

Nachweis von DNA-Schäden mittels Analyse von oxidierten Nukleosiden und deren Anwendung als Biomarker

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Literatur:

1. Marnett, L.J.: Oxyradicals and DNA damage. *Carcinogenesis* 21: 361-370 (2000).
2. Halliwell, B.: Can oxidative DNA damage be used as a biomarker of cancer risk in humans? Problems, resolution and preliminary results from nutritional supplementation studies. *Free Radical Res* 29: 469-486 (1998).
3. Dizdaroglu, M.: Chemical determination of free radical-induced damage to DNA. *Free Radical Bio Med* 10: 225-242 (1992).
4. Loft, S.; Poulsen, H.E.: Cancer risk and oxidative DNA damage in man. *J Mol Med* 74: 297-312 (1996).
5. Boveris, A.; Chance, B.: The mitochondrial generation of hydrogen peroxide. General properties and effect of hyperbaric oxygen. *Biochem J* 134: 707-716 (1973).
6. Sohal, R.S.: Aging, cytochrome oxidase activity, and hydrogen peroxide release by mitochondria. *Free Radical Bio Med* 14: 583-588 (1993).
7. Wallace, D.C.: Mitochondrial diseases in man and mouse. *Science* 283: 1482-1488 (1999).
8. Wei, Y.H.; Lu, C.Y.; Lee, H.C.; Pang, C.Y.; Ma, Y.S.: Oxidative damage and mutation to mitochondrial DNA and age-dependent decline of mitochondrial respiratory function. *Ann NY Acad Sci* 854: 155-170 (1998).
9. Ames, B.N.; Shigenaga, M.K.; Hagen, T.M.: Oxidants, antioxidants, and the degenerative diseases of aging. *P Natl Acad Sci USA* 90: 7915-7922 (1993).
10. Davies, K.J.A.: Oxidative stress: the paradox of aerobic life. In: Rice-Evans C., Halliwell B., Lunt G.G. (eds.): *Free Radicals and Oxidative Stress: Environment, Drugs and Food Additives*, Portland Press, London 1-31 (1995).
11. Ji, L.L.; Leeuwenburgh, C.; Leichtweis, S.; Gore, M.; Fiebig, R.; Hollander, J.; Beijma, J.: Oxidative stress and aging. Role of exercise and its influences on antioxidant systems. *Ann NY Acad Sci* 854: 102-117 (1998).
12. Kelly, E.J.; Mudway, I.; Krishna, M.T.; Holgate, S.T.: The free radical basis of air pollution: focus on ozone. *Respir Med* 89: 647-656 (1995).
13. Sies, H.: Strategies of antioxidant defense. *Eur J Biochem*. 215: 213-219 (1993).
14. Cutler, R.G.: Human longevity and aging: possible role of reactive oxygen species. *Ann NY Acad Sci* 621: 1-28 (1991).
15. Halliwell, B.; Gutteridge, J.M.C.: Oxygen toxicity, oxygen radicals, transition metals and disease. *Biochem J* 219: 1-14 (1984).
16. Halliwell, B.: Oxidative stress, nutrition and health. Experimental strategies for optimisation of nutritional antioxidant intake in humans. *Free Radical Res* 25: 57-74 (1996).
17. Pryor, W.A.: Vitamin E and heart disease: basic science to clinical intervention trials. *Free Radical Bio Med* 28: 141-164 (2000).
18. Sohal, R.S.; Weindruch, R.: Oxidative stress, caloric restriction, and aging. *Science* 273: 59-63 (1996).
19. Khan, A.U.; Wilson, T.: Reactive oxygen species as cellular messengers. *Chem Biol* 2: 437-445 (1995).
20. Ischiropoulos, H.; Zhu, L.; Beckman, J.S.: Peroxynitrite formation from macrophage-derived nitric oxide. *Arch Biochem Biophys* 298: 446-451 (1992).
21. DeRojas-Walker, T.; Tamir, S.; Ji, H.; Wishnok, J.S.; Tannenbaum, S.R.: Nitric oxide induces oxidative damage in addition to deamination in macrophage DNA. *Chem Res Toxicol* 8: 473-477 (1995).
