

PERSONAL INFORMATION	
SURNAME	KYRMIZI
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## EDUCATION

<b>10.2003 - 08.2006</b>	Department of Biology, University of Crete and IMBB-FORTH, Crete, Greece, PhD in Biology.  Title: <i>“Crossregulatory pathways of expression between hepatic transcription factors”</i>
<b>10.2001 - 09.2003</b>	Department of Biology, University of Crete and IMBB-FORTH, Crete, Greece, MSc in Molecular Biology- Biomedicine Grade: 9,27/10.  Title: <i>“Gene expression and morphology study in the liver of liver-specific HNFKO mouse”</i> .
<b>09.1997 - 09.2001</b>	Department of Biology, University of Crete, Crete, Greece, Bsc in Biology, Grade: 8,45/10.

## RESEARCH/WORKING EXPERIENCE

<b>12.2010 - Present</b>	<p><b>Current position</b></p> <p>Post-Doctoral research Fellow in Host Defense and Fungal Pathogenesis Laboratory, School of Medicine, University of Crete, Greece.</p> <p><u>Research interests:</u></p> <ul style="list-style-type: none"> <li>• Dissecting signaling pathways regulating phagosome biogenesis and macrophage immunity against airborne opportunistic human fungal pathogens.</li> <li>• Understanding molecular mechanisms of immunodeficiency in myeloid phagocytes with a central role in development of invasive fungal disease</li> <li>• Harnessing macrophage metabolism as a novel therapy in patients with immunodeficiency.</li> </ul>
<b>09.2006 – 11.2010</b>	<p><b>Previous position</b></p> <p>Post-Doctoral research Fellow in Rheumatology and Autoimmune diseases Lab, School of Medicine, University of Crete, Crete, Greece.</p> <p><u>Research interest:</u></p> <p>Role of Tpl2 kinase in signaling pathways downstream of FcγRs and in pathogenesis of systemic autoimmune diseases in mice.</p>

