



## Edward MocarSKI

Professor of Microbiology and Immunology, Emeritus  
Microbiology & Immunology

 NIH Biosketch available Online

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### Bio

#### BIO

Edward S. MocarSKI, Jr.

Department of Microbiology and Immunology (2006 – present)

Emory University Vaccine Center

Emory University School of Medicine

Atlanta, GA 30322

Robert W. Woodruff Professor of Microbiology & Immunology in the Emory Vaccine Center, Emory University. Professor and Chair of Microbiology & Immunology at Stanford University between 1983 and 2006 (now Emeritus). Distinguished Fellow at MedImmune, LLC, a division of AstraZeneca in 2009 and 2010 where he directed new pipeline vaccine research. His research interest is in the biology and pathogenesis of cytomegalovirus (CMV), and his group has made key contributions to the identification of replication functions, latent reservoir in myelomonocytic progenitors, immunomodulatory functions, and cellular response to viral infection. Most recently, study of viral functions that modulate host cell intrinsic activation and death pathways has brought understanding of cell death pathways in host defense and development.

PLEASE NOTE THAT ALL RESEARCH OCCURS AT EMORY UNIVERSITY (ATLANTA) AND NOT AT STANFORD UNIVERSITY (PALO ALTO).

#### ACADEMIC APPOINTMENTS

- Emeritus Faculty, Acad Council, Microbiology & Immunology

#### HONORS AND AWARDS

- Robert W. Woodruff Endowed Professor, Emory University (2006 - present)
- Distinguished Fellow, MedImmune, LLC. (2009-2011)
- See Biosketch for full list, Various (2016)

#### PROFESSIONAL EDUCATION

- AB, Rutgers University , Microbiology (1974)
- PhD, University of Iowa , Microbiology (1979)
- postdoc, The University of Chicago , Virology (1982)

#### COMMUNITY AND INTERNATIONAL WORK

- Emory Vaccine Center, Atlanta, GA

- Vaccine Research and Development, Mountain View
- International AIDS Vaccine Initiative, New York, NY

## LINKS

- Personal Web site: <http://cmgm.stanford.edu/micro/fac/mocarski.html>

## Research & Scholarship

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### CURRENT RESEARCH AND SCHOLARLY INTERESTS

Over the most recent decade my laboratory has focused on the infected cell response to infection, mainly the contribution of regulated cell death pathways to host defense. The phenomenal diversity of CMV-encoded modulators of the host response to infection provided an opening, with the cell death suppressors, which have been conserved in human and murine CMV, evolved as separate pathogens, contributing handily to the knowledge base. We recently discovered that caspase 8 can be eliminated from the mouse germ line, most likely because this protease evolved in mammals under the adaptive pressure of large viruses that encode suppressors of mitochondrial apoptosis. Our characterization of receptor interacting protein (RIP)3 kinase-dependent programmed necrosis as a “trap door” that opens when caspase 8 activity is compromised points to a multi-level and complementary contribution of programmed cell death pathways to host defense. These efforts show that CMV-encoded viral inhibitor of caspase 8 activation (vICA) and viral inhibitor of RIP activation (vIRA) block caspase-dependent apoptosis and RIP3-dependent necrosis, respectively. In the absence of vIRA, the pathogen sensor DAI senses input viral DNA and then oligomerizes with RIP3 to initiate programmed necrosis that eliminates infected cells. We have established that vICA suppression of caspase 8 activity is an essential part of this process, and that, together, vICA and vIRA represent key modulators of potent host defense pathways. These insights prompted our discovery that embryonic lethality due to germline deficiency in caspase 8 results from dysregulated RIP3 kinase-dependent necrosis. Because CMV is such a master manipulator of the host response to infection, other individual viral gene products have provided us with high impact observations, such as the virus-encoded chemokine whose function assures CMV-susceptible myeloid cells are recruited to sites of infection as vehicles for dissemination as well as to downmodulate the CD8 T cell response to infection. My research interests continue to be in CMV replication functions, characterization of the latent CMV reservoir in myelomonocytic progenitors, dissection of immunomodulatory pathways including the cellular response to viral infection as well as our most recent mechanistic studies focused on complementary and overlapping viral and host pathways.