22. Cottrell, D.A.; Blakely, E.L.; Borthwick, G.M.; Johnson, M.A.; Taylor, G.A.; Brierley, E.J.; Ince, P.G.; Turnbull, D.M.: Role of mitochondrial DNA mutations in disease and aging. *Ann NY Acad Sci* 908: 199-207 (2000).
23. Knight, J.A.: Diseases related to oxygen-derived free radicals. *Ann Clin Lab Sci* 25: 111-121 (1995).
24. Knight, J.A.: Free radicals: their history and current status in aging and disease. *Ann Clin Lab* 28: 331-346 (1998).
25. Knight, J.A.: The biochemistry of aging. *Adv Clin Chem* 35: 1-62 (2000).
26. Williams, L.R.: Oxidative stress, age-related neurodegeneration, and the potential for neurotrophic treatment. *Cerebrovasc Brain Met Rev* 7: 55-73 (1995).
27. Ames, B.N.; Gold, L.S.; Willett, W.C.: The causes and prevention of cancer. *Proc Natl Acad Sci USA* 92: 5258-5265 (1995).
28. Halliwell, B.; Gutteridge, J.M.C.: *Free radicals in biology and medicine*. 3rd ed. Oxford, United Kingdom: Oxford University Press, 1999.
29. Feig, D.I.; Reid, T.M.; Loeb, L.A.: Reactive oxygen species in tumorigenesis. *Cancer Res* 54: 1890-1894 (1994).
30. Seidel, C.A.M.; Schulz, A.; Sauer, M.H.M.: Nucleobase-specific quenching of fluorescent dyes. 1. Nucleobase one redox potentials and their correlation with static and dynamic quenching efficiencies. *J Phys Chem* 100: 5541-5553 (1996).
31. Dizdaroglu, M.: Chemical determination of oxidative DNA damage by gas chromatography-mass spectrometry. *Method Enzymol*. 234: 3-16 (1994).
32. Shigenaga, M.K.; Gimeno, C.J.; Ames, B.N.: Urinary 8-hydroxy-2'-deoxyguanosine as a biological marker of in vivo oxidative DNA damage. *P Natl Acad Sci USA* 86: 9697-9701 (1989).
33. Loft, S.; Vistisen, K.; Ewertz, M.; Tjønneland, A.; Overvad, K.; Poulsen, H.E.: Oxidative DNA-damage estimated by 8-hydroxydeoxyguanosine excretion in man: influence of smoking, gender and body mass index. *Carcinogenesis* 13: 2241-2247 (1992).
34. Loft, S.; Poulsen, H.E.: Markers of oxidative damage to DNA: antioxidants and molecular damage. *Method Enzymol* 300: 166-184 (1999).
35. Croteau, D.L.; Bohr, V.A.: Repair of oxidative damage to nuclear and mitochondrial DNA in mammalian cells. *J Biol Chem* 272: 25409-25412 (1997).
36. Floyd, R.A.: Antioxidants, oxidative stress, and degenerative neurological disorders. *Proc Soc Exp Biol Med* 222: 236-245 (1999).
37. Kasai, H.: Analysis of a form of oxidative DNA damage, 8-hydroxy-2'-deoxyguanosine, as a marker of cellular oxidative stress during carcinogenesis. *Mutat Res* 387: 146-163 (1997).
38. Ottender, M.; Lutz, W.K.: Correlation of DNA adduct levels with tumor incidence: carcinogenic potency of DNA adducts. *Mutat Res* 424: 237-247 (1999).
39. Wang, D.; Kreutzer, D.A.; Essigmann, J.M.: Mutagenicity and repair of oxidative DNA damage: insights from studies using defined lesions. *Mutat Res* 400: 99-115 (1998).
40. Shibutani, S.; Takeshita, M.; Grollman, A.P.: Insertion of specific bases during DNA synthesis past the oxidation damaged base 8-oxodG. *Nature* 349: 431-434 (1991).
41. Kuchino, Y.; Mori, E.; Kasai, H.; Inoue, H.; Iwai, S.; Miura, K.; Ohtsuka, E.; Nishimura, S.; Masutani, C.; Hanaoka, F.; Ohtsuka, E.: Misreading of DNA templates containing 8-hydroxydeoxyguanosine at the modified base and at adjacent residues. *Nature* 327: 77-79 (1987).
