

## Vassilis L. Souliotis

Research Associate Professor

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### Current Research interests

Since 2001, Dr Vassilis L. Souliotis has been a group leader at the Institute of Biology, Medicinal Chemistry and Biotechnology of the National Hellenic Research Foundation. His research interests focus on translational research in hematology/ oncology and autoimmunity. Areas of research include the network of DNA damage response (DDR) pathways, a comprehensive signaling process that determines the cell's ability to repair DNA damage or to undergo apoptosis. Over the past few years, Dr Souliotis aims at producing scientific knowledge on the molecular pathways that are implicated in the onset and progression of the disease and in the successful outcome of chemotherapy. He has a longstanding interest to translate this knowledge into novel selective and effective tools that could be used for the early diagnosis and prognosis of the disease as well as for prediction of response to therapy.

### Education

Institute and location	Degree	Year conferred	Field of study
University of Athens	B.Sc.	1981	Chemistry
University of Patras	Ph.D.	1987	Molecular Biology

### Research positions

- 2001-present: Research Associate Professor, Program of Chemical Carcinogenesis and Genetic Toxicology, IBMCB/NHRF
- 1994-2001: Functional Scientist, Grade A, Program of Chemical Carcinogenesis and Genetic Toxicology, IBMCB/NHRF

- 1987-1994: Postdoctoral Fellow, Program of Chemical Carcinogenesis and Genetic Toxicology, IBMCB/NHRF.

### **Team members**

- Dr Maria Gkatzamanidou, MD, PhD, 2009-present
- Dr Antonia Efstathiou, PhD, January 2016-present
- Margarita Bekyrou, 2006-present
- Christina Liakou, 2007-present
- Maria Pappa, MD, 2015-present
- Artemis Korovesi, 2014-present
- Varvara Galanaki, 2014-present
- Spyridoula Krikoni, 2014-2015

### **Collaborations**

- Prof Meletios A Dimopoulos, Department of Clinical Therapeutics, National and Kapodistrian University of Athens Medical School, Athens, Greece
- Prof Petros P Sfrikakis, Joint Rheumatology Program & First Department of Propedeutic Internal Medicine, National and Kapodistrian University of Athens Medical School, Athens, Greece
- Prof Vassilis Gorgoulis, Molecular Carcinogenesis Group, Department of Histology and Embryology, National and Kapodistrian University of Athens Medical School, Athens, Greece
- Prof Evangelos Terpos, Department of Clinical Therapeutics, National and Kapodistrian University of Athens Medical School, Athens, Greece
- Dr. Maria Gkatzamanidou, Department of Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA
- Dr Maria Fousteri, Biomedical Sciences Research Center (BSRC) "Alexander Fleming", Vari, Athens, Greece
- Prof. Munshi NC, Jerome Lipper Multiple Myeloma Center, Department of Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA
- Prof. Shammas MA, Department of Medical Oncology, Harvard (Dana Farber) Cancer Institute, VA Boston Health Care System, Boston, MA, USA
- Prof. San Miguel JF, Clinica Universidad de Navarra, Centro de Investigación Médica Aplicada (CIMA), Avenida Pio XII 55, Pamplona, Spain
- Prof. Einsele H, Division of Hematology, Department of Internal Medicine II, University Hospital of Würzburg, Würzburg, Germany

- Prof Mullenders LHF, Department of Toxicogenetics, Leiden University Medical Center, Leiden University, Leiden, the Netherlands
- Dr. Ocio EM, University of Salamanca, University Hospital & Cancer Research Center, Department of Hematology, Salamanca, Spain
- Dr Anderson LM, Laboratory of Comparative Carcinogenesis, National Cancer Institute (NCI), Frederick Cancer Research and Development Center, Ft Frederick, USA
- Prof Christina Bamia, Department of Hygiene, Epidemiology and Medical Statistics, School of Medicine, University of Athens, Athens, Greece
- Dr Konstantinos Vougas, Biomedical Research Foundation, Academy of Athens, Athens, Greece.