## Teaching

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### GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Cancer Biology (Phd Program)
- Microbiology and Immunology (Phd Program)

## Publications

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### PUBLICATIONS

- **Retinoic Acid Inducible Gene 1 Protein (RIG1)-Like Receptor Pathway Is Required for Efficient Nuclear Reprogramming** *STEM CELLS*  
Sayed, N., Ospino, F., Himmati, F., Lee, J., Chanda, P., Mocarski, E. S., Cooke, J. P.  
2017; 35 (5): 1197-1207
- **Mouse cytomegalovirus M36 and M45 death suppressors cooperate to prevent inflammation resulting from antiviral programmed cell death pathways** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*  
Daley-Bauer, L. P., Roback, L., Crosby, L. N., McCormick, A. L., Feng, Y., Kaiser, W. J., Mocarski, E. S.  
2017; 114 (13): E2786-E2795
- **A Phase 1 Study of 4 Live, Recombinant Human Cytomegalovirus Towne/Toledo Chimera Vaccines in Cytomegalovirus-Seronegative Men** *JOURNAL OF INFECTIOUS DISEASES*  
Adler, S. P., Manganello, A., Lee, R., McVoy, M. A., Nixon, D. E., Plotkin, S., Mocarski, E., Cox, J. H., Fast, P. E., Nesterenko, P. A., Murray, S. E., Hill, A. B., Kemble, et al  
2016; 214 (9): 1341-1348

- **RIPK3 Activates Parallel Pathways of MLKL-Driven Necroptosis and FADD-Mediated Apoptosis to Protect against Influenza A Virus** *CELL HOST & MICROBE*  
Nogusa, S., Thapa, R. J., Dillon, C. P., Liedmann, S., Oguin, T. H., Ingram, J. P., Rodriguez, D. A., Kosoff, R., Sharma, S., Sturm, O., Verbist, K., Gough, P. J., Bertin, et al  
2016; 20 (1): 13-24
- **T cell-intrinsic ASC critically promotes T(H)17-mediated experimental autoimmune encephalomyelitis** *NATURE IMMUNOLOGY*  
Martin, B. N., Wang, C., Zhang, C., Kang, Z., Gulen, M. F., Zepp, J. A., Zhao, J., Bian, G., Do, J., Min, B., Pavicic, P. G., El-Sanadi, C., Fox, et al  
2016; 17 (5): 583-?
- **Caspase-8 as an Effector and Regulator of NLRP3 Inflammasome Signaling** *JOURNAL OF BIOLOGICAL CHEMISTRY*  
Antonopoulos, C., Russo, H. M., El Sanadi, C., Martin, B. N., Li, X., Kaiser, W. J., Mocarski, E. S., Dubyak, G. R.  
2015; 290 (33): 20167-20184
- **Manipulation of apoptosis and necroptosis signaling by herpesviruses** *MEDICAL MICROBIOLOGY AND IMMUNOLOGY*  
Guo, H., Kaiser, W. J., Mocarski, E. S.  
2015; 204 (3): 439-448
