BIOGRAPHICAL SKETCH
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NAME: Georgios Chamilos

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

POSITION TITLE: Professor, Clinical Microbiology and Microbial Pathogenesis

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
University of Athens, Greece	M.D.	07/1996	Medicine
Department of Therapeutics, University of Athens	M.D.	03/2003	Residency
University of Texas MD Anderson Cancer Center	Postdoctoral	06/2005	Mycology
University of Texas MD Anderson Cancer Center	Postdoctoral	06/2009	Immunology
University of Texas MD Anderson Cancer Center		06/2009	Infectious Diseases Clinical Fellowship
University of Athens, Therapeutic Clinics	PhD	07/2007	Hematology, Immunocompromised patients
Laboratory of Infectious Diseases, University of Crete	Postdoctoral	06/2010	Immunology

A. Personal Statement

As a physical-scientist, I developed a strong interest on understanding pathogenesis of the most devastating human infectious diseases in the immunocompromised host, those caused by airborne filamentous fungi (molds). Focus of my research as a PI (2009-present) is to identify specialized effector mechanisms employed by professional phagocytes during dynamic interactions with *Aspergillus* and the Mucorales, and fungal pathogenetic strategies that subvert physiological immune responses. My research includes immunological studies in transgenic mice, animal models of invasive mold infections, and primary human phagocytes from healthy individuals and immunocompromised patients. Furthermore, our group is interested on molecular mechanisms of regulation of phagosome biogenesis in inflammation and immune homeostasis. Focus of ongoing research is understanding the role of LC3 associated phagocytosis (LAP) on decision making of professional phagocytic cells shaping innate and adaptive immunity. At the molecular level we aim to delineate the role of LAP in inter-organelle cross talk during phagocytosis, endomembrane repair, phagolysosome integrity and fusion, antigen presentation and optimal regulation of inflammatory cell signaling in health and disease.

The scientific implications of my work on molecular mechanisms of regulation of phagosome biogenesis during fungal infection have broad physiological relevance on phagocyte biology. The translational part of my research aims to develop (i) novel biomarkers of immune deactivation (immmunoparalysis) to stratify patients at high risk for invasive fungal diseases and (ii) host-directed therapies that restore immunometabolic defects in phagocytes, as a mean to enhance fungal clearance, prevent inflammatory immunopathology, and improve disease outcome.

B. Positions and Honors

Positions and Employment

2011- 2016 Attending Physician, Internal Medicine/Infectious Diseases Department, University Hospital of Heraklion, Crete

2016 – 2020 Associate Professor, Head of the Department of Clinical Microbiology and Microbial

Pathogenesis, School of Medicine, University of Crete, Greece

2020- Present Professor, Head of the Department of Clinical Microbiology and Microbial Pathogenesis, School of Medicine, University of Crete, Greece

2016 – Present Affiliated Professor, Department of Internal Medicine and Infectious Diseases, School of Medicine, University of Crete, Greece

2018 – Present Group Leader, Institute of Molecular Biology and Biotechnology (IMBB), Foundation for Research and Technology Hellas, Crete, Greece

2021 – 2022 Chairman of the Bioethics Committee of FORTH, Greece

2020 – Present Member of National Pharmacovigilance Committee (2/2020-present)

2023 – 2025 Member of the National Organization for Medicine (EOF)

2023 – Present Elected Vice Dean, Medical School, University of Crete, Greece

Licensures and Board Certifications

2003-Present Board-certified in Internal Medicine

1997-Present Licensed in as a Medical Doctor in Greece

Other Experience and Professional Memberships

2010 – Present Cretan Medical Society

2016 – Present Hellenic Society of Medical Mycology

2009 – Present Member of Infectious Diseases Society of America (IDSA)

2010 – Present Member of Faculty if 1000; field: Mycology

2018 – Present Member, EORTC infectious Diseases Group (European Organization for Research and Treatment of Cancer)

2018 – Present Member, European Hematology Association (EHA)

2020 – Present Member, International Immunocompromised Host Society (ICHS)

