

BIOGRAPHICAL SKETCH

NAME George VASSILOPOULOS Personal Info Email gvasilop@uth.gr Tel +30 241350 1034 FAX +30 241350 1625	POSITION TITLE - Professor, Hematology – Internal Medicine, U. of Thessaly Medical School - Head, Division of Hematology, Larisa University Hospital - Affiliate Investigator, BRFAA, Division of Genetics and Gene Therapy Current Address Larisa University Hospital Division of Hematology, Biopolis, Larisa 41110
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EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	MM/YY	FIELD OF STUDY
University of Athens, Greece	MD	01/83	Medicine
Royal Postgraduate Medical School, University of London	MSc (Diploma)	09/88	Hematology
University of Athens, Greece	PhD	05/95	Medical Genetics

1. PROFESSIONAL AND ACADEMIC POSITIONS

1986-1988	Research Fellow, Hematology Lab, Karolinska Hospital, Sweden.
1989-1995	Residency and PhD candidate; Laikon University Hospital, Athens Greece.
1995-1998	Fogarty Fellow, Division of Medical Genetics, U. of Washington, Seattle WA.
1998-2000	Clinical Research Fellow, FHCRC, Seattle WA, USA.
2000-2005	Acting Instructor, Division of Hematology, U. of Washington, Seattle, WA.
2005-	Affiliate Investigator, Division of Genetics and Gene Therapy, BRFAA, Athens, GR
2006-	Assistant Professor, Internal Medicine & Hematology, U. of Thessaly, Larisa, GR
2012-	Associate Professor, Internal Medicine & Hematology, U. of Thessaly, Larisa, GR
2013-	Head, Division of Hematology, Larisa University Hospital
2015-	Head, Division of Oncology, Larisa University Hospital
2016	Professor, Internal Medicine & Hematology, U. of Thessaly, Larisa, GR

2. PROFESSIONAL SOCIETIES

1992-	Member, Hellenic Society of Hematology
2018-20	President, Hellenic Soc. of Gene Therapy and Regenerative Medicine
2010-14	Board Member, Hellenic Society of Hematology
2010-12	Educational Committee Board Member, Hellenic Society of Hematology
1995-	Member, American Society of Hematology
1998-2005	Member, American Society for Gene Therapy

3. PERSONAL STATEMENT / RESEARCH INTERESTS

As a fellow in Hematology, I developed an interest for the potential of genetic interventions at the Hematopoietic stem cell (HSC) that would allow the permanent correction of genetic disorders. I studied globin gene regulation in my PhD years and later as a post-doctoral fellow in the US. My long-term goal was to develop vectors for the genetic correction of b-thalassemia. To this end, I was involved in dissecting basic HSC biology through retroviral marking and tracking of HSC in myeloablated hosts. For cell marking experiments, I focused in the development of Foamy Virus (FV) vectors for gene transfer into HSC and showed that the vectors can transduce murine and human HSC; I then used the FV technology to dissect

the mechanism of HSC plasticity i.e. the HSC potential to derive non-hematopoietic tissues. My work culminated in the description of cell-fusion as the mechanism underlying the change of fates observed in HSC development. Upon my return in Greece, I set up my lab at BRFAA with funding from European and Greek agencies. In the lab, we developed FV vectors for two genetic disorders, beta-thalassemia and chronic granulomatous disease; in addition, we developed vectors capable of delivering siRNA and vectors expressing two cDNA in a coordinated fashion from endogenous promoters. As a clinical scientist, I have focused in the dissection of tumor – initiating cells in leukemia and neuroblastoma. In leukemia, we are studying the role of the Wnt signaling pathway in the development of leukemia in the NOD/SCID model and in neuroblastoma we have focused on the role of the CD44 surface molecule using the same NOD/SCID assay. Since wnt is one of the key pathways involved in the cross talk between mesenchymal stem cells and HSC, we are exploring its role in the development of MDS, a disorder where the hematopoietic milieu has been shown to be deregulated. Another area of research involves the dissection of the role of MyD88, a common signal-transducer in the innate immunity TLR pathway, in lymphoma development; we have found a strong association between MyD88 haplotypes and risk of Hodgkin's disease while in a collaborative study, a strong association has emerged between sarcoidosis and certain MyD88 haplotypes. Currently, My lab has developed FV-based vectors for CAR-T receptor expression in preclinical B-NHL models.

