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A. EDUCATION AND TRAINING:

1998-03 Ph.D. PHYSIOLOGY & BIOPHYSICS, Joint program: Stony Brook University & Cold Spring Harbor Laboratory (CSHL), New York, USA
1991-95 B.Sc. CHEMISTRY, American University of Beirut, Beirut, Lebanon
2003-04 Post-doc Stony Brook University, Department of Physiology & Biophysics

B. EMPLOYMENT:

2011- **Assistant Professor of Neurosurgery & Cancer Biology**, Vanderbilt University, Nashville.
2008-10 **Assistant Professor**, Weill Medical College of Cornell University, New York.
2004-08 **Research Assistant Professor of Medicine**, Washington University in St. Louis, Missouri.
1995-98 **Research Assistant** (Lab technician), Department of Physiology, American University of Beirut.

C. ACADEMIC HONORS AND AWARDS:

2011-15 **American Cancer Society (ACS) Scholar Award ***
* the American Cancer Society (ACS) Scholar grant proposal scored '**OUTSTANDING**' and was approved for funding. Due to budget shortfall at the ACS, this award is placed in the '*pay if funds become available*' category and can be funded when/if research funds are secured.
2011-14 **Qatar Foundation**, National Priorities Research Program Award
2006-08 **American Heart Association (AHA) BGIA Award** (aka, *career development award*)
(Score: OUTSTANDING 94%)
2001-03 **US Department of Defense (DoD) Breast Cancer pre-doctoral Fellowship Award**
(Score: OUTSTANDING 96%)
2002 **International Society for Translational Research Young Investigator** (travel) Award
1998-00 **The Research Foundation**, full scholarship (Graduate), SUNY at Stony Brook
1991-95 **Hariri Foundation**, full scholarship (Undergraduate), American University of Beirut

Research work selected for reviews and commentaries in the following science media outlets:

- HIGHLIGHTS, *Nature Medicine* Vol 10:907, Sep. (2004)
- 'News and Views', *Nature Cell Biology* Vol 6:806, Sep. (2004),
- *Science* magazine Editors' Choice Issue 246, p. tw293 (2004).
- HIGHLIGHTS *Nature Reviews Mol. Cell. Biol.* 3: 889, Dec. (2002);
- HIGHLIGHTS *Nature Reviews Cancer.* 2: 892, Dec. (2002);
- Biology Reports Ltd, Faculty of 1000, (2002).

D. LANGUAGE SKILLS: Fluent in Arabic, French, and English

E. COMMUNITY INVOLVEMENT:

1993 - 95 **Chemistry Students Society, American University of Beirut (Lebanon)**

- President (Elected)

1995 - 98 **Hariri Foundation Alumni Association (HFAA)**

- Chair of the Education and Cultural Committee, Beirut chapter
- Recipient of the HFAA Leadership award

- 1995 - 98 **Syndicate of Chemists in Lebanon**
- Chair of the Public Relations Committee
- 1998 - 01 **Stony Brook University Hospital (USA)**
 Volunteer at the department of Radiation oncology; developed a mathematical model for assessing treatment efficacy of lymphedema in breast cancer patients. Model presented at the international Lymphedema conference:
- **Z A. Nahle**, A G. Meek, S A. Russo, J L. Andersen, D. Dahlgren, C. Tuppo. *Lymphedemic Arm Measurement (I): Application of a New Mathematical Model to Breast Cancer Patients (II)*. Lymphedema: Sharpening the Focus For The New Millennium (Sep.14-17, 2000) p52. The 4th National Lymphedema Network International Conference, New Orleans LA.
- 2001 - 03 **Graduate Student Organization, Stony Brook University (US)**
- Senator and Class representative (Elected)

F. MEMBERSHIP IN PROFESSIONAL ORGANIZATIONS:

- 2009- Diabetes Research Training Center (DRTC), Albert Einstein College of Medicine (elected)
- 2008- American Society of Biochemistry and Molecular biology (elected)
- 2007- American Heart Association
- AHA Council on Basic Cardiovascular Sciences
 - Interdisciplinary working group on Functional Genomics & Translational Biology
- 2003- American Association for Cancer Research AACR
- 2002- New York Academy of Science
- 1999- American Physiological Society
- 1995- American Chemical Society

G. EDITORIAL RESPONSIBILITIES:

Peer Reviewer for the following scientific journals: *Oncogene; Cell Research; Journal of Biotechnology Progress; Diabetes Obesity and Metabolism.*