2020 – Present Member, International Society for Human and Animal Mycology (ISHAM)

2009 – Present Ad Hoc reviewer for various peer reviewed journals including:

Cell Host and Microbe, Nature Communications, PLoS Pathogens, Frontiers in Cellular and Infection Microbiology, Clin Infect Dis, Antimicrobial Agents Chemotherapy, Journal of Antimicrobial Chemotherapy, Journal of Infectious Diseases, Clin Infect Dis, Medical Mycology, and more

2014 – Present Reviewer for the French National Research Agency (ANR)

2018 – Present Reviewer for the Hellenic National Council of Research & Technology

Honors

2005 - 1st place winner of the Bristol-Myers Squibb Award in Clinical/Translational Research 9th Trainee Recognition Day, The University of Texas M. D. Anderson Cancer Center (2005)

2006 - 1st place winner of Research Poster Competition. American College of Physicians (ACP) Associates Day 2006 - Texas Academy of Internal Medicine (TAIM), Clear Lake City, TX, USA

2008 - 1st place winner, basic research poster competition, 2nd Infections in Cancer Symposium, Houston, TX, USA

2007 - The Kimberly Patterson Fellowship in Leukemia Research award, The University of Texas M. D. Anderson Cancer Center (2007)

2010 - Postdoctoral Marie Curie Reintegration fellowship, (260210)

2014 - Winner for Best Abstract Submission, 6th Advances against Aspergillosis, Madrid

2014 - Greek Government, General Secretary for Research and Technology (525171)

2015 - Greek Government, Research Programs for Excellence IKY/Siemens (2894)

C. Contribution to Science

Major accomplishments as independent investigator (2009-present)

1). We were the first to demonstrate **the major role of a noncanonical autophagy pathway, termed LC3 associated phagocytosis (LAP), in antifungal host defense**. In this work we identified the selective mechanism of induction of LAP during intracellular swelling of *Aspergillus* conidia via Dectin-1/Syk/NADPH oxidase-mediated reactive oxygen species (ROS) production. In addition, these studies uncovered a novel immunosupressive mechanism of action of corticosteroids, a major risk factor for human aspergillosis, mediated via inhibition of Src/Syk phosphorylation and downstream NADPH oxidase-dependent activation of LAP *(**Kyrmizi et al., J Immunol 2013**)*. In a follow up collaborative work, we explored mechanisms of harnessing LAP defects in chronic granulomatous disease (CGD), a primary immmunodeficieny characterized by genetic defects in components of NADPH oxidase complex and unique susceptibility for invasive pulmonary asperigillosis. Importantly, we demonstrated that treatment with the IL1Ra inhibitor Anakinra markedly improved deregulated inflammatory responses and outcome of patients with CGD via restoration of LAP (***Smeekens et al., PNAS 2014***).

2). Our group also discovered that ***Aspergillus* cell wall melanin, a major virulent factor of fungal pathogens with unknown molecular mechanism of action, targets LAP to promote fungal pathogenicity** (**Akoumianaki *T et al., Cell Host Microbe 2016***). Specifically, we discovered that cell wall melanin removal that physiollogicaly occurs during intracellular swelling of *Aspergillus* conidia is a prerequisite for activation of LAP and subsequent killing of fungal conidia by macrophages. Furtehrmore, we demonstrated that the attenuated virulence of melanin-deficient *A. fumigatus* mutants is fully restored in LAP-deficient human macrophages and in mice upon conditional inactivation of LAP-related genes (*Atg5*) in hematopoietic cells. Importantly, this work also demonstrated that LAP blockade is a general property of melanin pigments.

