Michele Di Mascio
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Bethesda, MD, 20817

Education			
INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
University of Ancona, Ancona, Italy	B.S. + M.S.	1994	Electronic Engineering + Bioengineering, *cum laude*
University of Ancona, Ancona, Italy	B.S. + M.S.	1999	Biology + Biotechnology, *cum laude*
Pharmacological Research Institute, Mario Negri Sud, Santa Maria Imbaro, Chieti, Italy	Ph.D.	1999	Pharmacology

Research Interests
Dynamics of residual viral replication and immune activation in HIV-1 infected antiretroviral-treated patients and the development of non-invasive in vivo imaging technologies to study HIV pathogenesis.

Current position:

Chief, AIDS Imaging Research Section, Integrated Research Facility;

Acting Chief, Mathematical Biology Section, Biostatistics Research Branch;

Division of Clinical Research,

National Institute of Allergy and Infectious Diseases,

NIH, Bethesda, MD, USA

1999-2003: Post Doctoral Research Associate. Theoretical Division, Los Alamos National Laboratory, Los Alamos, NM, USA.

***Awards*:**
Imaging Probe for the *In Vivo* Assessment of HIV-1 Dynamics (NIH 2003-2004). Principal Investigator: Dr. Michele Di Mascio

Special Act Award: February 2008, from National Institute of Allergy and Infectious Diseases- for the establishment of an imaging laboratory.

2010 **NIAID Merit Award**: For outstanding contributions in the development of an imaging laboratory to study viral infections

Professional experience

2012 Chair for 2012 Brainstorming session “Imaging anatomic reservoirs of SIV using hematopoietic stem-cells-reconstituted nonhuman primates”. The National Institutes of Health, Bethesda, MD.

2011 Member of the International Working Group "Towards an HIV Cure", International AIDS Society

2011 Member scientific review European Commission: HIV/AIDS, malaria and tuberculosis

2010 Principal Investigator of Clinical Protocol: Imaging Neuroinflammation in HIV-1 infection using Arachidonic Acid and PET;

2005 Co-chair for 2005 International Workshop on T cell turnover and homeostasis in HIV infection. The National Institutes of Health, Bethesda, MD. Chairs: Michele Di Mascio and Zvi Grossman.

2004-present. Establishment and scientific supervision of an Imaging laboratory at NIAID to study HIV pathogenesis in vivo using Non-Human Primates. Authorized user of SPECT Imaging laboratory.

Co-chair for 1999 International School of Biomathematics "Delay Differential Equations in Physiologic modeling". Mario Negri Sud Institute, Santa Maria Imbaro, Chieti, Italy

Editorial services:
Referee for Journal of AIDS, Blood, Journal of Theoretical Biology, International AIDS Society

***Peer-reviewed publications*:**

1-**Di Mascio, M.** & Esposito, E. The degree of inhibition of dopaminergic neurons in the ventral tegmental area induced by selective serotonin reuptake inhibitors is a function of the density-power-spectrum of the interspike interval. *Neuroscience* **79**, 957-61. (1997).

2-Di Matteo, V., Di Giovanni, G., **Di Mascio, M.** & Esposito, E. Selective blockade of serotonin2C/2B receptors enhances dopamine release in the rat nucleus accumbens. *Neuropharmacology* **37**, 265-72 (1998).

3-**Di Mascio, M.**, Di Giovanni, G., Di Matteo, V., Prisco, S. & Esposito, E. Selective serotonin reuptake inhibitors reduce the spontaneous activity of dopaminergic neurons in the ventral tegmental area. *Brain Res Bull* **46**, 547-54. (1998).

4-Di Giovanni, G., **Di Mascio, M.**, Di Matteo, V. & Esposito, E. Effects of acute and repeated administration of amisulpride, a dopamine D2/D3 receptor antagonist, on the electrical activity of midbrain dopaminergic neurons. *J Pharmacol Exp Ther* **287**, 51-7. (1998).

