

**BIOGRAPHICAL SKETCH**

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NAME: Gennaro, Maria Laura

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POSITION TITLE: Professor of Medicine Professor of Medicine

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
London School Hygiene Tropical Medicine	M.Sc.	06/1981	Medical Microbiology
University of Palermo Medical School, Italy	M.D.	07/1977	Medicine

**A. Personal Statement**

I have conducted tuberculosis research since the mid-90s. I have led biomarker discovery projects funded by the NIH and through the Bill and Melinda Gates Foundation, with emphasis on studies of the antibody response to tuberculosis. This work has yielded numerous publications, including a seminal publication in *PNAS* in 2010 that defines the sero-proteome of *Mycobacterium tuberculosis*, i.e., all the bacterial proteins inducing antibody responses during human tuberculosis. Moreover, I have been the PI of two R01s on the use of RNA flow cytometry to study antigen-specific T cell activation in latent and active tuberculosis. One of these R01s was an academia-industry partnership grant to establish a new diagnostic platform, which was published in *Nature Protocols* in 2017. My laboratory has also studied many antigenic proteins of *M. tuberculosis*. One of these proteins is part of antigen cocktails currently utilized in all commercial interferon-gamma release assays for the diagnosis of latent tuberculosis infection.

I have spearheaded multidisciplinary research. I have been the PI of a multidisciplinary, systems biology program studying latency in tuberculosis, which participated in NHLBI-led interactions among five grantees and a data coordinating center. Within that program, my laboratory began to study the role of lipid metabolism in host-pathogen interactions in tuberculosis, which eventually led to the discovery that lipid accumulation in tuberculous foam cells (lipid-laden macrophages) involves triglycerides rather than cholesteryl esters, as it had been implied from the atherosclerosis literature. Foam cell biogenesis as a potential target for host-directed therapies for tuberculosis is the focus of an active R01 of which I am the PI.

Since the start of the COVID-19 pandemic, I have participated in a leadership role in studies on a longitudinal healthcare worker cohort called Rutgers Corona Cohort (RCC), I am PI of a COVID-19 emergency supplement to an NHLBI R01 to study the effects of convalescent plasma therapy in COVID-19. I am also MPI on an NIAID R01 award aiming to study biomarkers of COVID-19 severity, natural history, and reinfection in the RCC; and site PI on the CLOCK pediatric consortium participating in the NIH RECOVER initiative on post-acute sequelae of COVID-19. Moreover, my laboratory is serving as serological core for the Tier 1 and Tier 2 of the entire Pediatric RECOVER protocol. In addition, I serve as MPI in the Rutgers-led PreVAIL study funded by NICHD to study manifestations of pediatric SARS-CoV-2 infection.

Selected COVID-19 publications are:

- Horton D.B., Barrett E.S., Roy J., **Gennaro M.L.**, Andrews T., Greenberg P., Bruiners N., Datta P., Ukey R., Velusamy S.K., Fine D., Honnen W.J., Yin Y., Pinter A., Brooks A., Tischfield J., Hussein S., Jagpal S., Swaminathan S., Parmar V., Reilly N., Gaur S., Panettieri Jr. R.A., Carson J., Blaser M.J. Determinants and dynamics of SARS-CoV-2 infection in a diverse population: 6-month evaluation of a prospective cohort study. *Journal Infectious Diseases* jjab411 August 13 2021, <https://doi.org/10.1093/infdis/jjab411>
- Datta P., Ukey R., Bruiners N., Honnen W., Carayannopoulos M.O., Reichman R., Choudhary A., Onyuka A., Handler D., Guerrini V., Mishra P.K., Dewald. H.K., Lardizabal A., Lederer L., Leiser A.L., Hussain S., Jagpal S.K., Radbel J., Bhowmick T., Horton D.B., Barrett E.S., Xie Y.L., Fitzgerald-Bocarsly P., Weiss

S.H., Woortman W., Parmar H., Roy J., Dominguez-Bello M.G., Blaser M.J., Carson J.L., Panettieri R.A. Jr., Libutti S.K., Raymond H.F., Pinter A., **Gennaro M.L.** Highly versatile antibody binding assay for the detection of SARS-CoV-2 infection. *Journal Immunological Methods* 2021, 499, 113165 doi.org/10.1016/j.jim.2021.113165

• Ukey, R., Bruiners, N., Mishra, H., Mishra, P.K., McCloskey, D., Onyuka, A., Chen, F. Pinter, A., Weiskopf, D., Sette, A., Roy, J., Gaur, S., **Gennaro, M.L.** Dichotomy between the humoral and cellular responses elicited by mRNA and adenoviral vector vaccines against SARS-CoV-2. *BMC Medicine* 20, 32 10.1186/s12916-022-02252-0 (2022)