### Research Records

- Publications in international peer review journals: **53**
- Citations: **1074**
- Total Impact Factor: **267.6**
- h-Index: **18**
- Publications in proceedings of Greek and international conferences: **92**

### Publications in international peer review journals

1. **Souliotis VL**, Sfrikakis PP. Increased DNA double-strand breaks and enhanced apoptosis in patients with lupus nephritis. *Lupus* 2015;24:804-815.
2. Stefanou DT, Bamias A, Episkopou H, Kyrtopoulos SA, Likka M, Kalampokas T, Photiou S, Gavalas N, Sfrikakis PP, Dimopoulos MA, **Souliotis VL**. Aberrant DNA damage response pathways may predict the outcome of platinum chemotherapy in ovarian cancer. *PLoS One* 2015;10:e0117654.
3. Gkatzamanidou M, Terpos E, Bamia C, Kyrtopoulos SA, Sfrikakis PP, Dimopoulos MA, **Souliotis VL**. Progressive changes in chromatin structure and DNA damage response signals in bone marrow and peripheral blood during myelomagenesis. *Leukemia* 2014;28:1113-1121.
4. Gkatzamanidou M, Sfrikakis PP, Kyrtopoulos SA, Bamia C, Dimopoulos MA, **Souliotis VL**. Chromatin structure, transcriptional activity and DNA repair efficiency affect the outcome of chemotherapy in multiple myeloma. *Br J Cancer* 2014;111:1293-1304.
5. Stellas D, **Souliotis VL**, Bekyrou M, Smirlis D, Kirsch-Volders M, Degraffi F, Cundari E, Kyrtopoulos SA. Benzo[a]pyrene-induced cell cycle arrest in HepG2 cells is associated with delayed induction of mitotic instability. *Mutat Res* 2014;769:59-68.

6. Westberg EA, Singh R, Hedebrant U, Koukouves G, **Souliotis VL**, Farmer PB, Segerbäck D, Kyrtopoulos S, Törnqvist MA. Adduct levels from benzo[a]pyrenediol epoxide: Relative formation to histidine in serum albumin and to deoxyguanosine in DNA in vitro and in vivo in mice measured by LC/MS-MS methods. *Toxicol Lett* 2014;232:28-36.
7. Gkatzamanidou M, Christoulas D, **Souliotis VL**, Papatheodorou A, Dimopoulos MA, Terpos E. Angiogenic cytokines profile in smoldering multiple myeloma: no difference compared to MGUS but altered compared to symptomatic myeloma. *Med Sci Monit* 2013;19:1188-1194.
8. Stefanou DT, Episkopou H, Kyrtopoulos SA, Bamias A, Gkatzamanidou M, Bamia C, Liakou C, Bekyrou M, Sfikakis PP, Dimopoulos MA, **Souliotis VL**. Development and validation of a PCR-based assay for the selection of patients more likely to benefit from therapeutic treatment with alkylating drugs. *Br J Clin Pharmacol* 2012;74:842-853.
9. Episkopou H, Kyrtopoulos SA, Sfikakis PP, Dimopoulos MA, **Souliotis VL**. The repair of melphalan-induced DNA adducts in the transcribed strand of active genes is subject to a strong polarity effect. *Mutat Res* 2011;714:78-87.
10. Episkopou H, Kyrtopoulos SA, Sfikakis PP, Fousteri M, Dimopoulos MA, Mullenders LH, **Souliotis VL**. Association between transcriptional activity, local chromatin structure, and the efficiencies of both subpathways of nucleotide excision repair of melphalan adducts. *Cancer Res* 2009;69:4424-4433.
11. Dimopoulos MA, **Souliotis VL**, Anagnostopoulos A, Bamia C, Pouli A, Baltadakis I, Terpos E, Kyrtopoulos SA, Sfikakis PP. Melphalan-induced DNA damage in vitro as a predictor for clinical outcome in multiple myeloma. *Haematologica* 2007;92:1505-1512.
12. Sfikakis PP, **Souliotis VL**, Fragiadaki KG, Moutsopoulos HM, Boletis JN, Theofilopoulos AN. Increased expression of the FoxP3 functional marker of regulatory T cells following B cell depletion with rituximab in patients with lupus nephritis. *Clin Immunol* 2007;123:66-73.
13. **Souliotis VL**, Dimopoulos MA, Episkopou HG, Kyrtopoulos SA, Sfikakis PP. Preferential in vivo DNA repair of melphalan-induced damage in human genes is greatly affected by the local chromatin structure. *DNA Repair (Amst)* 2006;5:972-985.
14. Singh R, Gaskell M, Le Pla RC, Kaur B, Azim-Araghi A, Roach J, Koukouves G, **Souliotis VL**, Kyrtopoulos SA, Farmer PB. Detection and quantitation of benzo[a]pyrene-derived DNA adducts in mouse liver by liquid chromatography-tandem mass spectrometry: comparison with <sup>32</sup>P-postlabeling. *Chem Res Toxicol* 2006;19:868-878.

