BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Mocarski, Edward

eRA COMMONS USER NAME (credential, e.g., agency login): mocarski.edward

POSITION TITLE: Emeritus Professor of Microbiology and Immunology (Emory and Stanford Universities)

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Rutgers University, New Brunswick, NJ	A.B.	05/1974	Microbiology
The University of Iowa, Iowa City, IA	Ph.D.	05/1979	Microbiology
The University of Chicago, Chicago, IL	Postdoc	12/1982	Virology

A. Personal Statement

Dr. Mocarski has contributed significantly to the fields of virology, immunology, cell death and inflammation, initially at Stanford University (1983-2006), where he served as Chair of Microbiology & Immunology (19941999) and Associate Dean of Research (2000-2001), and currently as Emeritus Professor and then at Emory University (2006-2021), where he served as Robert W. Woodruff Professor of Microbiology and Immunology in the Emory Vaccine Center and currently is Emeritus Professor. Dr. Mocarski also served as Distinguished Fellow at MedImmune, LLC, a division of AstraZeneca (2009-2011). He is recognized as a world expert in herpesviruses, having edited Human Herpesviruses (2007), authored the Cytomegaloviruses in the Encyclopedia of Virology through three editions and Fields Virology through five editions, including the current 7th Edition (2021). Dr. Mocarski has directly mentored over 70 graduate and postdoctoral trainees and participated as a member of thesis or postdoctoral committees of several hundred scientists. He has served on the founding scientific advisory boards of biotechnology companies in vaccines (Aviron, GlobeImmune, Immune Design, Virothera, Omios Pharma), inflammatory disease (ChemoCentryx, Ribozyme Pharmaceuticals), and antiviral/cancer therapies (CoCrystal Pharma, Agenovir). He served on advisory boards to International AIDS Vaccine Initiative and the Nebraska Center for Virology and currently advises the National Institutes of Health NIAID Vaccine Research Center and serves as an inaugural member of the Board of Directors of the Access to Advanced Healthcare Initiative. He has advised other companies and nonprofits in the development of vaccines as well as interventions in inflammatory disease and cancer.

In addition to numerous discoveries in herpesvirus replication, persistence and latency processes, Dr. Mocarski pioneered efforts to dissect signaling that contributes to cell autonomous host defense, inflammation, and the relationship to tissue and organ damage. Host and viral pathways that contribute to the virus-host “stand-off” have been a major interest over the past three decades. The battle between host defense and viral modulation, cell death pathways stand out because these are not well understood and interface with inflammation and disease pathogenesis. The cell death suppressors encoded by herpesviruses are evolutionarily conserved broadly across rodent and human viruses. The targeted pathways are also conserved in these mammalian species. Initially focusing on pathways targeted by cytomegalovirus (CMV), with later studies on herpes simplex virus (HSV) and the poxvirus vaccinia, his research unveiled novel cell death strategies employed by the host to eliminate infected cells. These studies reveal the importance of viral suppression in driving the evolution of alternate cell death pathways in mammalian host defense.

The human or murine CMV-encoded viral inhibitor of caspase-8 activation (vICA) prevents extrinsic apoptosis and is crucial to sustain viral dissemination in myeloid cells as well as the establishment of latency. The viral inhibitor of apoptosis (vMIA) targets Bcl2 family members Bax and Bak to block mitochondrial steps in apoptosis (a caspase-dependent death pathway). Dr. Mocarski discovered the physiological role of vMIA is to prevent a caspase-independent programmed cell death pathway mediated by mitochondrial serine protease HtrA2 (also called Omi). Elaboration of vMIA prolongs the life of CMV-infected cells to allow optimal production of virus progeny. The activity of the caspase-8 inhibitor vICA in human and murine CMV lead to the discovery of an alternate cell death pathway, called virus-induced necroptosis. This most significant discovery emerged from studies on a murine CMV cell death suppressor that targets receptor interacting protein (RIP) homotypic interaction motif (RHIM) signal transduction. Necroptosis, a strikingly potent and inflammatory cell death pathway prevents infection by virus mutants that are unable to block RHIM signal transduction. The M45encoded viral inhibitor of activation (vIRA), a function conserved in murine CMV (and other rodent betaherpesviruses) well as herpes simplex viruses (and other primate alphaherpesviruses), suppresses necroptosis of cells during infection. This research has led to many firsts, including the elaboration of Z-nucleic acid binding protein (ZBP1) as a novel pathogen sensor that initiates RIPK3-mediated necroptosis in murine CMV, HSV and vaccinia virus-infected cells. Necroptosis suppression mechanisms in these three plus human CMV have been elaborated. Through these insights, necroptosis has become a well-recognized aspect of host defense against both DNA and RNA viruses.