- Brakhage A, Goldman M., Schmidt F, **Kyrmizi I**, Chamilos G. Isolation of *Aspergillus fumigatus* conidia-containing phagolysosomes and following immunofluorescence staining. *STAR Protocols* **2021** Vol2,100328. <https://doi.org/10.1016/j.xpro.2021.100328>
- Klionsky D. et al. Guidelines for the use and interpretation of assays for monitoring autophagy (4th edition). *Autophagy* **2021**, Jan;17(1):1-382. <https://doi.org/10.1080/15548627.2020.1797280>.
- **Kyrmizi I**, Ferreira H, Carvalho A., Landero Figueroa J.A., Zarmas P, Cunha C, Akoumianaki T, Stylianou K, Deepe G.S.Jr, Samonis G, Lacerda J.F., Campos A.Jr, Kontoyiannis D.P., Mihalopoulos N., Kwon-Chung K.J., El-Benna J., Valsecchi I., Beauvais A., Brakhage A.A., Neves N.M., Latge J.P., and Chamilos G. Ca<sup>2+</sup> sequestration by fungal melanin blocks Ca<sup>2+</sup>/Calmodulin-dependent activation of LC3-associated phagocytosis (LAP) **2018** (*Nature Microbiology* **2018** Vol 3, pages791–803). <https://doi.org/10.1038/s41564-018-0167-x>
- Andrianaki AM#, **Kyrmizi I**#, Samonis G., Kontoyiannis DP, Ibrahim AS and Chamilos G. "Iron restriction inside the phagosome of macrophages is an essential host defense mechanism against Mucorales" (*Nature Communications* **2018**, Vol. 9, Article number: 3333 )# equal contribution. <https://doi.org/10.1038/s41467-018-05820-2>
- Chamilos G, Akoumianaki T, **Kyrmizi I**, Axel Brakhage, Beauvais A. and Latge. J.P. Melanin targets LC3-associated phagocytosis (LAP): A novel pathogenetic mechanism in fungal disease. *Autophagy* **2016** Vol. 12, No. 5, 1-2. doi: [10.1080/15548627.2016.1157242](https://doi.org/10.1080/15548627.2016.1157242)  
Akoumianaki T, **Kyrmizi I**, Valsecchi I, Gresnigt MS, Samonis G, Drakos E, Boumpas D, Muszkietal, Prevost MC, Kontoyiannis DP, Chavakis T, Netea MG, van de Veerdonk FL, Brakhage AA, El-Benna J, Beauvais A, Latge JP, Chamilos G. Cell wall melanin regulates fungal pathogenicity via targeting non canonical autophagy *Cell Host Microbe* **2016** Jan 13;19(1):79-90. doi: [10.1016/j.chom.2015.12.002](https://doi.org/10.1016/j.chom.2015.12.002)
- Klionsky D.J et al. Guidelines for the use and interpretation of assays for monitoring autophagy (3rd edition). *Autophagy* **2016** Jan 2;12(1):1 222 (Co-author). doi: [10.1080/15548627.2015.1100356](https://doi.org/10.1080/15548627.2015.1100356).
- Ioannou P, Andrianaki A, Akoumianaki T, **Kyrmizi I**, Albert N, Perlin D, Samonis G, Kontoyiannis DP, Chamilos G. Albumin Enhances Caspofungin Activity against *Aspergillus* Species by Facilitating Drug Delivery to Germinating Hyphae. *Antimicrob Agents Chemother* **2015** Dec 7;60A(3):1226-33. doi: [10.1128/AAC.02026-15](https://doi.org/10.1128/AAC.02026-15)
- **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**191(3):1287-99. doi: [10.4049/jimmunol.1300132](https://doi.org/10.4049/jimmunol.1300132)
- **Kyrmizi I.**, Ioannou M., Hatziapostolou M., Boumpas D.T. Tschlis PN. and Tassioulas I Tpl2 kinase regulates FcγR signaling and Immune thrombo-cytopenia in mice. *J Leukoc Biol.* **2013**.94(4):751-7. doi: [10.1189/jlb.0113039](https://doi.org/10.1189/jlb.0113039)
- Martinez-Jimenez CP, **Kyrmizi I**, Cardot P, Gonzalez FJ and Talianidis I.. Hepatocyte nuclear factor 4α coordinates a transcription factor network regulating hepatic fatty acid metabolism. *Mol Cell Biol.* **2010** Feb;30(3):565-77. doi: [10.1128/MCB.00927-09](https://doi.org/10.1128/MCB.00927-09)
- Stanulović V.S., **Kyrmizi I.**, Kruihof-de Julio M., Hoogenkamp M., Jan M. Ruijter, Talianidis I., Hakvoort T.B.M., and Lamers W.H. Hepatic HNF4α Deficiency Induces Periportal Expression of Glutamine Synthetase and Other Pericentral Enzymes. *Hepatology.* **2007** 45(2):433-44. doi: [10.1002/hep.21456](https://doi.org/10.1002/hep.21456).

- **Kyrmizi I**, Hatzis P, Katrakili N, Tronche F, Gonzalez FJ, and Talianidis I.. Plasticity and expanding complexity of the hepatic transcription factor network during liver development. *Genes Dev.* 2006 20(16):2293-305. doi: 10.1101/gad.390906.
- Hatzis P#, **Kyrmizi I**# and Talianidis I. .Mitogen-Activated Protein Kinase-Mediated Disruption of Enhancer-Promoter Communication Inhibits Hepatocyte Nuclear Factor4{alpha}Expression. *Mol Cell Biol.* 2006 26(19):7017-29. ) # *equal contribution* doi: 10.1128/MCB.00297-06.
- Kouskouti A. and **Kyrmizi I.** (Talianidis lab). Chromatin Immunoprecipitation (ChIP) Assay. "*The Epigenome network of Excellence*" 2005.  
† Featured publication (Editorial Commentary)