H. GRANT REVIEW/STUDY SECTIONS:

Philip Morris USA external research programs review board

I. TEACHING RESPONSIBILITIES:

- Conference group leader (09/10); *Molecules, Genes and Cells (MGC)*, Weill Cornell Medical College
- Mentor: *prep for pre* program for minority students.
- Graduate teaching assistant (01/03); *Medical Physiology, Neuroscience*, SUNY at Stony Brook

J. RESEARCH PUBLICATIONS:

A. Fernandez-L, M. Squatrito, P. Northcott, E. C. Holland, M.D. Taylor², **Z. Nahlé**, A.M. Kenney. Oncogenic YAP promotes radioresistance and genomic instability in medulloblastoma through IGF2-mediated Akt activation (*submitted*)

B. Bhatia, M. Hsieh, A.M. Kenney and **Z. Nahlé***. Mitogenic Sonic hedgehog signaling activates E2F1-mediated lipogenesis in progenitor cells and medulloblastoma. *Oncogene*. Oct 4, 2010. [Epub ahead of print]
 * Corresponding author.

S R. Parathath, L Mainwaring, A Fernandez-L, C G. Guldal, **Z. Nahlé**, A M Kenney. β -Arrestin-1 links mitogenic Sonic hedgehog signaling to the cell cycle exit machinery in neural precursors. *Cell Cycle* 9, (19):4013-4024, 2010.

M. Hsieh, D. Das, M. Q. Zhang, N. Sambandam and **Z. Nahlé***. Transcriptional Regulation of the PDK4 Isozyme by the Rb/E2F1 Complex. *J Biol. Chem.* 283 (41):27410-7, 2008. * Corresponding author.

Z. Nahlé*, M. Hsieh, T. Pietka, C. C. Coburn, P. A. Grimaldi, M. Q. Zhang, D. Das, N. A. Abumrad. CD36-dependent regulation of FoxO1 and PDK4 in the PPAR δ / β -mediated adaptation to metabolic stress. *J Biol. Chem.* 283(21):14317-26, 2008. * Corresponding author.

D. Das, **Z. Nahlé** and M.Q. Zhang. Adaptively Inferring Human Transcriptional Network. *Molecular Systems Biology* E1-14, 2006.

C.C. Bastie, **Z. Nahlé**, T. McLoughlin, K. Esser, W. Zhang, T. Unterman, N. Abumrad. FoxO1 stimulates fatty acid uptake and oxidation in muscle cells through CD36-dependent and independent mechanisms. *J Biol Chem.* 8; 280(14):14222-9, 2005.

(**Z. Nahle'** *, E. Hernando*), G. Juan, M. Alaminos, E. Diaz-Rodriguez, M. Hemann, L. Michel, V. Mittal, R. Benezra, W. Gerald, S. W. Lowe, C. Cordon-Cardo. *Rb Inactivation promotes genomic Instability by Uncoupling Cell Cycle Progression from Mitotic Control.* *Nature* 430: 799-802, 2004. (*equal contribution)
Selected for HIGHLIGHTS, *Nature Medicine*. Vol 10:907, Sep. (2004); News and Views', *Nature Cell Biology*. Vol 6:806, Sep. (2004); and *Science* Editors' Choice Issue 246, p. tw293 (2004).

Z. Nahle', J. Polyakoff, R V. Davuluri, M E. McCurrach, M D. Jacobson, M. Narita, M Q. Zhang, Y. Lazebnik, D. Bar-Sagi, and S W. Lowe. *Direct coupling of the cell cycle and cell death machinery by E2F.* *Nature Cell Biology* 4: 28-33, 2002.
Selected for HIGHLIGHTS *Nature Reviews Mol. Cell. Biol.* 3: 889, Dec. (2002), HIGHLIGHTS *Nature Reviews Cancer.* 2: 892, Dec. (2002), and Biology Reports Ltd, Faculty of 1000. (2002).

G. E. Haddad, F A. Saadeh, L H. Sharaf, **Z A. Nahle'**, Abou Fares, M.F., Haddad, R.E., Bitar, K.M., Bikhazi, A.B. *Alterations in IGF-I binding on cardiac myofibers and capillary endothelium during chronic volume-overload-induced hypertrophy.* *Journal of Biochem Mol Biol Biophys* 3: 65-74, 1999.

A B. Bikhazi, R E. Haddad, **Z A. Nahle'**, and K M. Bitar. *Angiotensin II Delivery and Binding at the Microvascular Endothelium and Cardiac Myocyte Surfaces in Perfused Rat Hearts.* *Journal of Pharmaceutical Sciences* 87: 1363-1367, 1998.