42. Kamiya, H.; Murata-Kamiya, N.; Fujimuro, M.; Kido, K.; Inoue, H.; Nishimura, S.; Masutani, C.; Hanaoka, F.; Ohtsuka, E.: Comparison of incorporation and extension of nucleotides in vitro opposite 8-hydroxyguanine (7,8-dihydro-8-oxoguanine) in hot spots of the c-Ha-ras gene. *Jpn J Cancer Res* 86: 270-276 (1995).
43. Hollstein, M.; Sidransky, D.; Vogelstein, B.; Harris, C.C.: p53 mutations in human cancers. *Science* 253: 49-52 (1991).
44. Harris, C.C.; Hollstein, M.: Clinical implications of the p53 tumor-suppressor gene. *N*

- Engl J Med 329: 1318-1327 (1993).
45. Green, M.S.; Bennett, W.P.; Hollstein, M.; Harris, C.C.: Mutation in the p53 tumor suppressor gene: Clues to cancer etiology and molecular pathogenesis. *Cancer Res* 54: 4855-4878 (1994).
 46. Ramotar, D.; Demple, B.: Enzymes that repair oxidative damage to DNA: enzymology and biology. *Annu Rev Biochem* 63: 915-948 (1994).
 47. Bempel, B.; Harrison, L.: Repair of oxidative damage to DNA: enzymology and biology. *Annu Rev Biochem* 63: 915-948 (1994).
 48. Boiteux, S.; Gajewski, E.; Laval, J.; Dizdaroglu, M.: Substrate specificity of the Escherichia coli Fpg protein (formamidopyrimidine-DNA glycosylase): excision of purine lesions in DNA produced by ionizing radiation or photosensitization. *Biochemistry* 31: 106-110 (1992).
 49. Bohr, V.A.; Taffe, B.G.; Larminat, E.: DNA repair, oxidative stress and aging. In: Cutler RG, Packer L, Bertram J, Mori A (eds): *Oxidative stress and aging*. Birkhauser Basel (1995).
 50. Karakaya, A.; Jaruga, P.; Bohr, V.A.; Grollman, A.P.; Dizdaroglu, M.: Kinetics of excision of purine lesions from DNA by Escherichia coli FPG protein. *Nucleic Acids Res* 25: 474-479 (1997).
 51. Collins, A.R.; Ai-Guo, Ma; Duthie, S.J.: The kinetics of repair of oxidative DNA damage (strand breaks and oxidised pyrimidines) in human cells. *Mutat Res* 336: 69-77 (1995).
 52. Shigenaga, M.K.; Ames, B.N.: Assays for 8-hydroxy-2'-deoxyguanosine: A biomarker of in vivo oxidative DNA damage. *Free Radical Bio Med* 10: 211-216 (1991).
 53. Loft, S.; Wierik, E.J.M.V.; Van der Berg, H.; Poulsen, H.E.: Energy restriction and oxidative DNA damage. *Cancer Epidemiol Biomar Prev* 4: 515-519 (1995).
 54. Kasai, H.; Nishimura, S.: Hydroxylation of deoxyguanosine at the C-8 position by ascorbic acid and other reducing agents. *Nucleic Acid Res.* 12: 2137-2145 (1984).
 55. Hofer, T.; Möller, L.: Optimization of the workup procedure for the analysis of 8-oxo-7,8-dihydro-2'-deoxyguanosine with electrochemical detection. *Chem Res Toxicol* 15: 426-432 (2002).
 56. Berger, M.; Anselmino, C.; Mouret, J.-F.; Cadet, J.: High performance liquid chromatography-electrochemical assay for monitoring the formation of 8-oxo-7,8-dihydroadenine and its related 2'-deoxyribonucleoside. *J. Liq Chrom* 13: 929-940 (1990).
 57. Jaruga, P.; Dizdaroglu, M.: Repair of products of oxidative DNA base damage in human cells. *Nucleic Acids Res* 24: 1389-1394 (1996).
 58. Halliwell, B.; Dizdaroglu, M.: The measurement of oxidative damage to DNA by HPLC and GC/MS techniques. *Free Radical Res Commun* 16: 75-87 (1992).
 59. Hofer, T.; Möller, L.: Reduction of oxidation during the preparation of DNA and analysis of 8-hydroxy-2'-deoxyguanosine. *Chem Res Toxicol* 11: 882-887 (1998).