3). **Our group demonstrated the master regulatory role of Ca^{2+}/calmodulin (CaM) signaling on activation of LAP** and discovered that molecular mechanism of inhibition of LAP by melanin. Specifically, **we found that Ca^{2+} sequestration inside the phagosome by melanin abrogates CaM recruitment to inhibit LAP** (Kyrmizi et al., **Nat Microbiol 2018**). Specifically, we identifed a novel mechanism of Ca^{2+}/CaM signaling activation on the phagosome membrane that requires intracellular Ca^{2+} stores from the ER, ER-phagosome communication and periphagosomal Ca^{2+} release. We demonstrated that Ca^{2+}/CaM signaling is a master regulator of NADPH oxidase mediated ROS production and other downstream molecular components of LAP, and provided genetic evidence for the physiological importance of this pathway in development of human aspergillosis. In addition, we disocovered that Ca^{2+} sequestration by fungal melanin inside the phagosome abbrogates periphagosomal Ca^{2+} release and CaM recruitment to inhibit LAP (***Kyrmizi I t al., Nat Microbiology*, 2018 3(7):791-803**). These findings reveal the important role of Ca^{2+}-CaM signaling in antifungal immunity and identify an immunological function of Ca^{2+} binding by melanin pigments with broad physiological implications.

4) In collaboration with **Ibrahim and Bruno labs**, we **discovered a novel mechanism of prolonged intracellular persistence of Mucorales conidia inside macrophages via targeting LAP.** *(Andrianaki et al., **Nat Commun 2018).*** Dissecting **LAP-indepepent antifungal effector pathways in macrophages** has been aslo a research priority of our group. We identified **a novel mechanism of intracellular "persistance" of Mucorales** fungi, mediated via melanin-induced inhibition of LAP and **revealed the important role of nutritional immunity via iron starvation inside the phagosome** as an important effector mechanism to inhibit fungal growth and restrict pathogenicity ***(Andrianaki et al., Nat Commun 2018 9:3333).*** This work leads to a new pathogenetic model of fungal disease linking (i) phagosome biogenesis defects in LAP with (ii) abnormalities

in iron metabolism in macrophages as the two fundamental requirements for development of invasive fungal disease.

5) We identified **a novel mechanism of immune deactivation in sepsis (sepsis immunoparalysis)** linking defective **IL-6 signaling with microtubule disorganization, impaired ERK trafficking and LAP blockade** (***Akoumianaki et al.;* Cell Host Microbe 2021**). Another important direction of the lab is understanding the role of phagosome biogenesis defects in sepsis immunosupression, an aquired immunodeficiency of unknown etiology in patients recovering from severe infections associated with invasive mold infections. In this project we discovred **a selective defect in LAP pathway in phagocytes of a distinct cohort of sepsis patients** associated with increasesd severity of diseases and marked increase in susceptibility to secondary infections. These results were phenocopied in a mouse model of severe sepsis and associated with increased susceptibility for development of *Aspergillus* pulmonary infection. Mechanistically, we identifed a novel signaling pathway regulating LAP via ERK-dependent phosphoyrlation of p47phox subunit of NADPH oxidase complex, which is inhibited in late phase of sepsis. Notably, we also discovered that IL-6/JAK2 signaling regulates microtubule organization and ERK trafficking from the endosomal combartment to the phagosome of monocytes/macrophages and is selectively impaired in LAP defective macrophages following recovery from severe sepsis. This work delinates a novel mechanisms of sepsis immunosupression and provides **a new molecular link between cytokine signaling, endosomal traficking and LAP-dependent phagosome respones**.

6) Through an ERC Consolidator Grant (iMAC-FUN) we identified a novel host defense mechanism against Mucorales fungi, which is orchestrated by albumin. Specifically, we discovered that **albumin-bound FFAs display potent antifungal activity** selectively against Mucorales (A. Pikoulas, et al 2025). These physiological lipids target the pathogenicity program of Mucorales by inhibiting protein synthesis, rendering these pathogens avirulent in vivo. In parallel work, we delineated the **mechanism of antifungal activity of FFAs** via altering mitochondrial metabolism of Mucorales. Furthermore, we found that metabolic rewiring of macrophages towards OXPHOS **targets lipid droplets to Mucorales-containing phagosomes** and inhibits fungal growth through the activity of FFAs (submitted ms).