15. Dimopoulos MA, **Souliotis VL**, Anagnostopoulos A, Papadimitriou C, Sfikakis PP. Extent of damage and repair in the p53 tumor-suppressor gene after treatment of myeloma patients with high-dose melphalan and autologous blood stem-cell transplantation is individualized and may predict clinical outcome. *J Clin Oncol* 2005;23:4381-4389.
16. **Souliotis VL**, Sfikakis PP, Anderson LM, Kyrtopoulos SA. Intra- and intercellular variations in the repair efficiency of O6-methylguanine, and their contribution to kinetic complexity. *Mutat Res* 2004;568:155-170.
17. **Souliotis VL**, Dimopoulos MA, Sfikakis PP. Gene-specific formation and repair of DNA monoadducts and interstrand cross-links after therapeutic exposure to nitrogen mustards. *Clin Cancer Res* 2003;9:4465-4474.
18. Katsiari CG, Liossis SN, **Souliotis VL**, Dimopoulos AM, Manoussakis MN, Sfikakis PP. Aberrant expression of the costimulatory molecule CD40 ligand on monocytes from patients with systemic lupus erythematosus. *Clin Immunol* 2002;103:54-62.
19. **Souliotis VL**, Henneman JR, Reed CD, Chhabra SK, Diwan BA, Anderson LM, Kyrtopoulos SA. DNA adducts and liver DNA replication in rats during chronic exposure to N-nitrosodimethylamine (NDMA) and their relationships to the dose-dependence of NDMA hepatocarcinogenesis. *Mutat Res* 2002;500:75-87.
20. Chhabra SK, Anderson LM, Perella C, Desai D, Amin S, Kyrtopoulos SA, **Souliotis VL**. Coexposure to ethanol with N-nitrosodimethylamine or 4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone during lactation of rats: marked increase in O(6)-methylguanine-DNA adducts in maternal mammary gland and in suckling lung and kidney. *Toxicol Appl Pharmacol* 2000;169:191-200.
21. **Souliotis VL**, van Delft JH, Steenwinkel MJ, Baan RA, Kyrtopoulos SA. DNA adducts, mutant frequencies and mutation spectra in lambda lacZ transgenic mice treated with N-nitrosodimethylamine. *Carcinogenesis* 1998;19:731-739.
22. Sfikakis PP, Dimopoulos MA, **Souliotis VL**, Charalambopoulos D, Mavrikakis M, Panayiotidis P. Effects of 2-chlorodeoxyadenosine and gold sodium thiomalate on human bcl-2 gene expression. *Immunopharmacol Immunotoxicol* 1998;20:63-77.
23. Saunders MP, Salisbury AJ, O'Byrne KJ, **Souliotis VL**, Varcoe SM, Talbot DC, Kyrtopoulos SA, Harris AL. A phase II study evaluating the effect of tamoxifen on DNA repair in melanoma patients treated with dacarbazine. *Anticancer Res* 1997;17:4677-4680.
24. Kyrtopoulos SA, Anderson LM, Chhabra SK, **Souliotis VL**, Pletsa V, Valavanis C, Georgiadis P. DNA adducts and the mechanism of carcinogenesis and cytotoxicity of methylating agents of environmental and clinical significance. *Cancer Detect Prev* 1997;21:391-405.
25. Sfikakis PP, **Souliotis VL**, Akbar AN, Katsilambros N, Hoffbrand VA, Panayiotidis P. Regulation of bcl-2 and fas expression in primary activation of human peripheral