5-Di Matteo, V., Di Giovanni, G., **Di Mascio, M.** & Esposito, E. Role of the serotonergic system in the control of mesocorticolimbic dopaminergic function. *Current Topic in Pharmacology* **4**, 107-116 (1999).

6-Di Giovanni, G., De Deurwaerdere, P., **Di Mascio, M.**, Di Matteo, V., Esposito, E. & Spampinato, U. Se2lective blockade of serotonin-2C/2B receptors enhances mesolimbic and mesostriatal dopaminergic function: a combined in vivo electrophysiological and microdialysis study. *Neuroscience* **91**, 587-97 (1999).

7-Di Matteo, V., Di Giovanni, G., **Di Mascio, M.** & Esposito, E. SB 242084, a selective serotonin2C receptor antagonist, increases dopaminergic transmission in the mesolimbic system. *Neuropharmacology* **38**, 1195-205. (1999).

8-**Di Mascio, M.**, Di Giovanni, G., Di Matteo, V. & Esposito, E. Decreased chaos of midbrain dopaminergic neurons after serotonin denervation. *Neuroscience* **92**, 237-43 (1999).

9-**Di Mascio, M.**, Di Giovanni, G., Di Matteo, V. & Esposito, E. Reduced chaos of interspike interval of midbrain dopaminergic neurons in aged rats. *Neuroscience* **89**, 1003-8 (1999).

10-Di Giovanni, G., Di Matteo, V., **Di Mascio, M.** & Esposito, E. Preferential modulation of mesolimbic vs. nigrostriatal dopaminergic function by serotonin(2C/2B) receptor agonists: a combined in vivo electrophysiological and microdialysis study. *Synapse* **35**, 53-61. (2000).

11-Di Matteo, V., Di Giovanni, G., **Di Mascio, M.** & Esposito, E. Effect of acute administration of hypericum perforatum-CO2 extract on dopamine and serotonin release in the rat central nervous system. *Pharmacopsychiatry* **33**, 14-8. (2000).

12-Di Matteo, V., **Di Mascio, M.**, Di Giovanni, G. & Esposito, E. Acute administration of amitriptyline and mianserin increases dopamine release in the rat nucleus accumbens: possible involvement of serotonin2C receptors. *Psychopharmacology (Berl)* **150**, 45-51. (2000).

13-Di Matteo, V., Di Giovanni, G., **Di Mascio, M.** & Esposito, E. Biochemical and electrophysiological evidence that RO 60-0175 inhibits mesolimbic dopaminergic function through serotonin(2C) receptors. *Brain Res* **865**, 85-90. (2000).

14-Metzner, K.J., Jin, X., Lee, F.V., Gettie, A., Bauer, D.E., **Di Mascio, M.**, Perelson, A.S., Marx, P.A., Ho, D.D., Kostrikis, L.G. & Connor, R.I. Effects of in vivo CD8(+) T cell depletion on virus replication in rhesus macaques immunized with a live, attenuated simian immunodeficiency virus vaccine. *J Exp Med* **191**, 1921-31. (2000).

15-Percus, J.K., Percus, O.E., Markowitz, M., Ho, D.D., **Di Mascio, M.** & Perelson, A.S. The distribution of viral blips observed in HIV-1 infected patients treated with combination antiretroviral therapy. *Bull Math Biol* **65**, 263-77. (2003).

16-Louie, M., Hogan, C., **Di Mascio, M.**, Hurley, A., Simon, V., Rooney, J., Ruiz, N., Brun, S., Sun, E., Perelson, A.S., Ho, D.D. & Markowitz, M. Determining the relative efficacy of highly active antiretroviral therapy. *J Infect Dis* **187**, 896-900. (2003).

17-**Di Mascio, M.**, Dornadula, G., Zhang, H., Sullivan, J., Xu, Y., Kulkosky, J., Pomerantz, R.J. & Perelson, A.S. In a subset of subjects on highly active antiretroviral therapy, human immunodeficiency virus type 1 RNA in plasma decays from 50 to <5 copies per milliliter, with a half-life of 6 months. *J Virol* **77**, 2271-5. (2003).