Relevant Publications

1. Pikoulas A, Morianos I, Nidris VN, Hamdy R, López-López A, Moran-Garrido M, Muthu V, Halabalaki M, Papadovasilaki M, Irene K, Gu Y, Aerts R, Mercier T, Vanbiervliet Y, Cho SY, Spallone A, Samonakis D, Kastritis E, Drakos E, Tzardi M, Eliopoulos A, Georgila K, Carvalho A, Kurzai O, Rudramurthy S, Lanternier F, Petratos K, Maertens J, Bruno V, Kontoyiannis D, Barbas C, Soliman S, Ibrahim A, **Chamilos G*.** Albumin orchestrates a natural host defense mechanism against mucormycosis. Res Sq [Preprint]. 2024 Dec 3:rs.3.rs-5441197. doi: 10.21203/rs.3.rs-5441197/v1. *** Corresponding author**
2. Seldeslachts L, Staels F, Gkountzinopoulou M, Jacobs C, Tielemans B, Vanhoffelen E, Reséndiz-Sharpe A, De Herdt L, Haughton J, Prezzemolo T, Burton O, Feys S, van de Veerdonk FL, Carvalho A, Naesens L, Matthys P, Lagrou K, Verbeken E, **Chamilos G**, Wauters J, Humblet-Baron S, Vande Velde G. Damping excessive viral-induced IFN-γ rescues the impaired anti-Aspergillus host immune response in influenza-associated pulmonary aspergillosis. ***EBioMedicine.*** 2024 Oct;108:105347. doi: 10.1016/j.ebiom.2024.105347.
3. Akoumianaki T, Vaporidi K, Diamantaki E, Pène F, Beau R, Gresnigt MS, Gkountzinopulou M, Venichaki M, Drakos E, El-Benna J, Samonis G, Le KTT, Kumar V, Georgopoulos D, van de Veerdonk FL, Netea MG, Latge JP, **Chamilos G***. Uncoupling of IL-6 signaling and LC3-associated phagocytosis drives immunoparalysis during sepsis. ***Cell Host Microbe***. 2021 Aug 11;29(8):1277-1293.e6. doi: 10.1016/j.chom.2021.06.002. *** Corresponding author**
4. Soliman SSM, Baldin C, Gu Y, Singh S, Gebremariam T, Swidergall M, Alqarihi A, Youssef EG, Alkhazraji S, Pikoulas A, Perske C, Venkataramani V, Rich A, Bruno VM, Hotopp JD, Mantis NJ, Edwards JE Jr, Filler SG, **Chamilos G**, Vitetta ES, Ibrahim AS. Mucoricin is a ricin-like toxin that is critical for the pathogenesis of mucormycosis. ***Nat Microbiol***. 2021 Mar;6(3):313-326. doi: 10.1038/s41564-020-00837-0.