Bikhazi AB, **Nahlé ZA**, El-Sabban M, Bitar K. Measurement of the binding parameters of therapeutically active peptides (e.g., insulin, insulin-like growth factor-1 [IGF-1], endothelin-1 [ET1], angiotensin-II [ATII]) and their antagonists on the endothelium of the coronary vasculature and myocytes, in perfused heart models. *Expert Opinion on Therapeutic Targets* 2(1): 65-67, 1998.

A B. Bikhazi, **Z A. Nahle'**, M E. El-Sabban, and K M. Bitar. *Peptides and Their Antagonists in The Endothelium of The Coronary Vasculature and Myocytes.* *Emerging Therapeutic Targets* 2: 65-67, 1998.

A B. Bikhazi, F A. Saadeh, R E. Haddad, **Z A. Nahle'**, M F. Abou Fares, K M. Bitar, and A E. Birbari. *Insulin receptor binding characteristics in perfused SHR and WKY rat hearts.* *Comparative Biochemistry and Physiology* 120C:127-136, 1998.

A Bikhazi, **Z. Nahle'**, S. Kreydiyyeh, R. Haddad, K. Bitar, G. Haddad, A. Abdelnoor. *Endotoxin binding on capillary endothelium and myocyte plasma membranes in perfused rat heart.* *Journal of Endotoxin Research* 4: 45-51, 1997.

R.E Haddad, A R. Jurjus, M. Ibrahim, **Z A. Nahle'**, M M. El-Kasti, K M. Bitar, S I. Kreydiyyeh, F A. Saadeh, and A B. Bikhazi. *Binding of ¹²⁵I-Insulin on Capillary Endothelial and Myofiber Cell Membranes in Normal and Streptozotocin-Induced Diabetic Perfused Rat Hearts.* *Comparative Biochemistry and Physiology* 117A:523-530, 1997.

K. EDITORIALS, REVIEWS, CHAPTERS:

- 1- Bhatia, Z. **Nahlé**, and AM Kenney. Double trouble: when Sonic hedgehog signaling meets TSC inactivation. *Cell Cycle* 9 (3):456-9, 2010. (extra view)
- 2- **Zaher Nahlé**. PPAR trilogy from metabolism to cancer. *Curr. Opin. Clin. Nutr. Metab. Care* 7:397- 402, 2004. (Review)

L. LECTURES BY INVITATION:

May 2010	<i>Mitogenic Signaling in the Control of the Lipogenic/Lipolytic Balance</i> . New York Regional Diabetes Meeting, Albert Einstein College of Medicine, New York (host: Jeff Pessin, PhD).
Nov. 2009	<i>E2F in Cardiac Metabolism and Tumor Metabolism: Work in Progress</i> . Albert Einstein Diabetes and Research Training Center (DRTC), New York (host: Meredith Hawking, MD).
Jun. 2008	<i>Tumor Metabolism</i> . Weill Medical College of Cornell University, Department of Cardiothoracic Surgery, New York.
May 2008	<i>Novel Roles for the Rb/E2F Tumor Suppressor Complex in Metabolism and Cancer</i> . Saint Louis University, Department of Biochemistry, St Louis, Missouri (host: David Ford, PhD).
Mar. 2008	<i>Beyond Apoptosis and genomic instability:A role for E2F in Cellular Metabolism</i> . Stony Brook University, Department of Physiology & Biophysics, New York (host: Peter Brink, PhD).
Oct. 2007	<i>E2Fs and cellular metabolism</i> . Signaling/Cell Cycle Series, Siteman Cancer Center, Washington University in St. Louis (host: Helen Piwnica-Worms, PhD).
Sep. 2006	<i>Transcriptional Reprogramming in the Diabetic Heart</i> . Center for Cardiovascular Studies, Washington University in St. Louis (host: Dan Ori, MD).
Apr. 2005	<i>Fatty Acid flux and the control of apoptosis</i> . Center for Human Nutrition, Washington University in St. Louis (host: Sam Klein, MD).
Aug. 2002	<i>E2F-1 Directly Regulates Caspases Coupling Cell Cycle to Cell Death</i> . Cancer Genetics & Tumor Suppressor Genes, Cold spring Harbor Laboratory, New York (host: CSHL meetings).
Oct. 2002	<i>The Cell Cycle as a Target in Chemoprevention and Cancer Therapy</i> , International Society for Translational Research, Austin, Texas (host: Pablo Conti, MD).