- **Caspase-8 scaffolding function and MLKL regulate NLRP3 inflammasome activation downstream of TLR3** *NATURE COMMUNICATIONS*  
Kang, S., Fernandes-Alnemri, T., Rogers, C., Mayes, L., Wang, Y., Dillon, C., Roback, L., Kaiser, W., Oberst, A., Sagara, J., Fitzgerald, K. A., Green, D. R., Zhang, et al  
2015; 6
- **Necroptosis: The Trojan horse in cell autonomous antiviral host defense** *VIROLOGY*  
Mocarski, E. S., Guo, H., Kaiser, W. J.  
2015; 479: 160-166
- **Suppression of RIP3-dependent Necroptosis by Human Cytomegalovirus** *JOURNAL OF BIOLOGICAL CHEMISTRY*  
Omoto, S., Guo, H., Talekar, G. R., Roback, L., Kaiser, W. J., Mocarski, E. S.  
2015; 290 (18): 11635-11648
- **The immunological underpinnings of vaccinations to prevent cytomegalovirus disease** *CELLULAR & MOLECULAR IMMUNOLOGY*  
McCormick, A. L., Mocarski, E. S.  
2015; 12 (2): 170-179
- **The A, B, Cs of Herpesvirus Capsids** *VIRUSES-BASEL*  
Tandon, R., Mocarski, E. S., Conway, J. F.  
2015; 7 (3): 899-914
- **Herpes Simplex Virus Suppresses Necroptosis in Human Cells** *CELL HOST & MICROBE*  
Guo, H., Omoto, S., Harris, P. A., Finger, J. N., Bertin, J., Gough, P. J., Kaiser, W. J., Mocarski, E. S.  
2015; 17 (2): 243-251
- **MicroRNA miR-21 Attenuates Human Cytomegalovirus Replication in Neural Cells by Targeting Cdc25a** *JOURNAL OF VIROLOGY*  
Fu, Y., Liu, X., Li, X., Shen, Z., Yang, B., Wu, C., Li, J., Miao, L., Ye, H., Qiao, G., Rayner, S., Chavanas, S., Davrinche, et al  
2015; 89 (2): 1070-1082
- **TNFR1-dependent cell death drives inflammation in Sharpin-deficient mice** *ELIFE*  
Rickard, J. A., Anderton, H., Etemadi, N., Nachbur, U., Darding, M., Peltzer, N., Lalaoui, N., Lawlor, K. E., Vanyai, H., Hall, C., Bankovacki, A., Gangoda, L., Wong, et al  
2014; 3
- **RIP3 Induces Apoptosis Independent of Pronecrotic Kinase Activity** *MOLECULAR CELL*  
Mandal, P., Berger, S. B., Pillay, S., Moriwaki, K., Huang, C., Guo, H., Lich, J. D., Finger, J., Kasparcova, V., Votta, B., Ouellette, M., King, B. W., Wisnoski, et al  
2014; 56 (4): 481-495
- **RIP3 induces apoptosis independent of pronecrotic kinase activity.** *Molecular cell*  
Mandal, P., Berger, S. B., Pillay, S., Moriwaki, K., Huang, C., Guo, H., Lich, J. D., Finger, J., Kasparcova, V., Votta, B., Ouellette, M., King, B. W., Wisnoski, et al  
2014; 56 (4): 481-495

