BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Issam A. Awad	Professor of Surgery (Neurosurgery) Division of Biological Sciences and the Pritzker School of Medicine, University of Chicago
eRA COMMONS USER NAME (credential, e.g., agency login) ISSAMAWAD	

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
Loma Linda University, Loma Linda, CA	BA, MSc	1976, 1979	Biochemistry
Loma Linda University, Loma Linda, CA	MD	1980	Medicine
The Cleveland Clinic, Cleveland, OH	Residency	1986	Neurosurgery

A. Personal Statement

The proposed corresponding co-PI for this project has led major contributions in the study of cerebral cavernous malformations (CCMs) for nearly two decades. Dr. Awad and collaborators performed the early studies on lesion prevalence and clinical natural history, patholologic heterogeneity and mixed lesions, and the genetics of familial cases. His laboratory has characterized the cardinal features of human CCM lesion phenotype, including studies on angiogenesis and proliferative activity, ultrastructure, differential gene expression, genotype-phenotype correlations, and somatic mutations. More recent work has focused on the defined antigen mediated immune response associated with CCM lesions, and advanced imaging applications. Along with co-PI Marchuk at Duke, he has published the only studies of high field MRI screening of mutant mice *in vivo*, detecting CCM lesions that can be targeted therapeutically. In collaboration with co-PI Ginsberg, he has characterized markers of RhoA-kinase activity in the heterozygous state in human and murine CCM lesions. Dr Awad's clinical practice has focused on treatment advances in CCM disease, he edited the first textbook dedicated to CCM, and since 2002 he has been the Chairman of the Scientific Advisory Board of the Angioma Alliance (www.angioma.org), the organization advocating for research and advancing the clinical care of CCM patients.

B. Positions and honors.

Professional Experience

1985-1986 Neurovascular Fellow, Barrow Neurological Institute, Phoenix, AZ
1986-1987 Physician Specialist and Clinical Assistant Professor of Surgery (Neurosurgery), Stanford University School of Medicine, Stanford, CA
1986-1987 Associate Chief of Neurosurgery, Santa Clara Valley Medical Center, San Jose, CA
1987-1993 Attending Staff, Cleveland Clinic Foundation, Cleveland, OH
1988-1992 Head, Section of Epilepsy Surgery, Cleveland Clinic Foundation, Cleveland, OH
1992-1993 Head, Section of Cerebrovascular Surgery, Cleveland Clinic Foundation, Cleveland, OH
1992-1993 Vice-Chairman, Department of Neurological Surgery, Cleveland Clinic Foundation, Cleveland, OH
1993-1994 Associate Professor of Surgery, Yale University School of Medicine, New Haven, CT
1994-2001 Professor of Neurosurgery, Yale University School of Medicine, New Haven, CT
1997-2001 The Nixdorff-German Professor of Neurosurgery, Yale University School of Medicine, New Haven, CT
1993-2000 Head, Neurovascular Surgery Program, Yale University School of Medicine, New Haven, CT
1993-2000 Director, Neurovascular-Neuroscience ICU, Yale University School of Medicine, New Haven, CT
1993-2000 Co-Director, Yale Cerebrovascular Center, New Haven, CT
2001-2003 The Ogsbury-Kindt Chair in Neurosurgery, Professor with tenure of Neurosurgery, Neurology and Pathology, University of Colorado School of Medicine, Denver, CO
2003-2009 Professor of Neurological Surgery (with tenure), Vice-chairman for Research and Program Development; Northwestern University Feinberg School of Medicine, Chicago, IL

2003-2009 Director of Neurovascular Surgery, Neurocritical Care, Stereotactic Radiosurgery, and Surgical Neurosciences Research, NorthShore University HealthSystem (formerly Evanston Northwestern Healthcare), Evanston, IL

2009-present Adjunct Professor of Biomedical Engineering, McCormick School of Engineering, Northwestern University, Evanston, IL

2010-present Professor of Surgery in the Clinician Scholar Track, Division of Biological Sciences, and Director of Neurovascular Surgery, Section of Neurosurgery, The Pritzker School of Medicine, University of Chicago, Chicago, IL