Dr. Mocarski research first unveiled the ZBP1-RIPK3-MLKL and TRIF-RIPK3-MLKL necroptosis pathways as well as the ability of RIPK3 to trigger apoptosis via a complex consisting of RIPK1-FADD-CASP8. He has also contributed to understanding RIPK1-RIPK3-MLKL necroptosis. His laboratory was the first to recognize that the midgestational lethality of caspase-8 knockout mice and the perinatal lethality of RIPK1 knockout mice are the result of unleashed necroptosis and combined necroptosis/apoptosis, respectively. These discoveries brought innate immune cell death front and center in inflammatory disease manifestations that continue to dominate investigations into numerous and diverse disease processes. Using mice that lack components of extrinsic cell death machinery, Dr. Mocarski has shown that caspase-8 provides a damper on lymphocyte proliferation during the antiviral immune response, and investigated caspase-8, RIPK3 and RIPK1 signaling during bacterial infection and endotoxic shock, showing that caspase-8 must participate with caspase-11 during the execution of endotoxic shock in mice. The implications of this coordinated cell death and cross talk in treatment of cancer remain significant. Dr. Mocarski brings the understanding of cell death signaling and induction of inflammatory processes that have grown out of over 10 years of research efforts and publications that reveal the relative importance of pro-necroptotic RIPK3, pro-apoptotic caspase-8 and pro-pyroptotic caspase-1/caspase-11 signaling in both acquired and genetic inflammatory disease states. Importantly, it has become clear that cross talk in tissues, dependent on both cytokine signaling and cell death execution, contribute in a multifaceted manner to progression of both infectious and genetic diseases. These pathways may be harnessed to treat challenging cancers such as multiple myeloma as proposed here.

B. Positions and Honors

Experience and Employment:

1975-1981	USPHS Predoctoral and Postdoctoral Trainee
1981-1983	Leukemia Society of America Special Fellow
1983-1989	Assistant Professor, Department of Microbiology & Immunology, Stanford University, 1989-
1995	Associate Professor (with tenure)
1995-1999	Professor & Chair
2000-2001	Associate Dean of Research, Provost’s Office, Stanford University
1995-2006	Professor
2006 (May)	Professor Emeritus, Stanford University
2009-2011	Distinguished Fellow, MedImmune LLC (a wholly owned subsidiary of AstraZeneca)
2006-2021	Robert W. Woodruff Professor, Emory Vaccine Center, Emory University School of Medicine
2022-present	Professor Emeritus, Emory University

Honors, Awards and Service:

1981-1983 Leukemia Society Special Fellow
1984 Agnes Axtell Moule Faculty Scholar and Andrew Mellon Fellow
1984-1990 American Cancer Society Faculty Research Award
1989 NIH-NIAID Board of Scientific Counselors
1989-1993 USDA Biotechnology Study Section
1990-1994 Member, NIH Experimental Virology Study Section
1991-2015 *Journal of Virology* Editorial Board 1991-2016 *Virology* Editorial Board
1992-1994 ASM Foundation for Microbiology
1993 NIH Wallace Rowe Lecture
1995-1996 Advisory Panel to Office of AIDS Research on Opportunistic Infections
1995-1996 SmithKline Beecham Fellow
2000-2003 9th District US Federal Court Judicial Scientific Advisor
2000-2001 Associate Dean of Research in the Provost's Office at Stanford University
2000-2015 Nebraska Center for Virology COBRE External Advisory Board
2001-2015 *Journal of Biological Chemistry* Editorial Board
2001 Pfizer Visiting Professor in Infectious Diseases, Univ of Oklahoma
2001-2004 Chair, Stanford University School of Medicine Conflict of Interest Committee
2002-2004 Stanford University Fellow
2002 NIH-NHLBI Program Review Panel
2002-present NIH Reviewers Reserve (*ad hoc* reviews performed)
2003 Organizer, Keystone Conference, Pathogen:Host Standoff – Taos, NM
2004 NIH NIDCD Review Panel on CMV-related Hearing Loss
2004-2015 Louisiana Biomedical Research
Network INBRE External Advisory Board
2005 Organizer, Keystone Conference, Pathogen:Host Standoff – Keystone, CO
2006-2007 United Kingdom MRC Virology Focus Strategy Review Group
2006-2011 Georgia Cancer Coalition Distinguished Cancer Scholar
2007 Jamie McNew Lecture, University of Minnesota
2008 Hilleman Lecturer, University of Chicago
2009-2011 Distinguished Fellow, MedImmune, a division of Astra-Zeneca
2010 Keynote - Nebraska Virology Center 10th Anniversary Symposium
2011 Keynote - 13th International Cytomegalovirus/ 5th International Betaherpesvirus Workshop
2011 Keynote – Southeast IDeA Joint Program
2012 NCI-NIAID Joint EBV Vaccine Meeting
2012 NIH NCI Burkitt Lymphoma Workshop
2012 FDA-CDC-NIH Joint CMV Vaccine
2012 Fellow, American Academy of Microbiology
2012 Emory 1% Award
2013 NIH NCI Review Panel on Role of CMV in Glioblastoma
2013 Keynote - AACBNC Chair's Meeting
2014 Herpes Laison Award – Eastern Virginia Medical School
2014-2015 NIH Viral and Microbial Disease Study Section – ad hoc
2015 Weller-Smith Oration – CMV/Betaherpesvirus Workshop, Brisbane
2015 Nirit and Michael Shaoul Fellow (Visiting Professor), Tel Aviv University
2014-pres IAVI Scientific Advisory Committee
2016 Keynote - VISTRIE Symposium
2016 Nature Conference on Innate Immunity
2017 Banbury Conference on Necroptosis
2018 Keynote – Gertrude and Werner Henle Lectureship University of Pennsylvania
2019 Closing Keynote and Perspective – International Herpesvirus Workshop - Knoxville

C. Contribution to Science

1. Cytomegalovirus Replication. Dr. Mocarski was first to identify CMV replication and regulation functions, with many significant studies on HSV as well CMV gene function starting in the early 1980's. His laboratory at Stanford was the first to investigate any CMV gene function, and, starting in the mid-1990's, his contributions have included many "firsts", including investigation of the function of the major immediate early gene (1) and the mapping and function of the CMV DNA replication origin (2) Most recently, together with former trainee, Dr. Kaiser, found CRISPR screen to identify a cellular receptor for entry (3). Additional investigations into transcription control of late viral gene expression, post-transcriptional gene regulation, cleavage and packaging of the viral genome, virion assembly and egress of virions from cells are accessible through the PubMed:

(1) Greaves, R. F., and E.S. Mocarski (1998) Low multiplicity growth defect and gene expression during infection by a human cytomegalovirus *ie*1 mutant. J. Virol. 72:366-379. PMC109384

(2) Masse, M.J., S. Karlin, G.A. Schachtel and E.S. Mocarski (1992). Human cytomegalovirus origin of DNA replication (oriLyt) resides within a highly complex repetitive region. *Proc. Natl. Acad. Sci. USA* 89:5246-5250. PMC238285

(3) Lane, R. K., H. Guo, A. D. Fisher, J. Diep, Z. Lai, Y. Che, J. W. Upton, J. Carette, E. S. Mocarski and W. J. Kaiser (2020) Necroptosis-based CRISPR knockout screen reveals neuropilin-1 as a critical host factor for early staged of murine cytomegalovirus infection. *Proc. Natl. Acad. Sci. USA* 117:20109-20116. doi: 10.1073/pnas.1921315117. PMC7443917

2. Dissemination and Latency. Dr. Mocarski investigated marker-tagged HSV LAT mutants in mice in 1989 as well as human CMV in humanized mice in the mid-1990's, resulting in research that opened the critical understanding of myeloid cell progenitors in CMV latency, including the identification of unique latencyassociated transcripts in an experimental model that were later confirmed on natural samples from human bone marrow donors (4). His laboratory has contributed the only enumeration of CMV genomes in natural latency (5), which set the stage for pursuing CMV latency in hematopoietic cell progenitors that defines the field today. Studies on murine CMV as a model of CMV biology revealed seminal information on how a CMVencoded chemokine controls T cell immunity (6) as well as the recruitment of myelomonocytic cells that act as a taxi service for viral dissemination and the establishment of latency (7):