- **Caspase-8 Modulates Dectin-1 and Complement Receptor 3-Driven IL-1 beta Production in Response to beta-Glucans and the Fungal Pathogen, *Candida albicans*** *JOURNAL OF IMMUNOLOGY*  
Ganesan, S., Rathinam, V. A., Bossaller, L., Army, K., Kaiser, W. J., Mocarski, E. S., Dillon, C. P., Green, D. R., Mayadas, T. N., Levitz, S. M., Hise, A. G., Silverman, N., Fitzgerald, et al  
2014; 193 (5): 2519-2530
- **Cutting Edge: RIP1 Kinase Activity Is Dispensable for Normal Development but Is a Key Regulator of Inflammation in SHARPIN-Deficient Mice** *JOURNAL OF IMMUNOLOGY*  
Berger, S. B., Kasparcova, V., Hoffman, S., Swift, B., Dare, L., Schaeffer, M., Capriotti, C., Cook, M., Finger, J., Hughes-Earle, A., Harris, P. A., Kaiser, W. J., Mocarski, et al  
2014; 192 (12): 5476-5480
- **RIP1 suppresses innate immune necrotic as well as apoptotic cell death during mammalian parturition** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*  
Kaiser, W. J., Daley-Bauer, L. P., Thapa, R. J., Mandal, P., Berger, S. B., Huang, C., Sundararajan, A., Guo, H., Roback, L., Speck, S. H., Bertin, J., Gough, P. J., Balachandran, et al  
2014; 111 (21): 7753-7758
- **Caspase-8 and RIP kinases regulate bacteria-induced innate immune responses and cell death** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*  
Weng, D., Marty-Roix, R., Ganesan, S., Proulx, M. K., Vladimer, G. I., Kaiser, W. J., Mocarski, E. S., Pouliot, K., Chan, F. K., Kelliher, M. A., Harris, P. A., Bertin, J., Gough, et al  
2014; 111 (20): 7391-7396
- **Highly Acidic C-Terminal Region of Cytomegalovirus pUL96 Determines Its Functions during Virus Maturation Independently of a Direct pp150 Interaction** *JOURNAL OF VIROLOGY*  
Brechtel, T. M., Mocarski, E. S., Tandon, R.  
2014; 88 (8): 4493-4503
- **Cytomegalovirus Hijacks CX3CR1(hi) Patrolling Monocytes as Immune-Privileged Vehicles for Dissemination in Mice.** *Cell host & microbe*  
Daley-Bauer, L. P., Roback, L. J., Wynn, G. M., Mocarski, E. S.  
2014; 15 (3): 351-362
- **True grit: programmed necrosis in antiviral host defense, inflammation, and immunogenicity.** *Journal of immunology*  
Mocarski, E. S., Kaiser, W. J., Livingston-Rosanoff, D., Upton, J. W., Daley-Bauer, L. P.  
2014; 192 (5): 2019-2026
- **Transcription of True Late (gamma 2) Cytomegalovirus Genes Requires UL92 Function That Is Conserved among Beta- and Gammaherpesviruses** *JOURNAL OF VIROLOGY*  
Omoto, S., Mocarski, E. S.  
2014; 88 (1): 120-130
- **Natural antisense transcripts of UL123 packaged in human cytomegalovirus virions** *ARCHIVES OF VIROLOGY*  
Yang, C., Miao, L., Pan, X., Wu, C., Rayner, S., Mocarski, E. S., Ye, H., Luo, M.  
2014; 159 (1): 147-151
- **Priorities for CMV vaccine development** *VACCINE*  
Krause, P. R., Bialek, S. R., Boppana, S. B., Griffiths, P. D., Laughlin, C. A., Ljungman, P., Mocarski, E. S., Pass, R. F., Read, J. S., Schleiss, M. R., Plotkin, S. A.  
2013; 32 (1): 4-10
- **Apaf1 apoptotic function critically limits Sonic hedgehog signaling during craniofacial development** *CELL DEATH AND DIFFERENTIATION*  
Long, A. B., Kaiser, W. J., Mocarski, E. S., Caspar, T.  
2013; 20 (11): 1510-1520
- **Proapoptotic Chemotherapeutic Drugs Induce Noncanonical Processing and Release of IL-1 beta via Caspase-8 in Dendritic Cells** *JOURNAL OF IMMUNOLOGY*  
Antonopoulos, C., El Sanadi, C., Kaiser, W. J., Mocarski, E. S., Dubyak, G. R.  
2013; 191 (9): 4789-4803
- **Toll-like Receptor 3-mediated Necrosis via TRIF, RIP3, and MLKL** *JOURNAL OF BIOLOGICAL CHEMISTRY*  
Kaiser, W. J., Sridharan, H., Huang, C., Mandal, P., Upton, J. W., Gough, P. J., Schon, C. A., Marquis, R. W., Bertin, J., Mocarski, E. S.