Selected Honors

1979 Student Investigator of the Year Award, Loma Linda University
1980 Donald E. Griggs Award for Meritorious Scholarship, Loma Linda University
1985 Crile Traveling Fellowship, The Cleveland Clinic Foundation
1988 The Pudenz Award for Excellence in Hydrocephalus Research
1989 The Oldendorf Award for Outstanding Contribution to Neuro-imaging
1995 The Rasmussen Lecturer, Montreal Neurologic Institute
1995 Honorary Master of Arts (Privatim), Yale University
1997-2000 The Nixdorff-German Endowed Professorship in Neurosurgery, Yale University
1998 Invited Nominator, the Nobel Committee for Physiology and Medicine, Stockholm, Sweden
1999 The 4th Tindall Distinguished Professor, Emory University
1999 Honored Neuroscience Alumnus, The Cleveland Clinic Foundation
1999 Invited Nominator, the Nobel Committee for Physiology and Medicine, Stockholm, Sweden
2001 Invited Nominator, the Nobel Committee for Physiology and Medicine, Stockholm, Sweden
2001-2003 The Ogsbury Kindt Endowed Chair in Neurosurgery, University of Colorado
2000-2001 Chairman, Joint Section on Cerebrovascular Surgery of the American Association of Neurological Surgeons and the Congress of Neurological Surgeons
2000-2001 President, Congress of Neurological Surgeons
2002, 2003 2000 Outstanding Intellectuals of the 21st Century (Second and Third Editions)
2005-2007 Academic Excellence Award - Highest Academic Achievement in the Department of Surgery, Evanston Northwestern Healthcare, Evanston, IL (3 consecutive years)
2008 Co-Chairman, NIH/NINDS Workshop on "*Biology of Vascular Malformations of the Brain*"
1996-2010 Best Doctors in America

B. Selected peer-reviewed publications. (Selected from 240 papers and chapters, and 11 books)

1. Gunel M, Awad IA, Finberg K, Anson JA, Steinberg GK, Batjer HH, Kopitnik TA, Morrison L, Giannotta SL, Nelson-Williams C, Lifton RP: A founder mutation as a cause of cerebral cavernous malformation in Hispanic Americans.The New Eng J Med, 334: 946-51, 1996.
2. Rothbart D, Awad IA, Kim J, Lee J, Criscuolo G: Expression of angiogenic growth factors and structural matrix proteins in central nervous system vascular malformations. Neurosurgery 38: 915-925, 1996.
3. Skirgaudas M, Awad IA, Kim J, Criscuolo G: Expression of angiogenesis factors and selected vascular wall matrix proteins in intracranial saccular aneurysms. Neurosurgery 39: 537-547, 1996.
4. Baev N and Awad IA. Endothelial cell cultures from human cerebral cavernous malformations. Stroke 29: 2426-2434, 1998.
5. Craig HD, Gunel M, Cepeda O, et al., Awad IA, Lifton RP. Multilocus linkage identifies two new loci for a mendelian form of stroke, cerebral cavernous malformation, at 7p15-13 and 3q25.2-27. Human Mol Gen. 7: 1851-1858, 1998.
6. Abdulrauf SI, Keynar M and Awad IA. A comparison of the clinical profile of cavernous malformations with and without associated venous malformations. Neurosurgery 44: 41-47, 1999.
7. Wong J, Kim J, Awad IA. Ultrastructural pathology of cerebral vascular malformations: A preliminary report. Neurosurgery 46: 1454-1459, 2000.
8. Uranishi R, Baev NI, Kim JH, Awad IA. Vascular smooth muscle differentiation in human cerebral vascular malformations. Neurosurgery 49: 671-680, 2001.