(4) Kondo, K., H. Kaneshima, and E.S. Mocarski. (1994) Human cytomegalovirus latent infection of granulocyte-macrophage progenitors. *Proc. Natl. Acad. Sci. USA* 91:11879-11883. PMC45339 *and*
Hahn, G., R. Jores, and E.S. Mocarski (1998) Cytomegalovirus is latent in a common progenitor of dendric and myeloid cells. Proc. Natl. Acad. Sci. USA 95:3937-3942 PMC19941

(5) Slobedman, B., and E.S. Mocarski (1999) Quantitative analysis of latent human cytomegalovirus. *J. Virol.* 73:4806-4812. PMC112523

(**6**) Daley-Bauer, L. P., G. M. Wynn and E. S. Mocarski. (2012) Cytomegalovirus impairs antiviral $CD8^+$ T cell immunity by recruiting inflammatory monocytes. *Immunity* 37:122-133. PMC3412053

(7) Daley-Bauer, L. P., L. J. Roback, G. M. Wynn, and E. S. Mocarski (2014) Cytomegalovirus hijacks $CX3CR1^{hi}$ patrolling monocytes as immune-privileged vehicles for dissemination in mice. *Cell Host Microbe* 5:351-362. PMC3989205

3. Virus-encoded Inhibitors of Cell Death. Starting in the late 1990's and early 2000's, Dr. Mocarski pioneered the identification of virus-encoded cell death suppressors targeting the activation of mitochondrial Bcl2 proteins, cytosolic caspase-8 and cytosolic RIPK3. Of all the immune modulatory functions encoded by human and murine CMVs, only the cell death suppressors are conserved between distantly related betaherpesviruses and alphaviruses. The Mocarski laboratory demonstrated that the viral inhibitor of caspase8 activation (vICA) is interchangeable between the two CMVs, work published in the early 2000's that continues to the present (though not listed here). The Mocarski laboratory has been incisive by unveiling two novel caspase-independent programmed cell death pathways now known to contribute to host defense above and beyond apoptosis. First, the HtrA2 serine protease death pathway was shown in 2008 to be controlled by the human CMV UL37x1-encoded viral mitochondrial inhibitor of apoptosis (vMIA) through evaluation of viral mutants that disrupted this cell death suppressor but left others intact (8). A similar strategy unveiled necroptosis as a natural host defense pathway in murine CMV (9), observations that have had an enormous innovative impact on the general field of cell death signaling because this was the only natural example of the pathway. Experimental studies in the TNF field had first detected necroptosis when caspase-8 activity was compromised in experimental settings. Importantly, murine CMV-induced necroptosis proceeds independently of RIPK1 and so is distinct from TNF-induced necroptosis. Thus, Mocarski laboratory contributions nucleated the field of ZBP1-RIPK3 virus-induced necroptosis in host defense, inflammation and cell death signaling. The elaboration of RHIM-signaling suppressor vIRA in murine CMV brought to light the analogous HSV

UL39encoded inhibitor ICP6, which functions as a species-specific suppressor of apoptosis and necroptosis in human cells (10). Our identification of the poxvirus E3L-encoded inhibitor of ZBP1 activation in 2017 has recently allowed a detailed mechanism of Z-RNA formation and sensing in vaccinia-induced, ZBP1-mediated necroptosis (11).

(8) McCormick, A. L., L. Roback and E. S. Mocarski. (2008) vMIA control of intramitochondrial, HtrA2/Omidependent cytomegalovirus programmed cell death to terminate the replication cycle. *PLoS Pathogens* 4:e1000063 PMC2528007

(9) Upton J. W., W. J. Kaiser, and E. S. Mocarski. (2010) Viral inhibition of RIP3–dependent necrosis. *Cell Host Microbe* 22:302-313. PMC4279434 *and* Upton J. W., W. J. Kaiser, and E. S. Mocarski. (2012) DAI/ZBP1/DLM-1 complexes with RIP3 to mediate virus-induced programmed necrosis that is targeted by murine cytomegalovirus vIRA. *Cell Host Microbe* 11:290-297. PMC3531981

(10) Guo, H. S. Omoto, P. A. Harris, J. N. Finger, J. Bertin, P. J. Gough, W. J. Kaiser and E. S. Mocarski (2015) Herpes simplex virus suppresses necroptosis in human cells. *Cell Host Microbe* 17:243-251 PMC4382104 and Guo, H., R. P. Gilley, A. Fisher, V. J. Landsteiner, K. B. Ragan, C. M. Dovey, J. E. Carette, J. W. Upton, E. S. Mocarski, W. J. Kaiser. (2018) A species-independent role of DAI/ZBP1/DLM1-triggered necroptosis in host defense against HSV1. *Cell Death & Dis.* 9:816. PMC6062522.