 60. Hofer, T.: Oxidation of 2'-deoxyguanosine by H₂O₂-ascorbate: evidence against free OHO and thermodynamic support for two-electron reduction of H₂O₂. *J Chem Soc Perk T 2*: 210-213 (2001).
 61. Teixeira, A.J.R.; Gommers-Ampt, J.H.; Van de Werken, G.; Westra, G.J.; Stavenuiter, J.F.C.; De Jong A.P.J.M.: Method for the analysis of oxidized nucleosides by gas chromatography/mass spectrometry. *Anal Biochem* 214: 474-483 (1993).
 62. Frelon, S.; Douki, T.; Ravanat, J.-L.; Pouget, J.-P.; Tornabene, C.; Cadet, J.: High-performance liquid-chromatography-tandem mass spec-
 - trometry measurement of radiation-induced base damage to isolated and cellular DNA. *Chem Res Toxicol* 13: 1002-1010 (2000).
 63. Weinmann, A.; Belleng, D.; Poulsen, H.E.: Measurement of 8-oxo-2'-deoxyguanosine and 8-oxo-2'-deoxyadenosine in DNA and human urine by high performance liquid chromatography-electrospray tandem mass spectrometry. *Free Radical Bio Med* 30: 757-764 (2001).
 64. Park, E.-M.; Shigenaga, M.K.; Degan, P.; Korn, T.S.; Kitzler, J.W.; Wehr, C.M.; Kolachana, P.; Ames, B.N.: Assay of excised oxidative DNA lesions: Isolation of 8-oxoguanine and its nucleoside derivatives from biological fluids with a monoclonal antibody column. *P Natl Acad Sci USA* 89 (1992).
 65. Hattori, Y.; Nishigori, C.; Tanaka, T.; Uchida, K.; Nakaido, O.; Osawa, T.; Hiai, H.; Imamura, S.; Toyokuni, S.: 8-Hydroxy-2'-deoxyguanosine is increased in epidermal cells of hairless mice after chronic ultraviolet B exposure. *J Invest Dermatol* 107: 733-737 (1997).
 66. Soulánakis, R.P.; Melamede, R.J.; Bespalov, I.A.; Wallace, S.S.; Beckman, K.B.; Ames, B.N.; Taatjes, D.J.; Janssen-Heininger, Y.M.W.: Fluorescence detection of 8-oxoguanine in nuclear and mitochondrial DNA of cultured cells using a recombinant fab and confocal scanning laser microscopy. *Free Radical Bio Med* 28: 987-998 (2000).
 67. Collins, A.; Dobson, V.; Dusinka, M.; Kennedy, G.; Stetina, R.: The comet assay: what can it really tell us? *Mutat. Res* 375: 183-193 (1997).
 68. Collins, A.: The comet assay: a novel approach to measuring DNA oxidation. In: Aruoma, O.I.; Halliwell, B. (eds.): *DNA and Free Radicals: Techniques, Mechanisms & Applications*. OICA International, Saint Lucia (1998).
 69. Bhagwat, M. and Gerlt, J.A.: 3'- and 5'-strand cleavage reactions catalyzed by the Fpg protein from Escherichia coli occur via successive β- and α-elimination mechanisms, respectively. *Biochemistry* 35: 659-665 (1996).
 70. Tchou, J.; Grollman, A.P.: The catalytic mechanism of Fpg protein. *J Biol Chem* 270: 11671-11677 (1995).
 71. Gedik, M.; Wood, S.G.; Collins, A.R.: Measuring oxidative damage to DNA: HPLC and the comet assay compared. *Free Radical Res* 29: 609-615 (1998).
 72. Loft, S.; Deng, X.S.; Tuo, J.: Experimental study of oxidative DNA damage. *Free Radical Res* 29: 525-539 (1998).
 73. Cooke, M.S.; Evans, M.D.; Herbert, K.E.; Lunec, J.: Urinary 8-oxo-2'-deoxyguanosine-source, significance and supplements. *Free Radical Res* 32: 381-397 (2000).
 74. Lagorio, S.; Tagesson, C.; Forastiere, F.; Axelsson, O.; Carere, A.: Exposure to benzene and urinary concentrations of 8-hydroxydeoxyguanosine, a biological marker of oxidative damage to DNA. *Occup Environ Med* 51: 739-743 (1994).