18-Markowitz, M., Louie, M., Hurley, A., Sun, E., **Di Mascio, M.**, Perelson, A.S. & Ho, D.D. A novel antiviral intervention results in more accurate assessment of human immunodeficiency virus type 1 replication dynamics and T-cell decay in vivo. *J Virol* **77**, 5037-8. (2003).

19-Louie, M., Hogan, C., Hurley, A., Simon, V., Chung, C., Padte, N., Lamy, P., Baglatas, A., Flaherty, J., Coakley, D., **Di Mascio, M.**, Perelson, A.S. & Markowitz, M. Determining the antiviral activity of tenofovir DF in treatment-na.ve chronically HIV-1-infected individuals. *AIDS* 17: 1151-6 (2003).

20-Simon, V., Padte, N., Murray, D., Vanderhoeven, J., Wrin, T., Parkin, N., **Di Mascio, M.** & Markowitz, M. Infectivity and replication capacity of drug resistant HIV-1 variants isolated during primary infection. *J Virol* **77:** 7736-45 (2003).

21-**Di Mascio, M.**, Markowitz, M., Louie, M., Hurley, A., Ho, D.D. & Perelson, A.S. Viral Blip Dynamics during HAART. *J Virol* **77:** 12165-72 (2003).

22-**Di Mascio, M.**, Ribeiro, R., Markowitz, M., Ho, D. & Perelson, A.S. Modeling the long-term control of viremia in HIV-1 infected patients treated with antiretroviral therapy. *Math. Biosci.* **188:**47-62 (2003).

23-**Di Mascio, M.**, Markowitz, M., Louie, M., Hurley, A., Hogan, C., Simon, V., Follmann, D., Ho, D.D. & Perelson, A.S. Dynamics of Intermittent Viremia During HAART in Patients who Initiate Therapy During Chronic versus Acute and Early HIV-1 Infection. *J Virol* **78**:10566-73 (2004)

24-**Di Mascio, M.,** Percus, J.K., Percus, O.E., Markowitz, M., Ho, D.D., & Perelson, A.S. The duration of an intermittent episode of viremia. *Bull. Math. Biol.* **67**:885-900 (2005).

25-Kovacs, J.A., Lempicki, R.A., Sidorov, I., Adelsberger J., Sereti, I., Sachau, W., Kelly, G., Metcalf, J., Davey, R., Falloon, J., Polis, M., Tavel, J., Stevens, R., Lambert, L., Hosack, D., Issaq, H., Fox, S., Leitman, S., Baseler, M., Masur, H., **Di Mascio, M.**, Dimitrov, D., & Lane, C.H. Induction of Prolonged Survival of CD4+ T Lymphocytes by Intermittent IL-2 Therapy in Patients with HIV Infection. *J. Clin. Invest.* **115**: 2139-2148 (2005)

26-**Di Mascio M.**, Sereti I., Matthews L., Natarajan V., Yoder C., Jones E., Chow C., Sidorov I., Dimitrov D., Metcalf J.A., Polis M.A. & Kovacs J.A. Differential dynamics of TCR excision circles and naïve T cells during immune reconstitution suggest that HIV depletes naïve T cells by activation to memory cells. *J. Virol.* **80**: 2665-2674 (2006).

. 27-Chen, Y., **Di Mascio, M.**, Perelson, A.S., Gettie, A., Ho, D. & Zhang, L. Determination of virus burst size in vivo using a single-cycle SIV in rhesus macaques. *Proc Natl Acad Sci*. **104**:19079-84 (2007)

28-Kaur, A., **Di Mascio, M.**, Ribeiro R.M., Perelson, A.S., McClure, H.M. & Johnson R.P. Dynamics of T- and B-lymphocyte turnover in a natural host of simian immunodeficiency virus. *J Virol.* **82**:1084-93. (2008)

29-Read, S., Lempicki, R., **Di Mascio, M.**, Srinivasula, S., Cheng, Huang, C.Y., Kovacs, J. et al. Rate of CD4 T cell turnover following IL-2 therapy is predictive of change in CD4 T cell count. *J. Inf. Dis.* **198**: 843-50 (2008).