• Bruiners N., Guerrini V., Ukey R., Dikdan R., Yang J., Mishra P.K., Onyuka A., Handler D., Vieth J., Carayannopoulos M., Guo S., Pollen M., Pinter A., Tyagi S., Feingold D., Philipp C., Libutti S., **Gennaro M.L.** Longitudinal analysis of biologic correlates of COVID-19 resolution: case report. *Frontiers in Medicine* 2022 Jun 15;9:915367. doi: 10.3389/fmed.2022.915367.

### **Active and Recently Completed Projects**

R01 HL149450 Gennaro (PI) 08/01/2019-06/30/2023  
NIH/NHLBI

#### *Foam cells as drug targets in tuberculosis*

The goal of this program is to discover druggable targets in macrophage metabolic pathways involved in the development of foam cells-lipid-laden macrophages that are a hallmark of human tuberculosis lesions.

Role: PI

UL1 TR003017 Panettieri (PI) 03/11/2019-02/29/2024  
NIH/NCATS

#### *New Jersey Alliance for Clinical and Translational Science: NJ ACTS*

Our CTSA Hub focuses on two overarching themes: the heterogeneity of disease pathogenesis and response to treatment, and the value of linking large clinical databases with interventional clinical investigations to identify cause-and-effect and predict therapeutic responses. The biomarkers core will investigate biomarkers of progression to disease (tuberculosis) and exacerbation (asthma) by RNA flow cytometry.

Role: Core Lead, Biomarkers

R01HL149450-S1 Gennaro (PI) 08/15/2020-07/31/2021  
NIH/NHLBI

#### *Effects of donor plasma and recipient characteristics on convalescent plasma treatment outcome of COVID-19.*

The goal of this project is correlate the clinical outcome of convalescent plasma treatment of COVID-19 with the properties of the donor plasma.

Role: PI

R61/R33HD105619 Gennaro (MPI) 11/01/2020-10/31/2024  
NIH/NICHD

#### *COVID-19 Network of Networks Expanding Clinical and Translational approaches to Predict Severe Illness in Children (CONNECT to Predict SICK Children)*

Develops models and biomarkers that predict risk for severe disease in children and adolescents by systematically integrating social science, epidemiological, genetic, biochemical, immunological, and computational approaches.

Role: MPI (Contact PI - Kleinman)

RECOVER Phase II Kleinman (PI) 08/01/2021-07/31/2025  
*CLOCK Consortium for PASC Phase II RECOVER Pediatric Cohort*

The goal of the phase II of the NIH RECOVER initiative is to enroll 6,000 children for the study of post-acute sequelae of COVID-19. Our consortium, of which Rutgers University is the primary site, is tasked with the enrollment of 2,400 of these children.

Role: Site PI (Contact PI - Kleinman)

Contract awarded through the CLOCK Consortium for PASC

#### *Serologic analyses of RECOVER pediatric cohort -- Tier 1 and Tier 2*

03/25/2022 —

To screen by ELISA all pediatric participants to the RECOVER study and one caregiver per child (approx. 32,000 participants) for antibodies to SARS-COV-2 Spike Receptor Binding Domain and Nucleocapsid. To characterize the anti-SARS-CoV-2 antibody repertoire in children enrolled in the Tier 2 of the pediatric protocol.

Role: Program Director

R01AI158911  
NIH/NIAID

Gennaro (MPI)

09/01/2021-08/31/2024

*Cohort and biomarkers for COVID-19 severity, natural history, and reinfection*

The goal of this study is to follow-up well-characterized cohorts enrolled in March-April 2020 to monitor the evolution of SARS-CoV-2 infection and its sequelae in a rapidly evolving situation, including vaccination and emergence of virus variants.

09/01/2021 – 08/31/2024

Role: MPI (Contact PI – Blaser)

R01AG053961-S2  
NIH/NIA

Gluck (PI)

04/01/2021-03/31/2022

*Cognitive, Neural and Immunological Consequences of COVID-19 in Older African Americans and How They Relate to Risk for Alzheimer's Disease*

To investigate the cognitive, neural, and immunological consequences of COVID-19 in older African Americans and how they relate to risk for Alzheimer's disease.

Role: Co-Investigator

Danisco

Horton (PI)

01/27/2021-01/26/2022

*Live Microbials to Boost Anti-SARS-CoV-2 Immunity Clinical Trial (Live BASIC Trial)*

This pilot randomized controlled trial will test the preliminary efficacy and tolerability of a combination of probiotics given to boost the immunity of unvaccinated persons with prior confirmed SARS-CoV-2 infection.