 75. Hayakawa, M.; Hattori, K.; Sugiyama, S.; Ozawa, T.: Age associated oxygen damage and mutations in mitochondrial DNA in human hearts. *Biochem Biophys Res C* 189: 979-985 (1992).
 76. Mecocci, P.; MacGarvey, U.; Kaufman, A.E.; Koontz, D.; Shoffner, J.M.; Wallace, D.C.; Beal, M.F.: Oxidative damage to mitochondrial DNA shows marked age-dependent increases in human brain. *Ann Neurol* 34: 609-616 (1993).
 77. Tagesson, C.; Källberg, M.; Leanderson, P.: Determination of urinary 8-hydroxydeoxyguanosine by coupled-column high-performance liquid chromatography with electrochemical detection: a noninvasive assay for in vivo oxidative DNA damage in humans. *Toxicol Method* 1: 242-251 (1992).
 78. Loft, S.; Astrup, A.; Buemann, B.; Poulsen, H.E.: Oxidative DNA damage correlates with oxygen consumption in humans. *FASEB J* 8: 534-537 (1994).
 79. Inoue, T.; Mu, Z.; Sumikawa, K.; Adachi, K.; Okochi, T.: Effect of physical exercise on the content of 8-hydroxydeoxyguanosine in nuclear DNA prepared from human lymphocytes. *Jpn J Cancer Res* 84: 720-725 (1993).
 80. Suzuki, J.; Inoue, Y.; Suzuki, S.: Changes in urinary level of 8-hydroxyguanine by exposure to reactive oxygengenerating substances. *Free Radical Bio Med* 18: 431-436 (1995).
 81. Kasai, H.; Iwamoto-Tanaka, N.; Miyamoto, T.; Kawanami, K.; Kawanami, S.; Kido, R.; Ikeda, M.: Life style and urinary 8-hydroxydeoxyguanosine, a marker of oxidative DNA damage: Effects of exercise, working conditions, meat intake body mass index, and smoking. *Jpn J Cancer Res* 92: 9-15 (2001).
 82. Inoue, T.; Hayashi, M.; Takayanagi, K.; Morooka, S.: Oxidative DNA damage is induced by chronic cigarette smoking, but repaired by abstinence. *J Health Sci* 49: 217-220 (2003).
 83. Prieme, H.; Loft, S.; Karlsson, M.; Grønbæk, K.; Tonnesen, P.; Poulsen H.E.: Effect of smoking cessation on oxidative DNA modification estimated by 8-oxo-7,8-dihydro-2'-deoxyguanosine excretion. *Carcinogenesis* 19: 347-351 (1998).
 84. Kiyosawa, H.; Suko, M.; Okudaira, H.; Murata, K.; Miyamoto, T.; Chung, M.H.; Kasai, H.; Nishimura, S.: Cigarette smoking induces formation of 8-hydroxydeoxyguanosine, one of the oxidative DNA damages in human peripheral leucocytes. *Free Radical Res C* 11: 23-27 (1990).
 85. Asami, S.; Manabe, H.; Miyake, J.: Cigarette smoking induces an increase in oxidative DNA damage, 8-hydroxyguanosine, in a central site of the human lung. *Carcinogenesis* 18: 1763-1766 (1997).
 86. Takeuchi, T.; Nakajima, M.; Ohta, Y.; Mure, K.; Takeshita, T.; Morimoto, K.: Evaluation of 8-hydroxydeoxyguanosine, a typical oxidative DNA damage, in human leukocytes. *Carcinogenesis* 15: 1519-1523 (1994).
 87. Yin, B.; Whyatt, R.M.; Perera, F.P.; Randall, M.C.; Cooper, T.B.; Santella, R.M.: Determination of 8-hydroxydeoxyguanosine by an immunoaffinity chromatography-monoclonal antibodybased ELISA. *Free Radical Bio Med* 18: 1023-1032 (1995).
 88. Djuric, Z.; Heilbrun, L.K.; Reading, B.A.; Bömer, A.; Valeriote, F.A.; Martino, S.: Effects of low-fat diet on levels of oxidative damage to DNA in human peripheral nucleated blood cells. *J Natl. Cancer Inst.* 83: 766-769 (1991).