- lymphocytes is not sensitive to dexamethasone or cyclosporin-A. *Hum Immunol* 1996;50:121-126.
26. Kyrtopoulos SA, **Souliotis VL**, Chhabra SK, Anderson LM. DNA damage studies related to the assessment of the role of N-nitroso compounds in human cancer. *Eur J Cancer Prev* 1996;5:109-114.
  27. Farmer PB, Sepai O, Lawrence R, Autrup H, Sabro Nielsen P, Vestergård AB, Waters R, Leuratti C, Jones NJ, Stone J, Baan RA, van Delft JH, Steenwinkel MJ, Kyrtopoulos SA, **Souliotis VL**, et al. Biomonitoring human exposure to environmental carcinogenic chemicals. *Mutagenesis* 1996;11:363-381.
  28. Chhabra SK, **Souliotis VL**, Kyrtopoulos SA, Anderson LM. Nitrosamines, alcohol, and gastrointestinal tract cancer: recent epidemiology and experimentation. *In Vivo* 1996;10:265-284.
  29. **Souliotis VL**, Valavanis C, Boussiotis VA, Pangalis GA, Kyrtopoulos SA. Comparative study of the formation and repair of O6-methylguanine in humans and rodents treated with dacarbazine. *Carcinogenesis* 1996;17:725-732.
  30. Sfikakis PP, **Souliotis VL**, Katsilambros N, Markakis K, Vaiopoulos G, Tsokos GC, Panayiotidis P. Downregulation of interleukin-2 and alpha-chain interleukin-2 receptor biosynthesis by cisplatin in human peripheral lymphocytes. *Clin Immunol Immunopathol* 1996;79:43-49.
  31. Anderson LM, **Souliotis VL**, Chhabra SK, Moskal TJ, Harbaugh SD, Kyrtopoulos SA. N-nitrosodimethylamine-derived O(6)-methylguanine in DNA of monkey gastrointestinal and urogenital organs and enhancement by ethanol. *Int J Cancer* 1996;66:130-134.
  32. Philip PA, **Souliotis VL**, Harris AL, Salisbury A, Tates AD, Mitchell K, van Delft JH, Ganesan TS, Kyrtopoulos SA. Methyl DNA adducts, DNA repair, and hypoxanthine-guanine phosphoribosyl transferase mutations in peripheral white blood cells from patients with malignant melanoma treated with dacarbazine and hydroxyurea. *Clin Cancer Res* 1996;2:303-310.
  33. Bianchini F, Weiderpass E, Kyrtopoulos S, **Souliotis VL**, Henry-Amar M, Wild CP, Boffetta P. Detection of DNA methylation adducts in Hodgkin's disease patients treated with procarbazine. *Biomarkers* 1996;1:226-231.
  34. van Delft JH, Luiten-Schuite A, **Souliotis VL**, Kyrtopoulos SA, Ouwerkerk J, Keizer HJ, Baan RA. N7-Methylguanine and O(6)-methylguanine levels in DNA of white blood cells from cancer patients treated with dacarbazine. *Biomarkers* 1996;1:94-98.
  35. Chhabra SK, **Souliotis VL**, Harbaugh JW, Krasnow SW, Jones AB, Anderson LM, Kyrtopoulos SA. O6-methylguanine DNA adduct formation and modulation by ethanol in placenta and fetal tissues after exposure of pregnant patas monkeys to N-nitrosodimethylamine. *Cancer Res* 1995;55:6017-6020.

36. **Souliotis VL**, Chhabra S, Anderson LM, Kyrtopoulos SA. Dosimetry of O6-methylguanine in rat DNA after low-dose, chronic exposure to N-nitrosodimethylamine (NDMA). Implications for the mechanism of NDMA hepatocarcinogenesis. *Carcinogenesis* 1995;16:2381-2387.
37. Anderson LM, Chhabra SK, Nerurkar PV, **Souliotis VL**, Kyrtopoulos SA. Alcohol-related cancer risk: a toxicokinetic hypothesis. *Alcohol* 1995;12:97-104.
38. Pletsas V, Troungos C, **Souliotis VL**, Kyrtopoulos SA. Comparative study of mutagenesis by O6-methylguanine in the human Ha-ras oncogene in E. coli and in vitro. *Nucleic Acids Res* 1994;22:3846-3853.
39. **Souliotis VL**, Valavanis C, Boussiotis VA, Pangalis GA, Kyrtopoulos SA. Comparative dosimetry of O6-methylguanine in humans and rodents treated with procarbazine. *Carcinogenesis* 1994;15:1675-1680.
40. Valavanis C, **Souliotis VL**, Kyrtopoulos SA. Differential effects of procarbazine and methylnitrosourea on the accumulation of O6-methylguanine and the depletion and recovery of O6-alkylguanine-DNA alkyltransferase in rat tissues. *Carcinogenesis* 1994;15:1681-1688.
41. Theocharis SE, **Souliotis VL**, Panayiotidis PG. Suppression of interleukin-1 beta and tumour necrosis factor-alpha biosynthesis by cadmium in in vitro activated human peripheral blood mononuclear cells. *Arch Toxicol* 1994;69:132-136.
42. Kyrtopoulos SA, **Souliotis VL**, Valavanis C, Boussiotis VA, Pangalis GA. Accumulation of O6-methylguanine in human DNA after therapeutic exposure to methylating agents and its relationship with biological effects. *Environ Health Perspect* 1993;99:143-147.
43. Sfrikakis PP, **Souliotis VL**, Panayiotidis PP. Suppression of interleukin-2 and interleukin-2 receptor biosynthesis by gold compounds in in vitro activated human peripheral blood mononuclear cells. *Arthritis Rheum* 1993;36:208-212.
44. **Souliotis VL**, Zongza V, Nikolopoulou V, Dimitriadis GJ. Measurement of O6-methylguanine-type adducts in DNA and O6-alkylguanine-DNA-alkyltransferase repair activity in normal and neoplastic human tissues. *Comp Biochem Physiol B* 1992;101:269-275.
45. **Souliotis VL**, Boussiotis VA, Pangalis GA, Kyrtopoulos SA. In vivo formation and repair of O6-methylguanine in human leukocyte DNA after intravenous exposure to dacarbazine. *Carcinogenesis* 1991;12:285-288.
46. **Souliotis VL**, Patrino-Georgoula M, Zongza V, Dimitriadis GJ. The urea-soluble low molecular weight cuticle proteins from the different developmental stages of *Dacus oleae*. *Cell Differ Dev* 1990;31:23-29.
47. **Souliotis VL**, Kaila S, Boussiotis VA, Pangalis GA, Kyrtopoulos SA. Accumulation of O6-methylguanine in human blood leukocyte DNA during exposure to procarbazine and its relationships with dose and repair. *Cancer Res* 1990;50:2759-2764.