(11) Koehler H., S. Cotsmire, T. Zhang, S. Balachandran, J. W. Upton, J. Langland, D. Kalman, B. L. Jacobs and E. S. Mocarski (2021) Vaccinia virus E3 prevents sensing of Z-RNA to block ZBP1-dependent necroptosis. *Cell Host Microbe* 29:1266-1276. PMC9333947

4. Benefits of Eliminating Cell Death Signaling Pathways in Mammals. The recognition of virus-encoded inhibitors and the specific pathways that they inhibit led to incisive and novel understanding of the risk innate host defense mechanisms pose during mammalian development. First, RIPK3-induced necroptosis was shown to underlie the midgestational embryonic lethality in caspase-8-deficient mice (12). *Casp8$^{-/-}$Ripk3$^{-/-}$* mice develop into viable, fertile and immunocompetent adult mice. Further, very important mechanistic insights emerged studying mice carrying a mutation in the kinase activity of RIPK3 (15) as well as RIPK1 (13). Dr. Mocarski elaborated a third way to trigger this mechanism, the TRIF-RIPK3 pathway of necroptosis (13). He then showed that RIPK1 deficiency results in perinatal death because of the combined impact of necroptosis and apoptosis (14). *Casp8$^{-/-}$Ripk3$^{-/-}$Ripk1$^{-/-}$* mice develop into viable, fertile and immunocompetent adult mice. Furthermore, pronecrotic RIPK3 protein kinase unleashes very rapid apoptosis via RHIM signal transduction (15), information that explained the embryonic lethality of a RIPK3 mutant published by others and opened the door to studying crosstalk between cell death pathways:

(12) Kaiser, W. J., J. W. Upton, A. B. Long, D. Livingston-Rosanoff, L. P. Daley, R. Hakem, T. Caspary and E. S. Mocarski. (2011) RIP3 mediates the embryonic lethality of caspase-8-deficient mice. *Nature* 471:368-372. PMC3060292

(13) Kaiser, W. J., H. Sridharan, J. W. Upton, P. J. Gough, C. A. Sehon, R. W. Marquis, J. Bertin and E. S. Mocarski. (2013) Toll-like receptor 3-mediated necrosis via TRIF, RIP3 and MLKL. *J. Biol. Chem.* 288:31268-31279. doi: 10.1074/jbc.M113.462341. PMC3829437

(14) Kaiser, W. J., L. P. Daley-Bauer, R. J. Thapa, P. Mandal, S. B. Berger, C. Huang, A. Sundararajan, H. Guo, L. Roback, S. H. Speck, J. Bertin, P. J. Gough, S. Balachandran, and E. S. Mocarski (2014). RIP1 suppresses innate immune cell death during mammalian parturition. *Proc. Natl. Acad. Sci. (USA)* 111:77537758 PMC4040608

(15) Mandal, P., S. B. Berger, S. Pillay, K. Moriwaki, C. Huang, H. Guo, J. D. Lich, J. Finger, V. Kasparcova, B. Votta, M. Ouellette, B. W. King, D. Wisnoski, A. S. Lakdawala, M. P. DeMartino, L. N. Casillas, P. A. Haile, C. A. Sehon, R. W. Marquis, J. Upton, L. P. Daley-Bauer, L. Roback, N. Ramia, C. M. Dovey, J. E. Carette, F. Chan, J. Bertin, P. J. Gough, E. S. Mocarski and W. J. Kaiser. (2014) RIP3 induces apoptosis independent of pro-necrotic kinase activity. *Mol. Cell* 56:481-495 PMC4512186