2013; 288 (43): 31268-31279

- **Cytomegalovirus UL91 Is Essential for Transcription of Viral True Late (gamma 2) Genes** *JOURNAL OF VIROLOGY*  
Omoto, S., Mocarski, E. S.  
2013; 87 (15): 8651-8664
- **Viral modulation of programmed necrosis** *CURRENT OPINION IN VIROLOGY*  
Kaiser, W. J., Upton, J. W., Mocarski, E. S.  
2013; 3 (3): 296-306
- **Desirability and feasibility of a vaccine against cytomegalovirus** *VACCINE*  
Griffiths, P., Plotkin, S., Mocarski, E., Pass, R., Schleiss, M., Krause, P., Bialek, S.  
2013; 31: B197-B203
- **Gene products of the embedded m41/m41.1 locus of murine cytomegalovirus differentially influence replication and pathogenesis** *VIROLOGY*  
Crosby, L. N., McCormick, A. L., Mocarski, E. S.  
2013; 436 (2): 274-283
- **Multiplicity-dependent activation of a serine protease-dependent cytomegalovirus-associated programmed cell death pathway** *VIROLOGY*  
McCormick, A. L., Roback, L., Wynn, G., Mocarski, E. S.  
2013; 435 (2): 250-257
- **Cutting Edge: FAS (CD95) Mediates Noncanonical IL-1 beta and IL-18 Maturation via Caspase-8 in an RIP3-Independent Manner** *JOURNAL OF IMMUNOLOGY*  
Bossaller, L., Chiang, P., Schmidt-Lauber, C., Ganesan, S., Kaiser, W. J., Rathinam, V. A., Mocarski, E. S., Subramanian, D., Green, D. R., Silverman, N., Fitzgerald, K. A., Marshak-Rothstein, A., Latz, et al  
2012; 189 (12): 5508-5512
- **Antiviral T Cell Response Triggers Cytomegalovirus Hepatitis in Mice** *JOURNAL OF VIROLOGY*  
Livingston-Rosanoff, D., Daley-Bauer, L. P., Garcia, A., McCormick, A. L., Huang, J., Mocarski, E. S.  
2012; 86 (23): 12879-12890
- **Activation of Innate Immunity Is Required for Efficient Nuclear Reprogramming** *CELL*  
Lee, J., Sayed, N., Hunter, A., Au, K. F., Wong, W. H., Mocarski, E. S., Pera, R. R., Yakubov, E., Cooke, J. P.  
2012; 151 (3): 547-558
- **Mechanisms modulating immune clearance during human cytomegalovirus latency** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*  
Slobedman, B., Mocarski, E. S.  
2012; 109 (36): 14291-14292
- **Toll-Like Receptor 3 Activation Promotes Efficient Nuclear Reprogramming and Endothelial Differentiation** *Basic Cardiovascular Sciences Scientific Session*  
Sayed, N., Lee, J., Hunter, A., Au, K. F., Wong, W., Mocarski, E., Pera, R. R., Cooke, J. P.  
LIPPINCOTT WILLIAMS & WILKINS.2012
- **Viral and host control of cytomegalovirus maturation** *TRENDS IN MICROBIOLOGY*  
Tandon, R., Mocarski, E. S.  
2012; 20 (8): 392-401
- **Cytomegalovirus Impairs Antiviral CD8(+) T Cell Immunity by Recruiting Inflammatory Monocytes** *IMMUNITY*  
Daley-Bauer, L. P., Wynn, G. M., Mocarski, E. S.  
2012; 37 (1): 122-133
- **DAI/ZBP1/DLM-1 Complexes with RIP3 to Mediate Virus-Induced Programmed Necrosis that Is Targeted by Murine Cytomegalovirus vIRA** *CELL HOST & MICROBE*  
Upton, J. W., Kaiser, W. J., Mocarski, E. S.  
2012; 11 (3): 290-297
- **Viral infection and the evolution of caspase 8-regulated apoptotic and necrotic death pathways.** *Nature reviews. Immunology*  
Mocarski, E. S., Upton, J. W., Kaiser, W. J.