## CONFERENCES/WORKSHOPS

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- June 14-19 **2003**, Heraklion, Crete, Greece. "*Liver Development, Gene Regulation & Disease*"- EMBO Workshop.
- August 28- September 1, **2004**, Heidelberg, Germany, "*6<sup>th</sup> EMBL Transcription Meeting*". (Poster) "*Fundamental role of Hepatocyte Nuclear Factor 4 (HNF-4) in controlling transcription factor network operating in liver.*"
- September 10-13 **2006**, Athens, Greece "*1<sup>st</sup> International MUGEN Conference on Animal Models for Human Immunological Disease*"
- November 6-7, **2006**, Utrecht, Netherlands. "*TRANSREG STREP meeting*" (Oral presentation) "*Crossregulatory networks in hepatocytes*".
- October 24-27, **2007** Phoenix, Arizona **ACR** meeting. (Poster): "*FcγR and TLR-induced ERK1/2 activation and cytokine production in primary murine and human macrophages is regulated by the Tpl2 kinase.*"
- February 28 - March 1, **2008**, Toulouse, France, **EWRR** meeting (Poster): "*FcγR and TLR-induced ERK1/2 activation and cytokine production in primary murine and human macrophages is regulated by the Tpl2 kinase.*"
- February 26-28, **2009** Warsaw, Poland **EWRR** meeting. (Oral presentation and poster): "*FcγR and TLR-induced ERK1/2 activation and cytokine production in primary murine and human macrophages is regulated by the Tpl2 kinase*"
- June 10-13, **2009** Copenhagen, Denmark **EULAR** meeting. (Oral presentation): "*Tpl2 kinase regulates FcγR signaling and antibody-mediated pathogenic responses in vivo.*" (AWARDED)
- January 26-28 **2012**, Istanbul, Turkey, **5<sup>th</sup> Advances against Aspergillosis** meeting (Poster): "*β-glucan mediated autophagy induction regulates intracellular killing of Aspergillus fumigatus in human monocyte.*"
- February 27-March 1, **2014**, Madrid, Spain, **6<sup>th</sup> Advances against Aspergillosis** meeting (Poster): "*Noncanonical autophagy is a target of fungal cell wall melanin*".
- January 15-20, **2017 Galveston, TX, USA, GRC Conference** Immunology of Fungal Infections. *Novel molecular mechanisms regulating Aspergillus phagosome biogenesis*
- May 13-19 **2017**, La Colle-sur-Loup, France. **7<sup>th</sup> FEBS Advanced Lecture Course on Human Fungal Pathogens** (Accepted for poster presentation): "*Iron restriction inside the phagosome of macrophages is an essential host defense mechanism against Mucorales*".
- September 29-30 **2017**, Athens, Greece. **Master class: 'Advances in treatment of infections in immunocompromised patients with cancer'**. Oral presentation: A new protocol for immunophenotyping of cancer patients with infection.

## FELLOWSHIPS and AWARDS

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- 1997-2001:** State Scholarships Foundation (**IKY**) for undergraduate studies.
- 2001-2002:** Institute of Molecular Biology and Biotechnology (**IMBB**) Scholarship for post-graduate(MSc) studies.
- 2004-2006:** **“Alexander S. Onassis” Public Benefit Foundation Scholarship** for post-graduate (PhD) studies in IMBB,FORTH, Crete, Greece.
- 2009:** **Award** for Oral presentation in *EULAR* meeting, Copenhagen, Denmark,June10-13
- 2016-2018:** **Special Grant** and support for Scholars’ association members of **“Alexander S.Onassis” Public Benefit Foundation** for Post-Doctoral research in Host Defense and Fungal Pathogenesis ,Medical School, University of Crete, Greece. *Exploring novel mechanisms of killing of “persister” Mucorales conidia inside macrophages* Principal Investigator I.Kyrmizi, 20.000€, 24 months.

## SCIENTIFIC ACHIEVEMENTS

I identified that a specialized non-canonical autophagic pathway termed LC3 associated phagocytosis (LAP) plays a major role in phagosome maturation and killing of the human fungal pathogen *Aspergillus fumigatus*. Additionally, I discovered that corticosteroid receiving patients, which are susceptible to develop invasive aspergillosis, display a serious defect in LAP of *Aspergillus conidia* and further characterized the mechanism of this LAP blockade finding that corticosteroids target the Dectin-1/Src/Syk/NADPH oxidase signaling pathway (J Immunol. 2013; 191:1287-99).

I also identified that Calmodulin is a master regulator of phagosome biogenesis acting upstream of LC3 recruitment on *Aspergillus*-containing phagosomes. I discovered that fungal cell wall melanin of *Aspergillus conidia* interferes with this pathway by scavenging the intraphagosomal  $Ca^{+2}$ , supplied by the Endoplasmic Reticulum thus resulting in the blockade of Calmodulin activation, LC3 recruitment and phagosome maturation (Nature Microbiology,2018;3:791-803).

I am currently interested in investigating how lipid metabolism interferes with LC3-associated phagocytosis and efferocytosis. I identified that lipid modulation by cholesterol depletion reverses melanin-induced phagosome maturation arrest in *Aspergillus*-containing phagosomes. Most importantly I discovered that cholesterol depletion reverses LAP blockade in primary NADPH oxidase defective murine macrophages from CGD mice and human monocytes from CGD patients. (in preparation)