Role: Co-Investigator

## **B. Positions, Scientific Appointments, and Honors**

### **Positions and Scientific Appointments**

2020-present Full Member, Cancer Metabolism and Growth Program, Rutgers Cancer Institute of New Jersey  
2020-present Professor of Epidemiology, School of Public Health, Rutgers, The State University of New Jersey  
2018-2020 Director (interim), PHRI, NJMS, Rutgers, The State University of New Jersey  
2017-2018 Associate Director, PHRI, NJMS, Rutgers, The State University of New Jersey  
2011-present Professor of Medicine, New Jersey Medical School, Rutgers, The State University of New Jersey  
2007-present Member, Graduate School of Biomedical Sciences, Rutgers, The State University of New Jersey  
2004-2011 Associate Professor of Medicine, New Jersey Medical School, UMDNJ, Newark, NJ  
1996-2011 Adjunct Associate Professor, Department of Microbiology and Sackler Institute of Graduate Biomedical Sciences, New York University Medical Center, New York, NY  
1996-2007 Associate Member, Public Health Research Institute, New York, NY  
1989-1996 Assistant Member, Public Health Research Institute, New York, NY, and Adjunct Assistant Professor, Department of Microbiology and Sackler Institute of Graduate Biomedical Sciences, New York University Medical Center, New York, NY  
1984-1988 Associate, Department of Plasmid Biology, Public Health Research Institute, New York, NY  
1980-1986 Assistant Member, Laboratory of Bacteriology, Istituto Superiore Sanita', Roma, Italy  
1981-1982 Visiting Scientist, Molecular Genetics Laboratory, Centre for Applied Microbiology and Research, Public Health Laboratory Service, Porton Down, Salisbury, UK  
1980-1981 M. Sc. Student, Dept. of Microbiology, London School of Hygiene and Tropical Medicine, University of London, UK  
1978-1980 Postdoctoral Fellow, Istituto Superiore Sanita', Roma, Italy  
1977 Clinical Internship and Medical Board Exam Certification

### **Awards and Honors**

2020 Inaugural Chancellor Distinguished Biomedical Researcher Award  
1978 - 1980 Postdoctoral Fellowships awarded by Istituto Superiore Sanita', Roma, Italy  
1977 M.D. Magna cum Laude

### **Other Experience and Professional Membership**

Reviewer: more than 30 journals  
NSF: Prokaryotic Genetics and Biochemical Genetics Programs, International Programs  
NIH: ad-hoc (multiple cycles): NIGMS-MARC; BM1; ZA1 GB-I; CRSF; IDM-M; IDM-R; IDM-A; Indo-US Program; BACP; U-19 TBRU; IDIB-S02M. Standing member: BACP 2014 – 2018.  
Others: WHO (TBDI); Dept. Veterans Affairs; AIDS Research Program (Italy); Wellcome Trust (UK), Medical Research Council (UK)  
Member: American Society Microbiology, American Association Advancement of Science, New York Academy of Sciences

Advisor: World Health Organization TB Diagnostics Initiative  
Member: New Diagnostics Working Group -- Biomarker Task Force, Stop TB Partnership  
Director: Minority High School Student Research Apprentice Program (NIH) (1992-1997)  
Member: Board of Directors, Public Health Research Institute, New York, NY (1995-1997), Rutgers Global Health Institute Executive Committee (2018-present), NJ ACTS Advisory Board (2020), Rutgers Corona Cohort Leadership Committee (2020), Center for COVID Response and Pandemic Preparedness (CCRP2) Scientific Advisory Board (2020).