4. RESEARCH SUPPORT

1. Fogarty Fellowship Award (1995 –1997).
2. K12, Institutional Clinical Scientist Career Development Award from the Fred Hutchinson Cancer Research Center (FHCRC), Oncology Division, Seattle WA, USA (1998-2000).
3. K08, Mentored Career Development Award from the National Institute for Digestive and Kidney Diseases (NIDDK), National Institute of Health, USA (2000-2005).
4. Pilot and Feasibility Grant from FHCRC: Development of Foamy Virus Vectors for the Genetic Treatment of Immunodeficiencies (2003-4).
5. EPAN Grant from the Greek General Secretariat of Research & Technology (GENTHERNET) as a PI for the Development of a Gene Therapy Network in Greece (2005-2008).
6. Integrated Project Grant from EU (CONCERT, LSHB-CT-2004-005242) as a PI for the development of Gene Therapy based approached for genetic disorders (2005-2008).
7. Marie Curie International Reintegration Grant (EU); Development of FV vectors for CGD (2006-2007).
8. PENED Grant from the Greek General Secretariat of Research & Technology; Development of FV vectors for applications of RNAi in thalassemia (2007-2009).
9. ENTER Grant from the Greek General Secretariat of Research & Technology for the isolation of cancer stem cells in neuroblastoma (2006-2007).
10. SINERGASIA. Grant from the Greek General Secretariat of Research & Technology (2012-2015)

5. CLINICAL STUDIES (Completed GCP training, Nov 22, 2015)

1. AMBIGUARD, Phase III (GILEAD)
2. REVIEU Observational study in romiplostim treatment for ITP (GSK/NOVARTIS)
3. FN RISK10 Observational study for febrile neutropenia risk in NHL (AMGEN)
4. ASSIST FL Phase III, GP 13-301 (SANDOZ)
5. ENEST STOP, CAMN107A2408 (NOVARTIS)
6. ERASER (NOVARTIS)
7. ASPIRE (ASTELLAS)
8. MM4047 (CELGENE)
9. CC 5013 MDS Q10 (CELGENE)
10. CTP10 (CELLTRION)
11. ESCAPE (NOVARTIS)
12. TRC112121 (GSK/NOVARTIS)
13. LEOS (TEVA)
14. LEGEND (GENESIS)

6. ADVISORY BOARDS

Ad hoc for Bristol-Myers Squibb

Ad hoc for AMGEN
 Ad hoc for NOVARTIS
 Ad hoc for GILEAD
 Ad hoc for GENESIS Pharma
 Ad hoc for JANSSEN and JANSSEN Europe
 Ad hoc for ROCHE
 Ad hoc, Hellenic Bioethics Committee
 Permanent, Hellenic Cord Blood Bank

