BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
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NAME	POSITION TITLE
George K. Michalopoulos	Professor
eRA COMMONS USER NAME	
michalopoulosgk	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Athens University Medical School, Athens,	M.D.	1970	Medicine
University of Wisconsin, Madison, WS	Ph.D.	1977	Oncology
Board of Anatomic Pathology	Diploma	1977	Pathology

A. Positions and Honors. List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee.

1971-1972 Internship, Dept. of Pathology, University of Wisconsin, Madison, Wisconsin
1972-1977 Residency, Dept. of Pathology, University of Wisconsin, Madison, Wisconsin
1972-1976 Graduate Student, Oncology (McArdle Laboratories), Univ. of Wisconsin (Madison)
1977-1982 Assistant Professor, Dept. of Pathology, Duke University, Durham, NC
1983-1987 Associate Professor, Dept. of Pathology, Duke University, Durham, NC
1987-1991 Professor, Dept. of Pathology, Duke University, Durham, NC
1995-1998 Interim Dean, School of Medicine, University of Pittsburgh, Pittsburgh, PA
1991-Present Chairman, Dept. of Pathology, University of Pittsburgh, Pittsburgh, PA
Member, Duke University Academic Council (elected position), 1986-1990.
Director, FASEB Summer Research Conference on Molecular and Cellular Pathways of Liver Regeneration and Carcinogenesis, 1990, 1992, 1994, 1996.
President, Universities Associated for Research and Education in Pathology (UAREP), 1998-1999.
Member, Pathology B Study Section, 1980, 1994.
Member, Metabolic Pathology Study Section, 1985-1991.
NIH merit award 1992-2000.
Member, Chemical Pathology Study Section, 1996-2001.
Chairman of the Research Committee, Association of Pathology Chairs (1998-2004)
Member, Council for Association of Pathology Chairs, 2000-2002
Member, Gastrointestinal Cellular and Molecular Biology Study Section, 2005-Present
Member, BSC NIAAA, 2005-Present

B. Selected peer-reviewed publications (in chronological order). Do not include publications submitted or in preparation.

(Selected from a total of 225)

1. Loss of integrin linked kinase from mouse hepatocytes in vitro and in vivo results in apoptosis and hepatitis.Hepatology. 2007 Apr;45(4):1025-34. PMID: 17385211

2. Gkretsi V, Bowen WC, Yang Y, Wu C, Michalopoulos GK. Integrin-linked kinase is involved in matrix-induced hepatocyte differentiation. Biochem Biophys Res Commun. 2007 Feb 16;353(3):638-43. Epub 2006 Dec 20. PMID: 17194454

3. Tan X, Behari J, Cieply B, Michalopoulos GK, Monga SP. Conditional deletion of beta-catenin reveals its role in liver growth and regeneration. Gastroenterology. 2006 Nov;131(5):1561-72. PMID: 17101329

4. Luo JH, Ren B, Keryanov S, Tseng GC, Rao UN, Monga SP, Strom S, Demetris AJ, Nalesnik M, Yu YP, Ranganathan S, Michalopoulos GK. Transcriptomic and genomic analysis of human hepatocellular carcinomas and hepatoblastomas. Hepatology. 2006 Oct;44(4):1012-24. PMID: 17006932

5. Khan Z, Michalopoulos GK, Stolz DB. Peroxisomal localization of hypoxia-inducible factors and hypoxia-inducible factor regulatory hydroxylases in primary rat hepatocytes exposed to hypoxia-reoxygenation. Am J Pathol. 2006 Oct;169(4):1251-69. PMID: 17003483