5. Andrianaki AM, Kyrmizi I, Thanopoulou K, Baldin C, Drakos E, Soliman SSM, Shetty AC, McCracken C, Akoumianaki T, Stylianou K, Ioannou P, Pontikoglou C, Papadaki HA, Tzardi M, Belle V, Etienne E, Beauvais A, Samonis G, Kontoyiannis DP, Andreakos E, Bruno VM, Ibrahim AS, **Chamilos G***. Iron restriction inside macrophages regulates pulmonary host defense against Rhizopus species. ***Nat Commun***. 2018 Aug 20;9(1):3333. doi: 10.1038/s41467-018-05820-2. *** Corresponding author**
6. Kyrmizi I, Ferreira H, Carvalho A, Figueroa JAL, Zarmpas P, Cunha C, Akoumianaki T, Stylianou K, Deepe GS Jr, Samonis G, Lacerda JF, Campos A Jr, Kontoyiannis DP, Mihalopoulos N, Kwon-Chung KJ, El-Benna J, Valsecchi I, Beauvais A, Brakhage AA, Neves NM, Latge JP, **Chamilos G***. Calcium sequestration by fungal melanin inhibits calcium-calmodulin signalling to prevent LC3-associated phagocytosis. ***Nat Microbiol***. 2018 Jul;3(7):791-803. doi: 10.1038/s41564-018-0167-x. *** Corresponding author**
7. Akoumianaki T, Kyrmizi I, Valsecchi I, Gresnigt MS, Samonis G, Drakos E, Boumpas D, Muszkieta L, Prevost MC, Kontoyiannis DP, Chavakis T, Netea MG, van de Veerdonk FL, Brakhage AA, El-Benna J, Beauvais A, Latge JP, **Chamilos G***. Aspergillus Cell Wall Melanin Blocks LC3-Associated Phagocytosis to Promote Pathogenicity. ***Cell Host Microbe***. 2016 Jan 13;19(1):79-90. doi: 10.1016/j.chom.2015.12.002. *** Corresponding author**
8. Kyrmizi I, Gresnigt MS, Akoumianaki T, Samonis G, Sidiropoulos P, Boumpas D, Netea MG, van de Veerdonk FL, Kontoyiannis DP, **Chamilos G***. Corticosteroids block autophagy protein recruitment in Aspergillus fumigatus phagosomes via targeting dectin-1/Syk kinase signaling. ***J Immunol***. 2013 Aug 1;191(3):1287-99. doi: 10.4049/jimmunol.1300132. *** Corresponding author**
9. **Chamilos G**, Gregorio J, Meller S, Lande R, Kontoyiannis DP, Modlin RL, Gilliet M. Cytosolic sensing of extracellular self-DNA transported into monocytes by the antimicrobial peptide LL37. Blood. 2012 Nov 1;120(18):3699-707. doi: 10.1182/blood-2012-01-401364.
10. **Chamilos G**, Lewis RE, Hu J, Xiao L, Zal T, Gilliet M, Halder G, Kontoyiannis DP. Drosophila melanogaster as a model host to dissect the immunopathogenesis of zygomycosis. Proc Natl Acad Sci U S A. 2008 Jul 8;105(27):9367-72. doi: 10.1073/pnas.0709578105.

Complete List of Published Work in My Bibliography:

https://pubmed.ncbi.nlm.nih.gov/?term=chamilos+g+OR+hamilos+g&sort=date&size=200

D. Research Support

Ongoing Research Support and Projects

2023 - 2025: GSRI-11412. General Secretariat for Research and Innovation. MPI, Eliopoulos (Scientifi Coordinator), Chamilos (Scientific Coordinator). Project Acronym: Pro-sCAP. Title: A systems medicine approach to dissect mechanisms of immune dysfunction and develop biomarkers to predict and prevent complications of severe community acquired pneumonia (sCAP). **Budget:** 4.723.050,00 €. **Budget for the team** at University of Crete: 1, 700,000€. This is a multicenter National Study aiming to dissect pathogenesis and complications of severe CAP, including fungal superinfections. The major goal of this project is to generate a functional BioBank of patients with sCAP and identify underlying molecular mechanisms of immune dysfunction in phagocytes. The project will also collect biopsy proven invasive mold infection over the last 10 years.

2020 - 2026: European Research Council Consolidator Grant: ERC CoG 864957. Chamilos (PI). Acronym: iMAC-FUN. Title: Dissecting novel mechanisms of iron regulation during macrophage-fungal interplay. **Budget:** 2,000,000€. This project will evaluate molecular mechanisms of regulation of nutritional immunity in macrophages and dissect their role of deregulated iron homeostasis in development of invasive mold infections.

2020 - 2026: H2020-SC1-BHC-2018-2020. MPI, Veerdonk (Scientific Coordinator), Chamilos (PI, WP7). Acronym: HDM-FUN. Host-Directed-Medicine in Invasive Fungal Infections. **Budget for the team**: 300,000€. This project will evaluate mechanisms of immunoparalysis in sepsis aiming to develop host directed therapeutic strategies with cytokines. Our lab will study phagosome biogenesis and immunological responses in alveolar macrophages and monocyte derived macrophages obtained from cryopreserved samples.