7. PEER-REVIEWED PUBLICATIONS

1. **Vasilopoulos G**, Porwit A, Lauren L, Reizenstein P, Cazzola P: The effect of a calf-thymus acid lysate on bone marrow cell growth in vitro. *Immunopharmacology and Immunotoxicology*, 10:523-536, 1988.
2. **Vasilopoulos G**, Sjogren AM, Reizenstein P: Cytotoxic effects on viable human leukemic cells by combinations of lymphokine activated killer cells and monoclonal antibodies. *Leukemia Research*, 13:87-91, 1989.
3. Reizenstein P, **Vasilopoulos G**: Effect of CD3 antibodies on cytotoxicity against leukemic cells resistant to activated killer cells. *Leukemia Research*, 13:501-3, 1989.
4. Loudianos G, Cao A, Pirastu M, **Vassilopoulos G**, Kollia P, Loukopoulos D: Molecular basis of the $\delta\beta$ -thalassemia *in cis* to hemoglobin Knossos variant [letter]. *Blood*, 77:2087-8, 1991
5. Konstantopoulos K, **Vassilopoulos G**, Adamides S, Alexandrakis M, Zervas J: Stomatocytosis as a presenting symptom of myelodysplasia [letter]. *Medical Oncology and Tumor Pharmacotherapy*, 9:213-4, 1992.
6. Hussein IR, Temtamy SA, el-Beshlawy A, Fearon C, Shalaby Z, **Vassilopoulos G**, Kazazian HHJr: Molecular characterization of β -thalassemia in Egyptians. *Human Mutation*, 2:48-52, 1993.
7. Aessopos A, Voskaridou E, Kavouklis E, **Vassilopoulos G**, Rombos Y, Gavriel L, Loukopoulos D: Angioid streaks in sickle-thalassemia. *American Journal of Ophthalmology*, 117:589-92, 1994.
8. Aessopos A, Stamatelos G, Skoumas V, **Vassilopoulos G**, Mantzourani M, Loukopoulos D: Pulmonary hypertension and right heart failure in patients with β -thalassemia intermedia. *Chest*, 107:50-53, 1995
9. **Vassilopoulos G**, Papassotiriou I, Voskaridou E, Stamoulakatou A, Premetis E, Kister J, Marden M, Griffon N, Poyart C, Wajcman H, Galacteros F, Loukopoulos D: Hb Arta [β 45 (CD4) Phe-->Cys]: a new unstable haemoglobin with reduced oxygen affinity in trans with β -thalassaemia. *British Journal of Haematology*, 91:595-601, 1995.
10. Skarpidi E, **Vassilopoulos G**, Stamatoyannopoulos G, Li Q: Comparison of expression of human globin genes transferred into mouse erythroleukemia cells and in transgenic mice. *Blood*, 92:3416-3421, 1998.
11. **Vassilopoulos G**, Navas P, Skarpidi E, Peterson K, Lowrey C, Papayannopoulou T, Stamatoyannopoulos G: Correct function of the locus control region may require passage through a non-erythroid cellular environment. *Blood*, 93:703-712, 1999.
12. Skarpidi E, Yang Y, **Vassilopoulos G**, Li Q, Stamatoyannopoulos G: Novel in vitro assay for the detection of pharmacologic inducers of fetal hemoglobin. *Blood*, 96:321-326, 2000.
13. **Vassilopoulos G**, Trobridge GD, Josephson NC, Russell DW. Gene transfer into murine hematopoietic stem cells with helper-free foamy virus vectors. *Blood*, 98:604-609, 2001.
14. Trobridge G, **Vassilopoulos G**, Josephson N, Russell DW. Gene transfer with foamy virus vectors. *Methods in Enzymology*, 346:628-648, 2002.
15. Josephson NC, **Vassilopoulos G**, Trobridge GD, Priestley GV, Wood BL, Papayannopoulou T, Russell DW. Transduction of human NOD/SCID-repopulating cells with both lymphoid and myeloid potential by foamy virus vectors. *Proceedings of the National Academy of Sciences USA*, 99:8295-8300, 2002
16. Trobridge GD, Josephson NC, **Vassilopoulos G**, Mac J, Russell DW. Improved Foamy Virus Vectors with Minimal Viral Sequences. *Molecular Therapy*, 6:321-328, 2002.
17. **Vassilopoulos G**, Josephson NC, Trobridge G. Development of foamy virus vectors. *Methods Mol Med*. 2003;76:545-64.
18. **Vassilopoulos G**, Pei-Rong W, Russell DW. Transplanted bone marrow regenerates liver by cell fusion. *Nature*, 422:901-904, 2003.
19. **Vassilopoulos G**, Russell DW. Cell fusion: an alternative to stem cell plasticity and its therapeutic implications. *Current Opinion in Genetics and Development*, 13:480-485, 2003
20. **Vassilopoulos G**, Rethwilm A. The usefulness of a perfect parasite. *Gene Therapy*, 15(19):1299-1301, 2008.
21. V Mollaki, T Georgiadis, A Tassidou, M Ioannou, Z Daniil, A Koutsokera, A Papanthassiou, E Zintzaras & **G Vassilopoulos**. Polymorphisms and haplotypes in *TLR9* and *MYD88* are associated with the development of Hodgkin's lymphoma: a candidate-gene association study. *Journal of Human Genetics*. 54(11):655-9
22. A Andrianaki, EK Siapati, RK Hirata, DW Russell and **G. Vassilopoulos**. Dual transgene expression by foamy virus vectors carrying an endogenous bidirectional promoter. *Gene Therapy*, 2010 Mar;17(3):380-8.