30-Catalfamo M., **Di Mascio, M.**, Hu, Z., Srinivasula, S., Thaker, V., Adelsberger, J., Adam Rupert[3], Baseler, M., Roby, G., Follmann, D., & H.C. Lane. HIV infection leads to increased immune activation by two distinct pathways that differentially affect CD4 and CD8 T cell. *Proc Natl Acad Sci U S A*. **105**:19851-6 (2008).

31- Kiesewetter, D., Srinivasula, S., Knudson, K., Lim, E., & M. Di Mascio. *R* and *S* [$_{18}$F]FPMPA: Nucleotide Reverse Transcriptase Inhibitor for Biodistribution Studies. *J Labelled Compounds* **51**: 207-212 (2008)

32- Percus J.K., Percus, O.E. & **M. Di Mascio, M**. The amplitudes of viral blips in HIV-1 infected patients treated with antiretroviral therapy are power-law distributed. *J Theor Biol.* **257**: 2009

33- **Di Mascio, M**, Paik C., Carrasquillo J., Maeng J-S., Jang B-S Shin I. S., Srinivasula S., Byrum R., Neria A., Catalfamo M., Nishimura Y., Reimann K., Martin M. & H. Clifford Lane. Non-Invasive In Vivo Imaging of CD4 Cells in SHIV Infected Non-human Primates. *Blood* **114**: 328-37 (2009)

34- **Di Mascio**, **M**., S. Srinivasula, M. Collins, E. Lim, L.I. Cheng & D. Kiesewetter. Positron Emission Tomography agent for Non-Invasive Imaging of Antiretroviral Drug Penetration and Kinetics In Vivo. *Antimicrob, Agents Chemother.* **53**:4086-95 (2009)

35- Bray M, **Di Mascio M**, de Kok-Mercado F, Mollura DJ, Jagoda E. Radiolabeled antiviral drugs and antibodies as virus-specific imaging probes. Antiviral Res. 88:129-42 (2010)

36- Graf E.H., Mexas A.M., Yu J.J., Shaheen F., Liszewski M.K., **Di Mascio M.**, Migueles S., Connors M. and O'Doherty U. Elite Suppressors Harbor Low Levels of Integrated HIV DNA and High Levels of 2-LTR Circular HIV DNA Compared to HIV+ Patients on and off HAART (PLoS Pathog. 2011 February; 7(2): e1001300)

37- Hodge J. N., Srinivasula S., Hu Z., Sarah W. Read S.W., Porter B.O., Kim I., Mican J., Paik C., **Di Mascio M**. and Sereti I. Decreases in IL-7 levels during antiretroviral treatment of HIV infection suggest a primary mechanism of receptor-mediated clearance (Sep 22;118(12):3244-53)

38- Srinivasula S., Richard A. Lempicki R.A., Adelsberger J.W., Chiung-Yu Huang C-Y., Roark J., Lee P.I., Adam Rupert A., Stevens R., Sereti I., Lane H.C., **Di Mascio M.**, Joseph A. Kovacs J.A. In Vivo Labeling With Bromodeoxyuridine Identifies Differential Effects of HIV Viral load and CD4 Counts on Proliferation of Naïve and Memory CD4 and CD8 T Lymphocytes (Blood. 2011 Jul 14;118(2):262-70)

39- Concurrent measurements of total and integrated HIV DNA can be used to monitor reservoir size and detect ongoing replication in trials that target viral reservoirs. Mexas A.M., Graf E.H., Pace M.J., Papasavvas E., Azzoni L., Busch M., **Di Mascio M.**, Migueles A. M., Montaner L.J., O'Doherty U. (in preparation).