48. **Souliotis VL**, Kyrtopoulos SA. A novel, sensitive assay for O6-methyl- and O6-ethylguanine in DNA, based on repair by the enzyme O6-alkylguanine-DNA-alkyltransferase in competition with an oligonucleotide containing O6-methylguanine. *Cancer Res* 1989;49:6997-7001.
49. **Souliotis VL**, Giannopoulos A, Koufakis I, Kaila S, Dimopoulos C, Kyrtopoulos SA. Development and validation of a new assay for O6-alkylguanine-DNA-alkyltransferase based on the use of an oligonucleotide substrate, and its application to the measurement of DNA repair activity in extracts of biopsy samples of human urinary bladder mucosa. *Carcinogenesis* 1989;10:1203-1208.
50. **Souliotis VL**, Dimitriadis GJ. Identification and molecular analysis of the cuticle protein genes of *Dacus oleae*. *Insect Biochem* 1989;19:499-507.
51. **Souliotis VL**, Patrino-Georgoula M, Zongza V, Dimitriadis GJ. Cuticle proteins during the development of *Dacus oleae*. *Insect Biochem* 1988;18:485-492.
52. **Souliotis VL**, Patrino-Georgoula M, Zongza V, Dimitriadis GJ. Isolation and characterization of mRNAs coding for the third instar larvae cuticle proteins of *Dacus oleae*. *Insect Biochem* 1988;18:829-837.
53. Patrino-Georgoula M, **Souliotis VL**, Dimitriadis GJ. A study on the developmental appearance of serum proteins and its mRNA in the insect *Dacus oleae*. *Comp Biochem Physiol B* 1987;87:179-188.

#### **Submitted for publication**

1. **Souliotis VL**, Gorgoulis VG, Vougas K, Sfrikakis PP. Defective DNA repair and chromatin organization in patients with quiescent systemic lupus erythematosus, submitted for publication.
2. Gkatzamanidou M, Terpos E, Bamia C, Munshi NC, Dimopoulos MA, **Souliotis VL**. DNA repair of bone marrow plasma cells correlates with clinical outcome of myeloma therapy. The effect of the DNA repair inhibitor SCR7, submitted for publication.

#### **Manuscript in preparation**

1. Gkatzamanidou M, Terpos E, Bamia C, Dimopoulos MA, **Souliotis VL**. Changes in chromatin structure and key-molecules of the DNA damage response pathways affect the outcome of anti-myeloma therapy, manuscript in preparation.

#### **Chapters in collective volumes**



1. **Souliotis VL**, Kyrtopoulos SA. Dose-response relationships and potential thresholds in the induction of mutagenesis and the influence of DNA repair and cell cycle progression, in Dietrich C, Oesch F, Oesch-Bartlomowicz B, Waiss C (eds): Mechanisms of chemical carcinogenesis and their impact on dose-response relationships-the examples of dioxin and benzo(a) pyrene. ECNIS Reviews 2008, pp 31-42.
2. Kyrtopoulos SA, **Souliotis VL**, Ambatzi P, Pangalis G, Bousiotou V, Haritopoulos G, Davaris GI. Novel, sensitive assays for O-6-alkylguanine and its repair and their application to studies of the molecular epidemiology of this lesion in human populations, in O'Neill IK, Chen J, Bartsch H (eds): Relevance to human cancer of N-nitroso compounds, tobacco smoke and mycotoxins. IARC Scientific Publications 1991.