23. EK Siapati, M Papadaki, Z Kozaou, E Rouka, E Michali, I Savvidou, D Gogos, D Kyriakou, NI Anagnostopoulos and **G Vassilopoulos**. Proliferation and bone marrow engraftment of AML blasts is dependent on b-catenin signaling. *British Journal of Hematology* 2011 Jan;152(2):164-74.
24. **G. Vassilopoulos**, M. Palassopoulou, K. Zisaki, M. Befani, E. Bouronikou, N. Giannakoulas, E. Stathopoulou and P. Matsouka. Successful Control of Acute Myelofibrosis with Lenalidomide. *Case Reports in Medicine Volume 2010 (2010), Article ID 421239, doi:10.1155/2010/421239*
25. Ilenia Chatziandreou, Elena Konstantina Siapati and **George Vassilopoulos**. Genetic Correction of X-Linked Chronic Granulomatous Disease with Novel Foamy Virus Vectors. *Exp Hematol.* 2011 Jun;39(6):643-52.
26. Siapati EK, Rouka E, Kyriakou D and **Vassilopoulos G**. Neuroblastoma cells negative for CD44 possess tumor-initiating properties. *Cell Oncol (Dordr).* 2011 Jun;34(3):189-97.
27. Papadaki M, Siapati EK, **Vassilopoulos G**. A Foamy Virus Vector System for Stable and Efficient RNAi Expression in Mammalian Cells. *Hum Gene Ther.* 2011 Oct;22(10):1293-303.
28. I Morianos, EK Siapati, G Pongas and **G Vassilopoulos**. Comparative analysis of FV vectors with human α - or β -globin gene regulatory elements for the correction of β -thalassemia. *Gene Ther.* 2012 Mar;19(3):303-11.
29. Bouronikou E, Georgoulas P, Giannakoulas N, Valotassiou V, Palassopoulou M, **Vassilopoulos G**, Papadoulis N, Matsouka P. Metabolism-Related Cytokine and Hormone Levels in the Serum of Patients with Myelodysplastic Syndromes. *Acta Haematol.* 2013 Jan 31;130(1):27-33.
30. Zacharoulis D, Rountas C, Katsimpoulas M, Morianos J, Chatziandreou I, **Vassilopoulos G**. Efficient liver gene transfer with foamy virus vectors. *Med Sci Monit Basic Res.* 2013 Aug 14;19:214-20.
31. Daniil Z, Mollaki V, Malli F, Koutsokera A, Antoniou KM, Rodopoulou P, Gourgoulis K, Zintzaras E, **Vassilopoulos G**. Polymorphisms and haplotypes in MYD88 are associated with the development of sarcoidosis: a candidate-gene association study. *Mol Biol Rep.* 2013 Jul;40(7):4281-6.
32. Argentou N, **Vassilopoulos G**, Ioannou M, Germenis AE, Speletas M. Rapid detection of MYD88-L265P mutation by PCR-RFLP in B-cell lymphoproliferative disorders. *Leukemia.* 2013 Oct 18. doi: 10.1038/leu.2013.294.
33. Varela I, Karagiannidou A, Oikonomakis V, Tzetzis M, Tzanoudaki M, Siapati EK, **Vassilopoulos G**, Graphakos S, Kanavakis E, Goussetis E. Generation of human β -thalassemia induced pluripotent cell lines by reprogramming of bone marrow-derived mesenchymal stromal cells using modified mRNA. *Cell Reprogramming* 2014 Dec;16(6):447-55. doi: 10.1089/cell.2014.0050. Epub 2014 Oct 29.
34. Dumas S, Sakkas L, Panayiotidis P, Wozniak G, Vlychou M, **Vassilopoulos G**. Favorable outcome in non-Hodgkin lymphoma of the maxillary sinus treated with R-CHOP. *Arch Med Sci.* 2014 May 12;10(2):406-9. doi: 10.5114/aoms.2013.34986. Epub 2013 Apr 30.
35. Kotsianidis I, Kokkinou D, Siapati EK, Miltiades P, Lamprianidou E, **Vassilopoulos G**, Zoumpos NC, Spyridonidis A. Identification of a Chemoresistant, Oxidative State-Low, Leukemic Subpopulation in CD34+ Human Acute Myeloid Leukemia. *J Stem Cell Res Ther* 4:235. doi:10.4172/2157-7633.1000235
36. Vaiou M, Pangou E, Liakos P, Sakellari N, **Vassilopoulos G**, Dimas K, Papandreou C. Endothelin-1 (ET-1) induces resistance to bortezomib in human multiple myeloma cells via a pathway involving the ETB receptor and upregulation of proteasomal activity. *J Cancer Res Clin Oncol.* 2016 Oct;142(10):2141-58. doi: 10.1007/s00432-016-2216-2.
37. Aggelou K, Siapati EK, Gerogianni I, Daniil Z, Gourgoulis K, Ntanos I, Simantirakis E, Zintzaras E, Mollaki V, **Vassilopoulos G**. The -938C>A polymorphism in MYD88 is associated with susceptibility to tuberculosis: A pilot study. *Dis Markers.*;2016:4961086. doi: 10.1155/2016/4961086. Epub Dec 29, 2016.
38. Angelopoulou MK, Vassilakopoulos TP, Batsis I, Sakellari I, Gkirkas K, Pappa V, Giannoulia P, Apostolidis I, Apostolopoulos C, Roussou P, Panayiotidis P, Dimou M, Kyrtsionis MC, Palassopoulou M, **Vassilopoulos G** et al. Brentuximab vedotin in relapsed/refractory Hodgkin lymphoma. The Hellenic experience. *Hematol Oncol.*;36(1):174-181, 2018
39. Ampatzidou M, Papadimitriou SI, Paterakis G, Pavlidis D, Tsitsikas K, Kostopoulos IV, Papadakis V, **Vassilopoulos G**, Polychronopoulou S. ETV6/RUNX1-positive childhood acute lymphoblastic leukemia (ALL): The spectrum of clonal heterogeneity and its impact on prognosis. *Cancer Genet.*;224-225, 2018.
40. Tsirigotis P, Vassilakopoulos T, Batsis I, Bousiou Z, Gkirkas K, Sakellari I, Kaloyannidis P, Roussou P, Pangalis GA, Moschogiannis M, **Vassilopoulos G** et al. Positive impact of brentuximab vedotin on overall survival of patients with classical Hodgkin lymphoma who relapse or progress after autologous stem cell transplantation: A nationwide analysis. *Hematol Oncol.*;36(4):645-650, 2018.
41. Ampatzidou M, Paterakis G, Vasdekis V, Papadimitriou SI, Papadakis V, **Vassilopoulos G**, Polychronopoulou S. Prognostic significance of flow cytometry MRD log reduction during induction treatment of childhood ALL. *Leuk Lymphoma.* ;60(1):258-261, 2019. 10.1080/10428194.2018.1471603. Epub 2018 Jul 2. No abstract available.
42. Kamposioras K, Tsimplouli C, Verbeke C, Anthoney A, Daoukopoulou A, Papandreou CN, Sakellari N, **Vassilopoulos G** et al. Silencing of caveolin-1 in fibroblasts as opposed to epithelial tumor cells results in