9. Shenkar R, Elliott JP, Diener K, Gault J, Hu L-J, Cohrs RJ, Phang T, Hunter L, Breeze RE, Awad IA. Differential gene expression in human cerebral vascular malformations. Neurosurgery 52: 465-478, 2003.
10. Shenkar R, Sarin H, Awadallah NA, Gault J, Kleinschmidt-DeMasters BK, Awad IA. Variations in structural protein expression and endothelial cell proliferation in relation to clinical manifestations of cerebral cavernous malformations. Neurosurgery 56: 343-354, 2005.
11. Gault J, Shenkar R, Recksiek P, Awad IA. Biallelic somatic and germ line CCM1 truncating mutations in a cerebral cavernous malformation lesion. Stroke 36: 872-874, 2005.
12. Gault J, HU L-J, Sain S, Awad IA. Spectrum of genotype and clinical manifestations in human cerebral cavernous malformations. Neurosurgery. 59: 1278-1285, 2006.
13. Shenkar R, Venkatasubramanian PN, Zhao J-C, Batjer HH, Wyrwicz AM, Awad IA. Advanced magnetic resonance imaging in cerebral cavernous malformations: I. High-field imaging of excised human lesions. Neurosurgery 63: 782-789, 2008, NIHMS80963.
14. Shenkar R, Venkatasubramanian PN, Wyrwicz AM, Zhao J-C, Shi C, Akers A, Marchuk DA, Awad IA. Advanced magnetic resonance imaging in cerebral cavernous malformations: II. Imaging of lesions in murine models. Neurosurgery 63: 790-798, 2008.
15. Shi C, Shenkar R, Du H, Duckworth E, Raja H, Batjer HH, Awad IA. Immune response in human cerebral cavernous malformations. Stroke 40;1659-1665, 2009
16. Stockton RA, Shenkar R, Awad IA, Ginsberg MH. The interaction of KRIT-1 (CCM1) and CCM2 (Malcavernin, OSM) regulates vascular barrier function by inhibiting Rho Kinase. J Exp Med, in press 2010 (PMC Journal- in process).

C. Research support.

Ongoing Research Support

NIH/NINDS. R01 NS060748-01 Awad (co-PI) with Marchuk (co-PI, Duke University) 2009-2013
Genesis and Progression of Human Cerebral Cavernous Malformations

The co-PI's role on this project, approximately 15 % time commitment, is to oversee imaging of mutant mice with high field magnetic resonance, to identify cavernous malformation lesions, and to perform laser microdissection of lesional cells for molecular biologic studies in early versus late lesion stages. Expected results from this ongoing project will optimize the murine model to be used as a therapeutic platform in the current proposal, but there is no overlap in the aims or proposed experiments in the two projects.

NIH/NINDS/ Johns Hopkins Medical Institution. R01 NS046309. Awad (site PI) 2005-2012
Minimally Invasive Surgery plus rTPA for Intracerebral Hemorrhage Evacuation (MISTIE) Trial

The PI's role is to oversee recruitment of patients and to conduct minimally invasive evacuation of cerebral hemorrhage on enrolled cases at the PI's institution

NIH/NINDS U01 NS062851-01A1 2009-2013
"The CLEAR IVH Trial" (Intraventricular thrombolysis for intraventricular hemorrhage). Awad (trial co-PI)
Clot Lysis: Evaluating Accelerated Resolution of Intraventricular Hemorrhage (CLEAR III, IND 8523)

Phase III Randomized Double-Blinded Clinical trial of intraventricular thrombolytic versus placebo for clearance of intraventricular hemorrhage, with primary functional outcome endpoint. The study co-PI's role on this project, approximately 15% time commitment will oversee the trial's Surgical Center, developing surgical protocols and monitoring surgical endpoints for each of projected 500 enrolled subjects over 5 years, at 60 centers nationwide. The co-PI will co-lead the study's Steering and Protocol Committees, and will serve on its Recruitment Committee. Surgical Center subcontract to Johns Hopkins University.

Completed Research Support (past three years)

ENH Research Career Development Award, Mid-career. Awad (PI) 4/1/2005-3/31/2007

Advanced Imaging in Cerebral Cavernous Malformations

Intramural support for pilot studies on advanced imaging in human cerebral vascular malformations, including protected time for the P.I. to establish novel collaborations and collect preliminary data for the imaging of inflammatory cells in cavernous angiomas, imaging of lesions in transgenic mice, and high field imaging of vascular malformations in patients.

NINDS K24 NS02153 Awad (PI) 10/1/2001-3/31/2006
Phenotype-Genotype in Cerebral Vascular Malformations

Mid-career development grant to allow establishment of cerebrovascular malformation genotyping and phenotyping core group, and the mentoring of predoctoral and postdoctoral trainees in patient oriented research related to pathobiology and genetics of vascular malformations of the brain.
Role: PI

NIH/NINDS. R21-NS052285. Awad (PI). 2007-2008
Immune Response in Cerebral Cavernous Malformations

The PI's role on this project is to oversee recruitment of patients and securing and processing of surgical lesions for the proposed research, and to supervise experimental procedures for characterization of immune response in human lesional samples.