2012; 12 (2): 79-88

- **Viral infection and the evolution of caspase 8-regulated apoptotic and necrotic death pathways** *NATURE REVIEWS IMMUNOLOGY*  
Mocarski, E. S., Upton, J. W., Kaiser, W. J.  
2012; 12 (2): 79-88
- **Cytomegalovirus pUL96 Is Critical for the Stability of pp150-Associated Nucleocapsids** *JOURNAL OF VIROLOGY*  
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- **Inhibition of 2',5'-Oligoadenylate Synthetase Expression and Function by the Human Cytomegalovirus ORF94 Gene Product** *JOURNAL OF VIROLOGY*  
Tan, J. C., Avdic, S., Cao, J. Z., Mocarski, E. S., White, K. L., Abendroth, A., Slobedman, B.  
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- **Identification and Classification of Acute Cardiac Rejection by Intragraft Transcriptional Profiling** *CIRCULATION*  
Holweg, C. T., Potena, L., Luikart, H., Yu, T., Berry, G. J., Cooke, J. P., Valantine, H. A., Mocarski, E. S.  
2011; 123 (20): 2236-U154
- **Cytomegalovirus UL103 Controls Virion and Dense Body Egress** *JOURNAL OF VIROLOGY*  
Ahlqvist, J., Mocarski, E.  
2011; 85 (10): 5125-5135
- **RIP3 mediates the embryonic lethality of caspase-8-deficient mice** *NATURE*  
Kaiser, W. J., Upton, J. W., Long, A. B., Livingston-Rosanoff, D., Daley-Bauer, L. P., Hakem, R., Caspary, T., Mocarski, E. S.  
2011; 471 (7338): 368-?
- **Virus Inhibition of RIP3-Dependent Necrosis** *CELL HOST & MICROBE*  
Upton, J. W., Kaiser, W. J., Mocarski, E. S.  
2010; 7 (4): 302-313
- **Human Cytomegalovirus Exploits ESCRT Machinery in the Process of Virion Maturation** *JOURNAL OF VIROLOGY*  
Tandon, R., AuCoin, D. P., Mocarski, E. S.  
2009; 83 (20): 10797-10807
- **The spleen plays a central role in primary humoral alloimmunization to transfused mHEL red blood cells** *TRANSFUSION*  
Hendrickson, J. E., Saakadze, N., Cadwell, C. M., Upton, J. W., Mocarski, E. S., Hillyer, C. D., Zimring, J. C.  
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- **Human Herpesvirus Replication and Abnormal CD8+T Cell Activation and Low CD4+T Cell Counts in Antiretroviral-Suppressed HIV-Infected Patients** *PLOS ONE*  
Jacobson, M. A., Ditmer, D. P., Sinclair, E., Martin, J. N., Deeks, S. G., Hunt, P., Mocarski, E. S., Shiboski, C.  
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- **Receptor-Interacting Protein Homotypic Interaction Motif-Dependent Control of NF-kappa B Activation via the DNA-Dependent Activator of IFN Regulatory Factors** *JOURNAL OF IMMUNOLOGY*  
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- **Repression of human cytomegalovirus major immediate early gene expression by the cellular transcription factor CCAAT displacement protein** *VIROLOGY*  
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- **Cytomegalovirus m45 cell death suppression requires receptor-interacting protein (RIP) homotypic interaction motif (RHIM)-dependent interaction with RIP1** *JOURNAL OF BIOLOGICAL CHEMISTRY*  
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- **HtrA2/Omi terminates cytomegalovirus infection and is controlled by the viral mitochondrial inhibitor of apoptosis (vMIA)** *PLOS PATHOGENS*  
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- **Pathogen subversion of cell-intrinsic innate immunity** *NATURE IMMUNOLOGY*  
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- **Cyclosporine inhibits mouse cytomegalovirus infection via a cyclophilin-dependent pathway specifically in neural stem/progenitor cells** *JOURNAL OF VIROLOGY*  
Kawasaki, H., Mocarski, E. S., Kosugi, I., Tsutsui, Y.  
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- **Frequent occult infection with cytomegalovirus in cardiac transplant recipients despite antiviral prophylaxis** *JOURNAL OF CLINICAL MICROBIOLOGY*  
Potena, L., Holweg, C. T., Vana, M. L., Bashyam, L., Rajamani, J., McCormick, A. L., Cooke, J. P., Valantine, H. A., Mocarski, E. S.  
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- **Interplay between systemic inflammation and markers of insulin resistance in cardiovascular prognosis after heart transplantation** *JOURNAL OF HEART AND LUNG TRANSPLANTATION*  
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- **Changes in coronary arterial dimensions early after cardiac transplantation** *TRANSPLANTATION*  
Fearon, W. F., Potena, L., Hirohata, A., Sakurai, R., Yamasaki, M., Luikart, H., Lee, J., Vana, M. L., Cooke, J. P., Mocarski, E. S., Yeung, A. C., Valantine, H. A.  
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Melnick, M., Mocarski, E. S., Abichaker, G., Huang, J., Jaskoll, T.  
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