- increased tumor growth rate and chemoresistance in a human pancreatic cancer model. *Int J Oncol.*;54(2):537-549, 2019.
43. Christaki EE, Politou M, Antonelou M, Athanasopoulos A, Simantirakis E, Seghatchian J, **Vasilopoulos G**. Ex vivo generation of transfusable red blood cells from various stem cell sources: A concise revisit of where we are now. *Transfus Apher Sci.*;58(1):108-112, 2019.
 44. Giannopoulos A, Rougkala N, Loupis T, Mantzourani M, Viniou NA, Variami E, Vassilakopoulos TP, Dryllis G, Kotsianidis I, Gougopoulou T, Politou M, Konstantopoulos K, **Vasilopoulos G**. Detection of CALR Mutations Using High Resolution Melting Curve Analysis (HRM-A); Application on a Large Cohort of Greek ET and MF Patients. *Mediterr J Hematol Infect Dis.* 1;11(1):2019.
 45. Kotsopoulou M, Papadaki C, Anargyrou K, Spyridonidis A, Baltadakis I, Papadaki HA, Angelopoulou M, Pappa V, Liakou K, Tzanetakou M, Moustaka M, **Vasilopoulos G**. Effectiveness and Safety of Micafungin in Managing Invasive Fungal Infections among Patients in Greece with Hematologic Disorders: The ASPIRE Study. *Infect Dis Ther.*;8(2):255-268, 2019.
 46. Diamantopoulos P, Koumbi D, Kotsianidis I, Pappa V, Symeonidis A, Galanopoulos A, Zikos P, Papadaki HA, Panayiotidis P, Dimou M, Hatzimichael E, **Vasilopoulos G**, et al. Hellenic MDS study group. The prognostic significance of chromosome 17 abnormalities in patients with myelodysplastic syndrome treated with 5-azacytidine: Results from the Hellenic 5-azacytidine registry. *Cancer Med.* 8(5):2056-2063, 2019.
 47. Richardson PG, Oriol A, Beksac M, Liberati AM, Galli M, Schjesvold F, Lindsay J, Weisel K, White D, Facon T, San Miguel J, Sunami K, O'Gorman P, Sonneveld P, Robak P, Semochkin S, Schey S, Yu X, Doerr T, Bensmaine A, Biyukov T, Peluso T, Zaki M, Anderson K, Dimopoulos M; **OPTIMISMM trial investigators**. Pomalidomide, bortezomib, and dexamethasone for patients with relapsed or refractory multiple myeloma previously treated with lenalidomide (OPTIMISMM): a randomised, open-label, phase 3 trial. *Lancet Oncol.* 2019 Jun;20(6):781-794. doi: 10.1016/S1470-2045(19)30152-4. Epub 2019 May 13.