M. MEETING PROCEEDINGS (selected):

1. B. Bhatia, A.M. Kenney and **Z. Nahlé**. Mitogenic Sonic hedgehog signaling activates E2F1-mediated lipogenesis in progenitor cells and medulloblastoma. 2011 Pediatric Neuro-Oncology Basic and Translational Research Conference (May 19-20, **2011**), New Orleans, Louisiana
2. **Z. Nahlé**, R. Davuluri , M. McCurrach , J. Polyakoff , M. Jacobson ,M. Zhang , Y. Lazebnik , D. Bar-Sagi and S. Lowe. Direct Coupling of Cell cycle Progression and Apoptosis by E2F-1. Apoptosis and Cancer: Basic Mechanisms and Therapeutic Opportunities in the Post-Genomic Era (February 13-17, **2002**) Hawaii.
3. **Z. Nahlé**, M. McCurrach, R. Davuluri, M. Jacobson, J. Polyakoff, M. Zhang, Y. Lazebnik, D. Bar-Sagi and S. Lowe. E2F-1 Directly Regulates Caspases Coupling Cell Cycle to Cell Death. Cancer Genetics & Tumor Suppressor Genes (August 14-18, **2002**, pp.293) Cold spring Harbor Lab, NY.
4. **Z. Nahlé**. Cell Cycle and Cell Death. The Cell Cycle as a Target in Chemoprevention and Cancer Therapy (October 3-4, **2002**, pp.32) *Holiday Inn - Town Lake*, Austin, Texas.
5. **Z. Nahlé**, M. McCurrach, J. Polyakoff, R. Davuluri, M. Zhang, J. Pelletier, Y. Lazebnik, and S. Lowe. Oncogenic Induction of Caspases via an ARF-p53 Independent Pathway. Programmed Cell Death (November 9-11, **2001**) P.186, Cold Spring Harbor Laboratory, New York.
6. **Z. A. Nahlé**, A G.Meek, S A. Russo, J L. Andersen, D. Dahlgren, C. Tuppo. Lymphedemic Arm Measurement (I): Application of a New Mathematical Model to Breast Cancer Patients (II). Lymphedema: Sharpening the Focus For The New Millennium (Sep.14-17,**2000**) P52,. The 4th National Lymphedema Network International Conference, New Orleans LA.
7. J. Polyakova, **Z. Nahlé**, T. Lee, Y. Lazebnik, J. Pelletier and S. Lowe. Induction of Pro-Caspases by The E1A Oncogene. Cancer Genetics and Tumor Suppressor Genes (August 16- 20, **2000**) P147. Cold Spring Harbor Laboratory, New York.

8. G. Haddad, L. Sharaf, **Z. Nahlé**, K. Bitar, and A. Bikhazi. *IGF-I Receptor Kinetics During Regression of Cardiac Hypertrophy Following ACE-inhibitor or AT₁-antagonist Treatment*. The FASEB Journal Vol. 13(4), pp. A438, April **1999**. Experimental Biology' 99, Washington D.C.
9. G. Haddad, F. Saadeh, L. Sharaf, **Z. Nahlé**, M. Abou Fares, R. Haddad, K. Bitar, and A. Bikhazi. *Kinetics of IGF-I Binding on Cardiac Myofibers and Capillary Endothelium During Eccentric Hypertrophy*. The FASEB Journal Vol. 12 (4), pp. A709, April **1998**. Experimental Biology' 98, San Francisco, CA.
10. A. Bikhazi, **Z. Nahlé**, R. Haddad, K. Bitar. *Binding of Angiotensin II and DUP 753 on Capillary Endothelium and Myofibers in Perfused rat Hearts*. The FASEB Journal Vol. 2 (4), pp.A408, April **1998**. Experimental Biology' 98, San Francisco, CA.
11. A B. Bikhazi, **Z A. Nahlé**, M F. Abou Fares, R E. Haddad, and K M. Bitar. *Polypeptide Delivery at Myocyte-Surfaces in a Perfused Rat Heart Preparation*. Drugs Formulation and Delivery II pp.84, #84, Oct. **1997**. (presented at the American Chemical Society conference: La Jolla, CA.)
12. A. Bikhazi, **Z. Nahlé**, R. Haddad, K. Bitar. *Angiotensin II Binding on Capillary Endothelial and Myocyte Surfaces in Perfused Heart of Normal and Streptozotocin-Induced Diabetic Prefused Rats*. The FASEB Journal Vol. 11(3), pp. A498, Feb. **1997**. Experimental Biology'97, New Orleans, LA.
13. R E. Haddad, A B. Bikhazi, **Z A. Nahlé**, M. El-Kasti, and A M. Abdelnoor. *A Novel Rat Heart Perfusion Method to Assess Endotoxin Binding. Measurement of Binding and Residency Time on Capillary Endothelial and Myocyte Plasma Membrane*. Journal of Endotoxin Research Vol. 3, pp.57, **1996**. Fourth conference of the International Endotoxin Society, Nagoya, Japan.
14. R E. Haddad, A B. Bikhazi, **Z A. Nahlé**, and A M. Abdelnoor. *A Novel Rat Heart Perfusion Method to Assess Endotoxin Binding: Description of Perfusion Model (1)*. Journal of Endotoxin Research Vol. 3, pp.56, **1996**. International Endotoxin Society, Nagoya, Japan.