### C. Contributions to Science

1. My early publications were related to epidemiological studies of infections by *Enterobacteriaceae* and other bacteria that cause diarrheal diseases. I authored the first report on the cloning and nucleotide sequencing of the enterotoxin genes of *Vibrio cholerae*, the causative agent of cholera. This information was considered critical to the development of new cholera vaccines. When I joined the laboratory of Richard Novick, a member of the US Academy of Sciences, my interest shifted to the study of DNA replication in small, multi-copy plasmids of *Staphylococcus aureus*. I discovered two novel genetic elements on the multicopy plasmid pT181 – *cmp*, a cis-acting replication enhancer, and *pre*, a site-specific recombinase. I also contributed to the characterization of the plasmid's origin of replication.
  - a. **Gennaro M.L.** and Novick R.P. *cmp*, a cis-acting plasmid locus that increases the interaction between replication origin and initiator protein. *Journal of Bacteriology*.168, 160-166. (1986)
  - b. **Gennaro M.L.**, Kornblum J. and Novick R.P. A site-specific recombination function in *S. aureus* plasmids. *Journal of Bacteriology*. 169, 2601-2610. (1987)
  - c. **Gennaro M.L.** and Novick R.P. An enhancer of DNA replication. *Journal of Bacteriology* 170, 5709-5717. (1988)
  - d. **Gennaro M.L.**, Iordanescu S., Novick R.P., Murray R.W., Steck T.R. and Khan S.K. Functional organization of the plasmid pT181 replication origin. *Journal of Bacteriology* 205, 355-362. (1989)
2. When I established my own laboratory, I first continued the characterization of the replication enhancer *cmp* and of chromosomally encoded proteins that bound to it. At the time, the discovery of a replication enhancer established a new paradigm in biology.
  - a. **Gennaro M.L.** Genetic evidence for replication enhancement from a distance. *Proceedings of the National Academy of Science USA* 90, 5529-5533. (1993)
  - b. Henriquez V., Milisavljevic V., Kahn J.D. and **Gennaro M.L.** Sequence and structure of *cmp*, the replication enhancer of the *Staphylococcus aureus* plasmid pT181. *Gene* 134, 93-98. (1993)
  - c. Colombo D., Iordanescu S. and **Gennaro M.L.** Replication enhancer requirement for recognition of heterologous replication origin by an initiator protein. *Plasmid* 33, 232-234. (1995)
  - d. Zhang Q, Soares de Oliveira S., Colangeli R. and **Gennaro M.L.** Binding of a novel host factor to the pT181 plasmid replication enhancer. *Journal of Bacteriology*. 179, 684-688. (1997)
3. In the mid-eighties, tuberculosis became rampant in New York City, prompting new interest in research on this global disease. I started working on immunological markers of tuberculosis disease. Work from my laboratory led to the realization that tuberculosis is associated with a diverse antibody repertoire, to identifying novel serodominant antigens of *M. tuberculosis*, to devising dedicated rapid serology methods, and eventually to characterizing the entire seroreactive immunoproteome of *M. tuberculosis* using high-throughput methods and systems biology data analyses. My work in biomarker research has also contributed the development of RNA flow cytometry, a novel method that achieves high-throughput measurement of single-cell gene expression by combining in-situ nucleic acid hybridization with flow cytometry. I also recently contributed to a multidisciplinary study leading to the isolation and characterization of human monoclonal antibodies against mycobacterial lipoarabinomannan.
  - a. Lyashchenko K., Colangeli R., Houde M., Al Jahdali H., Menzies D. and **Gennaro M.L.** Heterogeneous antibody responses in tuberculosis. *Infection and Immunity* 66, 3936-3940. (1998)
  - b. Kunnath-Velayudhan S., Salamon H., Wang H.-Y., Davidow A.L., Molina D.M., Huynh V.T., Cirillo D.M., Michel G., Elizabeth A. Talbot E.A., Mark D. Perkins M.D., Philip L. Felgner P.L., Liang X., **Gennaro M.L.** Dynamic antibody responses to the Mycobacterium tuberculosis proteome. *Proceedings of the National Academy of Sciences USA* 107:14703-14708. (2010)
  - c. Kunnath-Velayudhan S., Davidow A.L., Wang H.-Y., Molina D.M., Huynh V.T., Salamon H., Pine R., Michel G., Perkins M.D., Liang X., Felgner P.L., Flynn J.L., Catanzaro A., and **Gennaro M.L.** Proteome-scale antibody responses and outcome of Mycobacterium tuberculosis infection in non-human primates and in tuberculosis patients. *Journal of Infectious Diseases* 206:697-705. (2012)