2023 – 2026 HORIZON-MSCA-2023-PF-01 Research Project to Support Post-Doctoral Fellows. Akrivi Dimitra Daskalaki PI. **(Chamilos Co-I, Scientific Coordinator).** Project Acronym: POLAR. Title: Phagosomal LC3's

alternative role**. Budget:** 153,486.72€. This project investigates a novel mechanism of prolonged and pulsatile LC3 lipidation on *Aspergillus* phagosomes, a process mediated upon sensing of a unique cell wall polysaccharide by a specialized C-type lectin receptor.

Completed Research (Previous 5 years)

2022 – 2024: General Secretariat for Research and Innovation (GSRI) and the Hellenic Foundation for Research and Innovation (HFRI): 3rd Call for H.F.R.I. Research Projects to Support Post-Doctoral Fellows. 7054. Morianos (PI), Chamilos (Co-I, Scientific Coordinator). Project Acronym: ALANTIN. Title: Exploring a novel role of Albumin in Antimicrobial Immunity. **Budget:** 120,000€. Following the seminal discovery of the MUCOR_ADVANCE group on the major role of albumin-bound FFAs in host defense against Mucorales, this project will explore the role of albumin in cellular immunity against bacterial and fungal pathogens.

2022 - 2025: Hellenic Foundation for Research and Innovation (HFRI): 3rd Call for H.F.R.I. 11056. Chamilos (PI). Research Projects to Support PhD stundents (award to Stavroula Baimba, PhD student). **Budget:** €32400.Title Dissecting the Molecular mechanisms of neutrophil-Mucorales interplay. This project is studying molecular mechanisms regulating coordinated clustering (swarming) of neutrophils against Mucorales.

2020 - 2023: "La Caixa" Banking Foundation call Health Research. 225186004. MPI, Carhvalo (PI), Barbas (PI), Veerdonk (PI), Chamilos (PI, WP4). Acronym: TRANS-CPA. A Transdisciplinary Approach to the Identification of Personalized Biomarkers and Therapeutic Targets for Chronic Pulmonary Aspergillosis (CPA). **Budget for the team**: 100,000€. This project will evaluate mechanisms of deregulation of macrophage immunity in chronic pulmonary aspergillosis. Our lab will explore the role of LAP defects in pathogenesis of CPA

2015 - 2018: Merieux Institute Advanced Research Grant. 4719. Chamilos: PI. Exploring the role of LC3 associated phagocytosis in sepsis induced immunosuppression. **Budget:** 100, 000 €. This project explored the role of LAP defects in pathogenesis of sepsis immmunoparalysis and the underlying molecular mechanisms.

2016 - 2018: SPECIAL GRANT AND SUPPORT PROGRAM FOR SCHOLARS' ASSOCIATION MEMBERS from Onassis Foundation. R ZM 003-1/2016-2017. Kyrmizi (PI), Chamilos (co-I, Scientific Coordinator) Exploring novel mechanisms of killing of "persister" Mucorales conidia inside macrophages. **Budget:** 20,000 €. This project evaluated the molecular mechanisms of intracellular persistence of Mucorales spores inside macrophages during pulomonary infection.

2017 - 2019: Ministry of Development, Special Account for Research University of Crete. Chamilos (PI), 4759. Dissecting Novel Molecular Pathways regulating PHAGOsome biogenesis during host-FUNgal interplay: PHAGO-FUN. **Budget**: 10, 000€. This project evaluated the role of LAP pathway in immunity against *Aspergillus*.

2018 - 2021: Hellenic Foundation for Research and innovation (H.F.R.I). 1787. 1st Call for H.F.R.I. Research Projects to Support Post-Doctoral Fellows. Akoumianaki (PI), Chamilos: (co-I, Scientific Coordinator). Acronym: Phago-FUN. **Title:** Delineating molecular mechanisms of PHAGOsome dysFUNction underlying Sepsis Immunossupression: A Roadmap to Personalized Medicine in Sepsis. **Budget:** 180, 000 €. This project explored the molecular mechanisms of immune dysfunction in sepsis phagocytes induced by sepsis and identified a central role of IL-6 in regulation of cytoskeleton organization, endosomal trafficking and phagosome biogenesis.