N. GRANT SUPPORT AND FUNDING:

PAST SUPPORT

No.	Name of Grant	Period of Award	Grant Category	Role in Grant	% Effort	Funding Source	Annual Direct Cost
1	<i>Analysis of the ARF-p53 Pathway During Oncogenic Stimulation</i>	12/01 to 05/03	Federal Grant	Principal Investigator	98%	Department of Defense (DoD)	\$33,000
2	<i>Fatty Acid Transporter: Regulation, identification</i>	03/03 to 02/08	Federal Grant	Co-Investigator	15%	National Institute of Health (NIH)	\$250,000
3	<i>Metabolic Regulation in Cell Growth and Apoptosis</i>	08/04 to 08/07	Private Foundation	Co-Investigator	85%	Philip Morris External Research Programs	\$250,000
4	<i>Potential Roles for E2F1 in the Pathogenesis of the Diabetic Heart</i>	01/07 to 12/08	Nonprofit Organization	Principal Investigator	10%	American Heart Association (AHA)	\$75,000

CURRENT SUPPORT

No.	Name of Grant	Period of Award	Grant Category	Role in Grant	% Effort	Funding Source	Annual Direct Cost
1	<i>Nicotine Signaling in Obesity-Induced Diabetic Cardiomyopathies</i>	05/11 to 04/14	Nonprofit Organization	Principal Investigator	10%	Qatar Foundation	\$290,000
2	<i>Hedgehog and Hippo signaling as drivers of medulloblastoma & cell division-associated metabolic choices</i>	10/10 to 10/13	Nonprofit Organization	Co-Investigator	10%	James S. McDonnell Foundation	\$150,000

PENDING SUPPORT

No.	Name of Grant	Period of Award	Grant Category	Role in Grant	% Effort	Funding Source	Annual Direct Cost
1	<i>Hedgehog Signaling and Rb/E2F regulation in development and cancer</i> 'Pay if' mechanism	01/11 to 12/14	Nonprofit Organization	Principal Investigator	20%	American Cancer Society (ACS)	\$200,000

Synopsis of selected grants:

Qatar National Research Foundation (QNRF)

5/2011-4/2014

Role: Lead Principal Investigator

'Nicotine Signaling in Obesity-Induced Diabetic Cardiomyopathies'

This proposal investigates new aspects of the Rb/E2F transcriptional complex as a nodal switch-like regulator coupling Nicotine sensing and signal integration -in the context of elevated fatty acid flux- to ensuing maladaptive cellular activities. Novel roles for Nicotine, the most addictive substance in cigarette smoke, in the regulation of mitochondrial bioenergetics and substrate utilization patterns are explored using *in-vivo* and *ex-vivo* methodologies. The work is a natural extension to earlier studies (supported by the AHA) where new functions for E2F1 and Rb in the regulation of PDK4, a critical nutrient sensor and an inhibitor of glucose oxidation, were identified. Potential mechanisms contributing to the adverse effects of Nicotine signaling and increased fatty acid uptake in exacerbating insulin resistance and associated metabolic inflexibilities are also explored. Collectively, these studies will advance the knowledge within the fields of cardiovascular metabolism and obesity research and will promote the understanding of key transcriptional networks and their function across numerous disciplines, including the areas of developmental and cancer biology.