5. Inflammation and Disease Pathogenesis. Dr. Mocarski has contributed to understanding infectious and genetic disease in animal models and in human transplant recipients. He has overseen studies concerning the contribution of human CMV and virus-specific T cell immunity to prevention of cardiac allograft disease in manuscripts published throughout the early 2000's showing that an overwhelming majority of at-risk heart transplant recipients encounter active human CMV infection, studies that included identification of a candidate gene signature to predict acute cardiac rejection, all published before 2012. Starting in the 1980's, his laboratory has used rodent models to unveil viral and immunological principles. More recently, the contribution of the T cell-mediated immune response to disease pathogenesis (16), and the importance of cell death as a determinant of inflammation and immunity (17). An important publication (18) brings to light the role of combined cell death pathways in the execution of inflammatory shock by showing (i) that the myeloid compartment initiates the signaling independent of pro-pyroptotic caspase-11 and gasdermin D, pronecroptotic RIPK3 and pro-apoptotic caspase-8, but (ii) that execution of lethal tissue damage in mice is due to the combined action of interferon-activated Casp11 and TNF-activated caspase-8, independent of RIPK3, properties that are shared with MCMV infection (20):

(16) Livingston-Rosanoff, D., L. P. Daley, A. Garcia, A. L. McCormick, J. Huang and E. S. Mocarski. (2012) Antiviral T cell response triggers cytomegalovirus hepatitis in mice. *J. Virol.* 86:12879-12890. PMC3497643

(17) Daley-Bauer, L. P., L. Roback L. Crosby, A. L. McCormick, Y. Fang, W. J. Kaiser and E. S. Mocarski. (2017) Cytomegalovirus M36 and M45 death suppressors cooperate to block proinflammatory consequences of combined apoptotic-necroptotic signaling. *Proc. Natl. Acad. Sci. (USA)*114:E2786-E2795. doi: 10.1073/pnas.1616829114. PMC28292903

(18) Mandal, P., Y. Feng, J. D. Lyons, S. B. Berger, S. Otani, A. Delaney, G. K. Tharp, K. Maner-Smith, E. Burd, M. Schaeffer, S. Hoffman, C. Capriotti, L. Roback, C. B. Young, Z. Liang, E. A. Ortlund, N. C. Di Paolo, J. Bertin, P. J. Gough, I. E. Brodsky, C. M. Coopersmith, D. M. Shayakhmetov, E. S. Mocarski. (2018) Caspase-8 collaborates with caspase-11 to drive tissue damage and execution of endotoxic shock. *Immunity* 49:42-55.e6. doi: 10.1016/j.immuni.2018.06.011. PMC30021146

(19) Feng Y, L. P. Daley-Bauer, L. Roback, M. Potempa, H. Guo, H. S. Koehler, L. L. Lanier and E. S. Mocarski (2019) Caspase-8 restricts antiviral CD8 T cell hyperaccumulation. *Proc. Natl. Acad. Sci.* 116: 15170-15177. doi: 10.1073/pnas.1904319116. PMC6660791

(20) Mandal, P., A. L. McCormick and E. S. Mocarski (2021) TNF signaling dictates myeloid and non-myeloid cell crosstalk to execute MCMV-induced extrinsic apoptosis. *Viruses* 12:1221. doi: 10.3390/v12111221. PMC7693317

PublicBibliography:http://www.ncbi.nlm.nih.gov/sites/myncbi/edward.mocarski.1/bibliography/41345455/public/?sort=date&direction=ascending

D. Research Support (Two most recent past NIH grants)

Project Number: 5 RO1 AI020211-33 (Mocarski, PI) **Dates of Entire Project:** 12/01/85-11/30/21
Source: NIH/NIAID. **Title:** Cytomegalovirus DNA replication and inversion.
Major Goals: (1) Study cell death pathways controlling cytomegalovirus dissemination. (2) Investigate cell death pathways controlling cytomegalovirus latency and persistence. (3) Elaborate the contribution of cell death to innate and adaptive immunity to cytomegalovirus.

Project Number: 2 R01 AI118853-04 (Mocarski, PI) **Dates of Project:** 6/01/15-5/31/19
Source: NIH/NIAID Director's Transformative Award
Title: Innate activation and death signals in health and disease.
Major Goals: (1) Optimize allogeneic engraftment by manipulating cell death pathways by controlling cell death. (2) Enhance nuclear reprogramming by eliminating detrimental innate cell death. (3) Determine the contribution of apoptosis and necroptosis to inflammatory disease in mouse models.