6. Bell AW, Michalopoulos GK. Phenobarbital regulates nuclear expression of HNF-4alpha in mouse and rat hepatocytes independent of CAR and PXR. Hepatology. 2006 Jul;44(1):186-94. PMID: 16799975
7. Xia JL, Dai C, Michalopoulos GK, Liu Y. Hepatocyte growth factor attenuates liver fibrosis induced by bile duct ligation. Am J Pathol. 2006 May;168(5):1500-12. PMID: 16651617
8. Giannopoulou M, Iszkula SC, Dai C, Tan X, Yang J, Michalopoulos GK, Liu Y. Distinctive role of Stat3 and Erk-1/2 activation in mediating interferon-gamma inhibition of TGF-beta1 action. Am J Physiol Renal Physiol. 2006 May;290(5):F1234-40. PMID: 16332928
9. Tan X, Apte U, Micsenyi A, Kotsagrelos E, Luo JH, Ranganathan S, Monga DK, Bell A, Michalopoulos GK, Monga SP. Epidermal growth factor receptor: a novel target of the Wnt/beta-catenin pathway in liver. Gastroenterology. 2005 Jul;129(1):285-302. PMID: 16012954
10. Michalopoulos GK, Barua L, Bowen WC. Transdifferentiation of rat hepatocytes into biliary cells after bile duct ligation and toxic biliary injury. Hepatology. 2005 Mar;41(3):535-44. PMID: 15726663
11. Kohler C, Bell AW, Bowen WC, Monga SP, Fleig W, Michalopoulos GK. Expression of Notch-1 and its ligand Jagged-1 in rat liver during liver regeneration. Hepatology. 2004 Apr;39(4):1056-65. PMID: 15057910
12. Micsenyi A, Tan X, Sneddon T, Luo JH, Michalopoulos GK, Monga SP. Beta-catenin is temporally regulated during normal liver development. Gastroenterology. 2004 Apr;126(4):1134-46. PMID: 15057752
13. Hussain SZ, Sneddon T, Tan X, Micsenyi A, Michalopoulos GK, Monga SP. Wnt impacts growth and differentiation in ex vivo liver development. Exp Cell Res. 2004 Jan 1;292(1):157-69. PMID: 14720515
14. Michalopoulos GK, Bowen WC, Mule K, Luo J. HGF-, EGF-, and dexamethasone-induced gene expression patterns during formation of tissue in hepatic organoid cultures. Gene Expr. 2003;11(2):55-75. PMID: 12837037
15. Schoedel KE, Tyner VZ, Kim TH, Michalopoulos GK, Mars WM. HGF, MET, and matrix-related proteases in hepatocellular carcinoma, fibrolamellar variant, cirrhotic and normal liver. Mod Pathol. 2003 Jan;16(1):14-21. PMID: 12527708
16. Monga SP, Monga HK, Tan X, Mule K, Pediaditakis P, Michalopoulos GK. Beta-catenin antisense studies in embryonic liver cultures: role in proliferation, apoptosis, and lineage specification. Gastroenterology. 2003 Jan;124(1):202-16. PMID: 12512043
17. Michalopoulos GK, Bowen WC, Mule K, Lopez-Talavera JC, Mars W. Hepatocytes undergo phenotypic transformation to biliary epithelium in organoid cultures. Hepatology. 2002 Aug;36(2):278-83. PMID: 12143035
18. Monga SP, Mars WM, Pediaditakis P, Bell A, Mule K, Bowen WC, Wang X, Zarnegar R, Michalopoulos GK. Hepatocyte growth factor induces Wnt-independent nuclear translocation of beta-catenin after Met-beta-catenin dissociation in hepatocytes. Cancer Res. 2002 Apr 1;62(7):2064-71. PMID: 11929826
19. Wang X, DeFrances MC, Dai Y, Pediaditakis P, Johnson C, Bell A, Michalopoulos GK, Zarnegar R. A mechanism of cell survival: sequestration of Fas by the HGF receptor Met. Mol Cell. 2002 Feb;9(2):411-21. PMID: 11864613
20. Pediaditakis P, Monga SP, Mars WM, Michalopoulos GK. Differential mitogenic effects of single chain hepatocyte growth factor (HGF)/scatter factor and HGF/NK1 following cleavage by factor Xa. J Biol Chem. 2002 Apr 19;277(16):14109-15. Epub 2002 Feb 6. PMID: 11832492
21. Michalopoulos GK, Bowen WC, Mule K, Stolz DB. Histological organization in hepatocyte organoid cultures. Am J Pathol. 2001 Nov;159(5):1877-87. PMID: 11696448
22. Pediaditakis P, Lopez-Talavera JC, Petersen B, Monga SP, Michalopoulos GK. The processing and utilization of hepatocyte growth factor/scatter factor following partial hepatectomy in the rat. Hepatology. 2001 Oct;34(4 Pt 1):688-93. PMID: 11584364
23. Monga SP, Pediaditakis P, Mule K, Stolz DB, Michalopoulos GK. Changes in WNT/beta-catenin pathway during regulated growth in rat liver regeneration. Hepatology. 2001 May;33(5):1098-109. PMID: 11343237
24. Rao UN, Gollin SM, Beaves S, Cieply K, Nalesnik M, Michalopoulos GK. Comparative genomic hybridization of hepatocellular carcinoma: correlation with fluorescence in situ hybridization in paraffin-embedded tissue. Mol Diagn. 2001 Mar;6(1):27-37. PMID: 11257209
25. Jo M, Stolz DB, Esplen JE, Dorko K, Michalopoulos GK, Strom SC. Cross-talk between epidermal growth factor receptor and c-Met signal pathways in transformed cells. J Biol Chem. 2000 Mar 24;275(12):8806-11. PMID: 10722725