 89. Djuric, Z.; Lewis, S.M.; Lu, M.H.; Mayhugh, M.; Tang, N.; Hart, R.W.: Effect of varying dietary fat levels on rat growth and oxidative DNA damage. *Nutr Canc* 39: 214-219 (2001).
 90. Loft, S.; Thorling, E.B.; Poulsen, H.E.: High fat diet induced oxidative DNA damage estimated by 8-oxo-7,8-dihydro-2'-deoxyguanosine excretion in rats. *Free Radical Res* 29: 595-600 (1998).
 91. Verhagen, V.; Poulsen, H.E.; Loft, S.: Reduction of oxidative DNA damage in humans by Brussels sprouts. *Carcinogenesis* 16: 969-970 (1995).
 92. Deng, X.S.; Tuo, J.; Poulsen, H.E.; Loft, S.: Prevention of oxidative DNA damage in rats by Brussels sprouts. *Free Radical Res* 28: 323-333 (1998).
 93. Rehman, A.; Bourne, L.C.; Halliwell, B.; Rice-Evans, C.: Tomato consumption modulates

- oxidative DNA damage in humans. *Biochem Biophys Res C* 262: 828-831 (1999).
94. Prestera, T.; Holtzclaw, W.D.; Zhang, Y.; Talalay, P.: Chemical and molecular regulation of enzymes that detoxify carcinogens. *P Natl Acad Sci USA* 90: 2965-2969 (1993).
95. Zhang, Y.; Kensler, T.W.; Cho, C.G.; Posner, G.H.; Talalay, P.: Anticarcinogenic activities of sulforaphane and structurally related synthetic norbornyl isothiocyanates. *P Natl Acad Sci USA* 91: 3147-3150 (1994).
96. Thompson, H.J.; Heimendinger, J.; Haegele, A.; Sedlack, S.M.: Effect of increased vegetable and fruit consumption on markers of oxidative cellular damage. *Carcinogenesis* 20: 2261-2266 (1999).
97. Van Poppel, G.; Poulsen, H.E.; Loft, S.; Verhaegen, H.: No influence of beta-carotene on oxidative DNA damage in male smokers. *J Natl Cancer Inst* 87: 310-311 (1995).
98. Huang, H.-Y.; Helzsouer, K.J.; Appel, L.J.: The effects of vitamin C and vitamin E on oxidative DNA damage: Results from a randomized controlled trial. *Cancer Epidemiol Biomar* 9: 647-652 (2000).
99. Porkkala-Sarataho, E.; Salonen, J.T.; Nyssönen, K.; Kaikkonen J.; Salonen R.; Ristonmaa U.; Diczfalusy U.; Brigelius-Flohe R.; Loft S.; Poulsen H. E.: Long-term effects of vitamin E, vitamin C, and combined supplementation on urinary 7-hydro-8-oxo-2'-deoxyguanosine, serum cholesterol oxidation products, and oxidation resistance of lipids in nondepleted men. *Arterioscler Thromb Vasc Biol* 20: 2087-2093 (2000).
100. Beatty, E.R.; England, T.G.; Geissler, C.A.; Aruoma, O.I.; Halliwell, B.: Effect of antioxidant vitamin supplementation on markers of DNA damage and plasma antioxidants. *P Nutr Soc* 58: 44A (abstr) (1999).
101. Sakamoto, W.; Isoura, H.; Fujie, K.: Coffee increases levels of urinary 8-hydroxydeoxyguanosine in rats. *Toxicology* 183: 255-263 (2003).
102. Olinski, R.; Zastawny, T.; Budzbon, J.; Skokowski, J.; Zegarski, W.; Dizdaroglu, M.: DNA base modification in chromatin of human cancerous tissues. *FEBS Lett* 309: 193-198 (1992).
103. Malins, D.C.; Haimanot, R.: Major alterations in the nucleotide structure of DNA in cancer of the female breast. *Cancer Res* 51: 5430-5432 (1991).
104. Malins, D.C.; Holmes, E.H.; Polissar N.L.; Gunselman, S.: The etiology of breast cancer. Characteristic alterations in hydroxyl radical-induced DNA base lesions during oncogenesis with potential for evaluating incidence risk. *Cancer Lett* 71: 3036-3042 (1993).