40- Towards an HIV cure: a global scientific strategy.The International AIDS Society Scientific Working Group on HIV Cure, Deeks SG, Autran B, Berkhout B, Benkirane M, Cairns S, Chomont N, Chun TW, Churchill M, **Di Mascio M.**, Katlama C, Lafeuillade A, Landay A, Lederman M, Lewin SR, Maldarelli F, Margolis D, Markowitz M, Martinez-Picado J, Mullins JI, Mellors J, Moreno S, O'Doherty U, Palmer S, Penicaud MC, Peterlin M, Poli G, Routy JP, Rouzioux C, Silvestri G, Stevenson M, Telenti A, Lint CV, Verdin E, Woolfrey A, Zaia J, Barré-Sinoussi F. Nat Rev Immunol. 2012 Jul 20;12(8):607-614

CHAPTER OF BOOK: M. Di Mascio, G. Di Giovanni and E. Esposito. Fourier analysis applied to the study of the electrical activity of midbrain dopaminergic neurons. In: International School of Biopysics: Neural circuit and Network (Eds. Torre, V. and Nicholls, J.), serie F: Computer and Systems, Vol. 167, pp. 41-51.

Imaging Anatomic Reservoirs of SIV using Hematopoietic-Stem-Cells Reconstituted Non-human Primates

The National Institutes of Health, Bethesda, MD.
April 20th 2012

Chair: Michele Di Mascio

9:00 AM- **Welcome**- **Cliff Lane (NIAID)**

9:10 AM- **Introduction**- Michele Di Mascio

9:30 AM **The ongoing debate towards HIV eradication**- **Michele Di Mascio (NIAID)**
[What are the current theories behind the persistence of HIV in the body and how in vivo imaging in NHPs can help to accelerate research in this area?]

9:50 **The second Berlin patient**- **Una O'Doherty (U Penn)**
[What are the lessons learned from the clinical outcome of this intervention and what could be learned from mimicking this model in NHPs?]

10:10 **HSC transplantation in NHPs**- **Robert Donahue (NHLBI)**
[What are the current strategies to reconstitute the immune system in NHPs through HSCs? How in vivo imaging could help research in HSC transplantation?]

10:30 - ----------*Break*----------

10:50 **Transfection and transduction efficiencies in HSC research**- **John Tisdale (NHLBI)**
[What are the advantages of random insertion of reporter genes; how many reporter genes can be transfected with a single vector and what is the expected interference between them?]

11:10 **Positive selection in vivo and site specific insertion of reporter genes**- **Peter-Hans Kiem (FHCRC)**
[How can we increase the percentage of modified cells in vivo? can we deliver a reporter gene while disrupting a specific gene (e.g. the site specific insertion of a reporter gene while disrupting the CCR5 gene)?]

11:30 **Can we image SIV infected cells: reporter gene under the control of LTR**- **Fatah Kashanchi (George Mason University)**
[What are the limits of this approach in terms of specificity and sensitivity? And what could be done to improve specificity and/or sensitivity?]

11:50 **Can we image SIV infected cells: trans-splicing with or without recombinant SIV**- **Lloyd Mitchell (Retrotherapy)**
[What are the limits of this approach in terms of specificity and sensitivity? And what could be done to improve specificity and/or sensitivity?]

12:10- ----------*Lunch Break*----------

1:10 **Engineered T-cells to control HIV infection**- **James Riley (U Penn)**
[How imaging can help to accelerate this area of research?]

1:30 **In vivo imaging of the immune system using mAb**- **Michele Di Mascio (NIAID)**
[How can we image CD4 and CD8 T cells in vivo through labeling of mAb directed against CD4/CD8 receptors? What is the sensitivity of this approach and can we perform longitudinal analysis?]

1:50 **In vivo imaging using reporter genes**- **Stephen Russell (Mayo Clinic)**
[What would be the advantage of transfecting a reporter gene (such as hNIS) in immune cells for in vivo imaging with an unbound radionuclide? Could we place in sequence a reporter gene to image immune cells and a reporter gene to image cells infected by SIV?]

2:10 **Towards transgenic NHP models**- **Marisa St Claire (NIAID)**
[What are the challenges today behind the design of an NHP model to answer a specific question of pathogenesis using transgenic technology?]

2:30----------*Break*----------

2:45- **Constraints in quantifying in vivo images** – **Richard Reba (Clinical Center)**

Discussion and Closing Remarks