26. Kim TH, Mars WM, Stolz DB, Michalopoulos GK. Expression and activation of pro-MMP-2 and pro-MMP-9 during rat liver regeneration. Hepatology. 2000 Jan;31(1):75-82. PMID: 10613731
27. Runge DM, Runge D, Foth H, Strom SC, Michalopoulos GK. STAT 1alpha/1beta, STAT 3 and STAT 5: expression and association with c-MET and EGF-receptor in long-term cultures of human hepatocytes. Biochem Biophys Res Commun. 1999 Nov 19;265(2):376-81. PMID: 10558875
28. Stolz DB, Mars WM, Petersen BE, Kim TH, Michalopoulos GK. Growth factor signal transduction immediately after two-thirds partial hepatectomy in the rat. Cancer Res. 1999 Aug 15;59(16):3954-60. PMID: 10463591
29. Runge D, Runge DM, Daskalakis N, Lubecki KA, Bowen WC, Michalopoulos GK. Matrix-mediated changes in the expression of HNF-4alpha isoforms and in DNA-binding activity of ARP-1 in primary cultures of rat hepatocytes. Biochem Biophys Res Commun. 1999 Jun 16;259(3):651-5. PMID: 10364473
30. Runge DM, Bowen WC, Katyal S, Runge D, Suski V, Michalopoulos GK. Expression of the human hepatocyte growth factor cDNA in primary cultures of rat hepatocytes. Biochem Biophys Res Commun. 1999 Apr 2;257(1):199-205. PMID: 10092533
31. Michalopoulos GK, Bowen WC, Zajac VF, Beer-Stolz D, Watkins S, Kostrubsky V, Strom SC. Morphogenetic events in mixed cultures of rat hepatocytes and nonparenchymal cells maintained in biological matrices in the presence of hepatocyte growth factor and epidermal growth factor. Hepatology. 1999 Jan;29(1):90-100. PMID: 9862855
32. Runge D, Runge DM, Drenning SD, Bowen WC Jr, Grandis JR, Michalopoulos GK. Growth and differentiation of rat hepatocytes: changes in transcription factors HNF-3, HNF-4, STAT-3, and STAT-5. Biochem Biophys Res Commun. 1998 Sep 29;250(3):762-8. PMID: 9784420
33. Kim TH, Bowen WC, Stolz DB, Runge D, Mars WM, Michalopoulos GK. Differential expression and distribution of focal adhesion and cell adhesion molecules in rat hepatocyte differentiation. Exp Cell Res. 1998 Oct 10;244(1):93-104. PMID: 9770353
34. Shima N, Stolz DB, Miyazaki M, Gohda E, Higashio K, Michalopoulos GK. Possible involvement of p21/waf1 in the growth inhibition of HepG2 cells induced by hepatocyte growth factor. J Cell Physiol. 1998 Oct;177(1):130-6. PMID: 9731753
35. Petersen BE, Zajac VF, Michalopoulos GK. Hepatic oval cell activation in response to injury following chemically induced periportal or pericentral damage in rats. Hepatology. 1998 Apr;27(4):1030-8. PMID: 9537443
36. Stolz DB, Michalopoulos GK. Differential modulation of hepatocyte growth factor-stimulated motility by transforming growth factor beta1 on rat liver epithelial cells in vitro. J Cell Physiol. 1998 Apr;175(1):30-40. PMID: 9491778
37. Petersen BE, Goff JP, Greenberger JS, Michalopoulos GK. Hepatic oval cells express the hematopoietic stem cell marker Thy-1 in the rat. Hepatology. 1998 Feb;27(2):433-45. PMID: 9462642
38. Petersen BE, Zajac VF, Michalopoulos GK. Bile ductular damage induced by methylene dianiline inhibits oval cell activation. Am J Pathol. 1997 Oct;151(4):905-9. PMID: 9327722
39. Kim TH, Mars WM, Stolz DB, Petersen BE, Michalopoulos GK. Extracellular matrix remodeling at the early stages of liver regeneration in the rat. Hepatology. 1997 Oct;26(4):896-904. PMID: 9328311
40. Runge D, Runge DM, Bowen WC, Locker J, Michalopoulos GK. Matrix induced re-differentiation of cultured rat hepatocytes and changes of CCAAT/enhancer binding proteins. Biol Chem. 1997 Aug;378(8):873-81. PMID: 9377484
41. Michalopoulos GK, DeFrances MC. Liver regeneration. Science. 1997 Apr 4;276(5309):60-6. Review. PMID: 9082986