105. Jaruga, P.; Zastawny, T.H.; Skokowski, J.; Dizdaroglu, M.; Olinski, R.: Oxidative DNA base damage and antioxidant enzyme activities in human lung cancer. *FEBS Lett* 341: 59-64 (1994).
106. Nagashima, M.; Tsuda, H.; Takenoshita, S.; Nagamachi, Y.; Hirohashi, S.; Yokota, J.; Kasai, H.: 8-hydroxydeoxyguanosine levels in DNA of human breast cancer are not significantly different from those of non-cancerous breast tissues by the HPLC-ECD method. *Cancer Lett* 90: 157-62 (1995).
107. Tagesson, C.; Kallberg, M.; Klintenberg, C.; Starkhammar, H.: Determination of urinary 8-hydroxydeoxyguanosine by automated coupled-column high performance liquid chromatography: a powerful technique for assaying in vivo oxidative DNA damage in cancer patients. *Eur J Cancer* 31A: 934-940 (1995).
108. Bergold, D.S.; Berg, C.D.; Simic, M.G.: Urinary biomarkers in radiation therapy of cancer.
- Adv Exp Med Biol 264: 311-316 (1990).
109. Rozalski, R.; Gackowski, D.; Roszkowski, K.; Foksinski, M.; Olinski, R.: The level of 8-hydroxyguanosine, a possible repair product of oxidative DNA damage, is higher in urine of cancer patients than in control subjects. *Cancer Epidemiol Biomarkers Prev* 11: 1072-1075 (2002).
110. Shimoda, R.; Nagashima, M.; Sakamoto, M.; Yamaguchi, N.; Hirohashi, S.; Yokota, J.; Kasai, H.: Increased formation of oxidative DNA damage, 8-hydroxy-deoxyguanosine, in human livers with chronic hepatitis. *Cancer Res* 54: 3171-3172 (1994).
111. Bashir, S.; Harris, G.; Denman, M.A.; Blake D.R.; Winyard, P.G.: Oxidative DNA damage and cellular sensitivity to oxidative stress in human autoimmune diseases. *Ann Rheum Dis* 52: 659-666 (1993).
112. Tsuboi, H.; Kouda, K.; Takeuchi, H.; Takigawa, M.; Masamoto, Y.; Takeuchi, M.; Ochi, H.: 8-Hydroxyguanosine in urine as an index of oxidative damage to DNA in the evaluation of atopic dermatitis. *Brit J Dermatology* 138: 1033-1035 (1998).
113. Dandona, P.; Thusu, K.; Cook, S.; Snyder, B.; Makowski, J.; Armstrong, D.; Nicotera, T.: Oxidative damage to DNA in diabetes mellitus. *Lancet* 347: 444-445 (1996).
114. Hinokio, Y.; Suzuki, S.; Hirai, H.; Suzuki, C.; Suzuki, M.; Toyota, T.: Urinary excretion of 8-oxo-7,8-dihydro-2'-deoxyguanosine as a predictor of the development of diabetic nephropathy. *Diabetologia* 45: 877-882 (2002).
115. Shohji, H.; Oguchi, S.; Shimizu, T.; Yamashiro, Y.: Effect of human breast milk on urinary 8-hydroxy-2'-deoxyguanosine excretion in infants. *Pediatr Res* 53: 850-852 (2003).
116. Cooke, M.S.; Evans, M.D.; Podmore, I.D.; Herbert, K.E.; Mistry, N.; Mistry, P.; Hicknbotham, P.T.; Hussieni, A.; Griffiths, H.R.; Lunec, J.: Novel repair action of vitamin C upon in vivo oxidative DNA damage. *FEBS Letters* 363: 363-367 (1998).
117. Okamoto, K.; Toyokuni, S.; Uchida, K.; Ogawa, O.; Takenewa, J.; Kahehi, Y.; Kinoshita, H.; Hattori-Nakakuki, Y.; Hiai, H.; Yoshida, O.: Formation of 8-hydroxy-2'-deoxyguanosine and 4-hydroxy-2-nonenal-modified proteins in human renal-cell carcinoma. *Int J Cancer* 58: 825-829 (1994).
118. Watzl, B.; Reckemmer, G.: Phenolsäuren. *Ernährungs-Umschau* 48: 413-416 (2001).

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