James S. McDonnell Foundation (JSMF)

10/2010-9//2013

Role: Co-investigator

AM Kenney, MSKCC (PI)

'Hedgehog and Hippo signaling as drivers of medulloblastoma and cell division-associated metabolic choices'

The overall objective of this proposal is to establish the requirement for Shh-induced Hippo pathway target YAP1 in expansion of neural progenitor cells and medulloblastoma cells and to determine whether targeting the Hippo pathway or downstream metabolic pathways may represent future therapeutic approaches to medulloblastoma. Specifically, this proposal aims to use region-specific ablation of YAP1 to characterize how it contributes to the development of the central nervous system

in general and specifically that of the granule neuron precursors in the cerebellum, proposed medulloblastoma cells-of-origin. Furthermore, the proposal investigates the requirement for YAP1 in mouse models for medulloblastoma formation, using YAP1 conditional mice and also manipulation of Hippo pathway components in mouse medulloblastoma cells followed by intracranial implantation into host mice. The grant explores how YAP1 can contribute to radio-resistance of medulloblastoma tumor repopulating cells, through its effects on survival and DNA repair pathways. Finally, the proposal explores how YAP1 integrates medulloblastoma cell survival and proliferation with metabolic pathways regulating synthesis of lipids required for cell growth and division.

(pending) American Cancer Society (ACS)

Role: Principal Investigator

‘Hedgehog Signaling and Rb/E2F regulation in development and cancer’

This proposal investigates the mechanism(s) through which the Shh→Rb/E2F oncogenic axis regulates *de novo* lipid synthesis and biomass accumulation, to fuel oncogenic transformation. Emphasis is placed on elucidating critical activities coupling Hedgehog signaling to the basal metabolic machinery controlling lipid homeostasis, in particular those mediating *de novo* lipid synthesis. Unconventional ‘metabolic-based’ therapeutic modalities are also explored using *in vivo* and *ex-vivo* analyses, including relevant animal models of pediatric brain cancer. Broad insights into cell cycle regulation and cancer etiologies arising from hedgehog-dependent precursor populations will result from this work.

(Completed) American Heart Association (AHA), BGIAA

1/1/2007 - 12/31/2008

Role: Principal Investigator

“Potential Roles for E2F1 in the Pathogenesis of the Diabetic Heart”

Abstract of AHA Award: Obesity and diabetes are lethal pathological conditions if combined with cardiovascular diseases. Adults with diabetes are two to four times more likely to have heart disease or stroke compared to their non-diabetic counterparts. Concordantly, heart disease is the leading cause of death from diabetes-related illnesses. In this application, we focus on studying the molecular basis of this significant and urgent health problem. Specifically, we investigate two aspects directly relevant to diabetic cardiomyopathy: i) the regulation of myocardial metabolic shifts and substrate utilization patterns in the diabetic heart, and ii) the reprogramming of the apoptotic network in the diabetic myocardium. Throughout, our experimental design comprises both mechanistic investigations paralleled with therapeutic modalities and interventions *in vivo*. Nevertheless, deregulated expression in the diabetic myocardium of a gene like E2F1 with established role in promoting apoptosis, inducing aneuploidy, deregulating the cell cycle, and influencing metabolic activities is, we propose, at the heart of the genetic reprogramming of the diabetic myocardium.

(Completed) Department of Defense (DoD)/Breast Cancer Program

12/1/2001 - 1/30/2003

Role: Principal Investigator

This is a pre-doctoral fellowship. Laboratory of Scott W. Lowe, Cold Spring Harbor Lab. New York

“Analysis of the ARF-p53 Pathway During Oncogenic Stimulation”

The purpose of this project was to identify new targets involved in the process of oncogene-induced apoptosis. The research was centered on microarray studies using the adenovirus E1A oncoprotein. For this project, we have locally manufactured, tested and successfully used spotted cDNA microarray chips to analyze gene expression profiles of E1A induced primary mouse fibroblasts, either wild-type or deficient for the ARF and/or p53 genes. A myriad of targets involved in many cellular functions such as apoptosis, cell cycle progression, checkpoint control, DNA replication, angiogenesis, biosynthesis, as well as structural and cytoskeletal elements were found to be regulated by oncogenic stimulation. This revealed the pleiotropic role of E1A and generated a databank of potential apoptotic targets that can be studied and characterized. Following up on some targets, we demonstrated that E1A can coordinately up-regulate caspase expression through E2F via a direct transcriptional mechanism. This work illustrates how programmed cell death can be ‘hardwired’ to cell-cycle progression as part of a fail-safe mechanism. Studies also shed lights on the manner in which the oncogene-induced apoptosis network and proceeds through a highly coordinated series of events and how p53-generated signals (e.g., cytochrome C release from mitochondria) can cooperate with p53-independent apoptotic activities in executing efficient cell death.