C. Research Support. List selected ongoing or completed (during the last three years) research projects (federal and non-federal support). Begin with the projects that are most relevant to the research proposed in this application. Briefly indicate the overall goals of the projects and your role (e.g. PI, Co-Investigator, Consultant) in the research project. Do not list award amounts or percent effort in projects.

ONGOING

R01-CA035373 Michalopoulos (PI) 7/15/83-12/31/06
NIH/NCI

HGF and Extracellular Matrix in Liver Development Regeneration and Neoplasia

HGF is a multifunctional cytokine with mitogenic, motogenic and morphogenic effects on many organs and cell types. The grant investigates the role of HGF (released through matrix remodeling and newly synthesized) in different stages of liver regeneration. There is no overlap between this grant and the proposed research.

R01-CA103958 Michalopoulos (PI) 4/1/04-3/31/09
NIH
HGF and Signaling Pathways in Hepatic Tissue Assembly

The purpose of this grant application is to explore new findings from our work as well as new models recently developed in our lab, in order to understand the mechanisms controlling assembly and formation of liver tissue. Gene array analysis of organoid cultures, composed of reassembled hepatic cellular elements, led to better understanding of the mechanisms by which dexamethasone, HGF and EGF regulate hepatic tissue assembly.

COMPLETED

U01-CA088110 Michalopoulos (PI) 08/29/00-1/31/05
NIH/NCI
Molecular Reclassification of Prostatic Cancer

This grant investigates gene expression patterns in the prostate for normal and cancerous conditions.*Please Note: Though Dr. Michalopoulos was the PI of this grant, all work was conducted in the laboratories of the associate members of the grant. The laboratory of Dr. Michalopoulos did not utilize any of the resources of this grant.* There was no overlap between this grant and the proposed research.