- d. Arriguucci R., Bushkin Y., Radford F., Lakehal K., Vir P., Pine R., Martin D., Sugarman J., Zhao Y., Yap G.S., Lardizabal A.A., Tyagi S., **Gennaro M.L.** FISH-Flow, a protocol for the concurrent detection of mRNA and protein in single cells using fluorescence in situ hybridization and flow cytometry. *Nat Protoc.* 12:1245-1260. doi: 10.1038/nprot.2017.039. (2017) Epub 2017 May 18.
4. To understand how the pathogen withstands host insult, my laboratory has used in vitro and animal models to study stress responses of *M. tuberculosis*. We reported key aspects of the transcriptional remodeling of *M. tuberculosis* that occurs during mouse lung infection, including changes in mycobacterial central metabolism and respiratory pathways. These observations contribute to the identification of targets for antibacterial compounds. We recently reported a novel envelope stress response system in *M. tuberculosis* that was previously found in Gram-negative bacteria. The work provided a novel example of convergent evolution of critical bacterial stress response mechanisms. Moreover, we reconstructed the full network of regulatory interactions among *M. tuberculosis* sigma factors, proteins that drive transcriptional remodeling under stress conditions. This work uncovered regulatory network dynamics that underlie mycobacterial metabolic reprogramming during stress.
- a. Shi L., Jung Y.-J., Tyagi S., **Gennaro M.L.\***, and North R. Expression of Th1-mediated immunity in mouse lung induces a Mycobacterium tuberculosis transcription pattern characteristic of nonreplicating persistence. *Proceedings of the National Academy of Sciences USA* 100, 241-246. (2003) (\*Corresponding author)
- b. Shi L., Sohaskey C.D., Kana B.D., Dawes S., North R.J., Mizrahi V. and **Gennaro M.L.** Changes in energy metabolism in Mycobacterium tuberculosis in mouse lung and under in vitro conditions affecting aerobic respiration. *Proceedings of the National Academy of Sciences USA* 102:15629-34. (2005)
- c. Datta P., Ravi J., Guerrini V., Chauhan R., Neiditch M.B., Shell S.S., Fortune S.M., Hancioglu B., Igoshin O., **Gennaro M.L.** The Psp system of Mycobacterium tuberculosis integrates envelope stress sensing and envelope preserving functions. *Molecular Microbiology* 97:408-422. (2015)
- d. Manganelli R. and **Gennaro M.L.** Protecting from Envelope Stress: Variations on the Phage-Shock-Protein Theme. *Trends Microbiol.* 2016 PMID: 27865622 DOI: 10.1016/j.tim.2016.10.001
5. We have also studied the dysregulation of macrophage lipid metabolism in *M. tuberculosis* infection, which is central to the formation of the tuberculosis granuloma (the hallmark lung lesion). We demonstrated that the antibacterial action of vitamin D is explained by a novel anti-lipogenic effect, in addition to the known induction of host antibacterial peptides. We also found that macrophages and other immune cells in lesions of the murine tuberculous lung undergo reprogramming of central metabolism, similar to that found in cancer cells (Warburg effect). Moreover, our discovery that the lipid-lowering statins have antimycobacterial effects when used to treat infected cells has led to discovering an adjunctive effect of statins in anti-tuberculosis therapy and the underlying mechanism and opened the way to an NIH-funded clinical trial in South Africa. Thus, our work has been contributing to the burgeoning field of host-directed tuberculosis therapy. Our recent characterization of tuberculous foam cells (lipid-laden macrophages) breaks new ground in foam cell research by revealing that foam cell biogenesis in tuberculosis occurs differently from the atherogenic foam cell formation, which has been the paradigm for foam cell biology. We have recently commented on foam cell biogenesis in EVALI (vaping-associated lung injury) in *Lancet Resp Dis*.
- a. Salamon H., Bruiners N., Lakehal K., Shi L., Ravi J., Yamaguchi K.D., Pine R., and **Gennaro M.L.** Cutting Edge: Vitamin D regulates lipid metabolism in Mycobacterium tuberculosis infection. *Journal of Immunology* 193:30-34. (2014)
- b. Guerrini V., Prideaux B., Blanc L., Bruiners N., Arriguucci R., Singh S., Ho-Liang H.P., Salamon H., Chen P.Y., Lakehal K., Subbian S., O'Brien P., Via L.E., Barry C.E. 3rd, Dartois V., **Gennaro M.L.** Storage lipid studies in tuberculosis reveal that foam cell biogenesis is disease-specific. *PLoS Pathog.* 14:e1007223 (2018) doi: 10.1371/journal.ppat.1007223. eCollection 2018 Aug.
- c. Guerrini V. and **Gennaro M.L.** Foam cells: one size doesn't fit all. *Trends Immunol.* (2019) Dec;40(12):1163-1179. doi: 10.1016/j.it.2019.10.002. Epub 2019 Nov 12.
- d. Bruiners N., Dutta N.K., Guerrini V., Salamon H., Yamaguchi K.D., Karakousis P.C., **Gennaro M.L.** The anti-tubercular activity of simvastatin is mediated by cholesterol-dependent regulation of autophagy via the AMPK-mTORC1-TFEB axis. *J. Lipid Res.* 2020 Aug 26; jlr.RA120000895. doi: 10.1194/jlr.RA120000895.

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