping" phenomenon in ES cells was associated with enhanced activity of the 20S proteasome – a structure which is essential for the degradation of the oxidatively damaged proteins in cells (4). This poses the question: if ES cells can accomplish the task of purging themselves of these damaged proteins why this phenomenon is not observed in fully differentiated cells?

One explanation is that there is an overall decline (1.5-2 fold) in proteasomal activity in aged cells or there may be significant overload of oxidative damage against which the antioxidant defences can not protect. Also non enzymatic glycation of proteins is not only a hyperglycemia dependent process but also aging contributes significantly to the reaction, so that young age (embryonic) may have an ability to overcome this by some defence mechanism which is compromised in adult life. Dissection of these issues in ES and progenitor cell pathobiology during diabetes and aging are critical since the reparative and regenerative potential of these cells is now widely recognised in medicine.

References

1. Kume S, Kato S, Yamagishi S, Inagaki Y, Ueda S, Arima N, Okawa T, Kojiro M, Nagata K (2005) Advanced glycation end-products attenuate human mesenchymal stem cells and prevent cognate differentiation into adipose tissue, cartilage, and bone. *J Bone Miner Res* 20(9):1647-58.

2. Oldfield MD, Bach LA, Forbes JM, Nikolic-Paterson D, McRobert A, Thallas V, Atkins RC, Osicka T, Jerums G, Cooper ME (2001) Advanced glycation end products cause epithelial-myofibroblast transdifferentiation via the receptor for advanced glycation end products (RAGE).*J Clin Inves* 108(12):1853-63

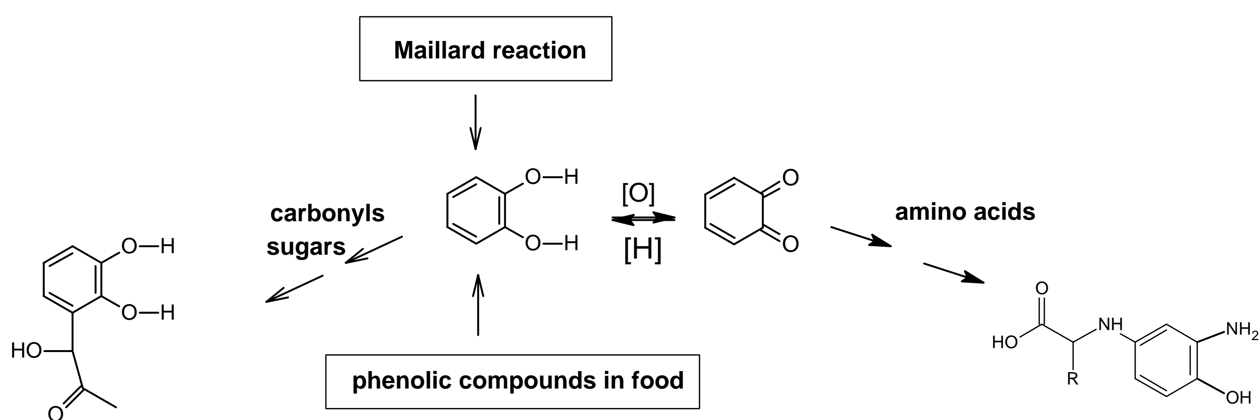
3. Fehrenbach H, Weiskirchen R, Kasper M, Gressner AM (2001) Up-regulated expression of the receptor for advanced glycation end products in cultured rat hepatic stellate cells during transdifferentiation to myofibroblasts. *Hepatology* 34(5):943-52

4. Hernebring M, Brolen G, Aguilaniu H, Semb H, Nystrom T (2006) Elimination of damaged proteins during differentiation of embryonic stem cells. *Proc Natl Acad Sci U S A.* 103(20):7700-5.

MAILLARD REACTION: COLLATERAL DAMAGE

by Varoujan Yaylayan

Information regarding the interaction of primary Maillard reaction precursors such as reducing sugars and amino acids with aromatic compounds, in addition to the generation of hydroxylated aromatic compounds through Maillard reaction has emerged in recent years. These oxygenated aromatic compounds not only can alter the pH and the redox potential of the media in which they are generated, but also can act as scavengers of amino acids and carbonyl compounds as demonstrated in several recent publications.



Phenolic compounds in food are receiving considerable attention due to their antioxidant and anticancer properties. Simple phenolics such as hydroxylated benzene derivatives have been shown to be generated in different Maillard model systems (1, 2) with their carbon rings mainly originating from the six carbon atoms of hexoses (2). In addition, polyphenols such as catechin or epicatechin are abundant in many food products such as tea, coffee and different fruits and vegetables. Recent studies (3, 4) have shown that oxidized phenolic compounds such as *o*-quinone moieties can scavenge amino acids and form adducts such as the structure shown above (5). On the other hand, their reduced forms can scavenge not only the carbonyls and dicarbonyls such as pyruvaldehyde (6) generated through the Maillard reaction, but also reducing sugars to form C-glycosides (7). These findings demonstrate that the scope of damage inflicted by the Maillard reaction far exceeds the known effects on proteins and amino acids and touches also the phenolics, in addition to the already documented interactions with the lipid peroxidation products. These studies further indicate that Maillard reaction plays a significant role in modulating the reaction pathways of both lipid and phenolic components in food during thermal treatment thus extending the molecular damage to other food components.

References

1. Lang R, Mueller C and Hofmann T (2006) Development of a stable isotope dilution analysis with liquid chromatography-tandem mass spectrometry detection for the quantitative analysis of di- and trihydroxybenzenes in foods and model systems. *J. Agric. Food Chem*. 54: 5755-5762.

2. Haffenden LJ and Yaylayan VA (2005) Mechanism of formation of redox-active hydroxylated benzenes and pyrazine in 13C-labeled glycine/D-glucose model systems. *J. Agric. Food Chem*. 53: 9742-9746.

3. Rizzi GP (2006) Formation of strecker aldehydes from polyphenol-derived quinones and alpha-amino acids in a nonenzymic model system. *J. Agric. Food Chem.* 54: 1893-1897.

4. Bittner S (2006) When quinones meet amino acids: chemical, physical and biological consequences. *Amino acids*, 30: 205-224.

5. Yaylayan VA (2006) Expanding the horizons of the Strecker reaction. *IMARS Highlights* 1: 6.

6. Totlani VM and Peterson DG. (2006) Epicatechin carbonyl-trapping reactions in aqueous Maillard systems: identification and structural elucidation *J. Agric. Food Chem.* (epub 8/29/2006) in press.

7. Hofmann, T. (2006) Taste-active glycol-conjugates and their formation upon thermal food processing. COST-IMARS Joint Workshop, Napoli, Italy.

INTERNATIONAL MAILLARD REACTION SOCIETY

Charting the future of carbonyl research in food and medicine

THANKS TO OUR GENEROUS SPONSORS

Nestlé

Good Food, Good Life

PRESCRIPTIVES A DIVISION OF ESTEE LAUDER COMPANIES

Firmenich

L'ORÉAL