

PAGGETTI Jérôme



Group Leader - Tumor Stroma Interactions
Department of Cancer Research
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Date of birth: March 1st 1982
Nationality: French



EDUCATION

- 2020 **Full ADR (« Autorisation à diriger les recherches », right to supervise PhD candidates)**
University of Luxembourg, Luxembourg, Luxembourg
- 2018 **Junior ADR (« Autorisation à diriger les recherches », right to supervise one PhD candidate)**
University of Luxembourg, Luxembourg, Luxembourg
- 2009 **Ph.D. in Biochemistry, Cellular and Molecular Biology obtained with highest honors (mention très honorable).**
Faculty of Life Sciences, University of Burgundy, Dijon, France
- 2005 **Research Master of Science in Biology and Health (specialized in Biochemistry, Cellular and Molecular Biology) obtained with highest honors (mention très Bien) (1st of 29).**
Faculty of Life Sciences, University of Burgundy, Dijon, France

WORK EXPERIENCE

- Since January 2017 **Luxembourg Institute of Health - Department of Cancer Research - Tumor Stroma Interactions group.** Luxembourg.
Group Leader / Principal Investigator. Research on the interaction between leukemic cells and their microenvironment.
- January 2014- December 2016 **Luxembourg Institute of Health - Department of Oncology - Laboratory of Experimental Cancer Research.** Luxembourg.
Researcher in hemato-oncology. Research on the interaction between leukemic cells and their microenvironment.
- January 2010 to December 2013 **Luxembourg Institute of Health (formerly CRP-Santé) - Department of Oncology - Laboratory of Experimental Hemato-Oncology.** Luxembourg.
Post-doctoral researcher in hemato-oncology. Research on extracellular vesicles in chronic lymphocytic leukemia.
- October 2005 to December 2009 **INSERM (French National Institute of Health and Medical Research) Research Center 866, research group « Chromatin Dynamics in Hematopoiesis and Leukemogenesis »**
Faculty of Medicine, University of Burgundy, Dijon, France.
Ph.D. internship aimed at studying the role of the leukemia associated histone acetyltransferase MOZ in hematopoiesis and leukemogenesis, under the supervision of Dr. Laurent Delva and Pr. Jean-Noël Bastie.
Funding from the French department of higher education and research (October 2005 to September 2008).
Funding from the French Association for Cancer Research (ARC) (October 2008 to September 2009).

SCIENTIFIC ACHIEVEMENT

AWARD OBTAINED

- **Prix « Legs Kanning »** (2019) - Action LIONS Vaincre le Cancer and Banque Internationale à Luxembourg
- **FNR Award for Outstanding Publication** (2016) - Fonds National de la Recherche Luxembourg
- **Prix de la Recherche Médicale Translationnelle** (2016) - Centre Hospitalier du Luxembourg
- **ASH Abstract Achievement Award** (2013) - 55th American Society of Hematology (ASH) Annual Meeting
- **ASH Travel Award** (2008) - 50th American Society of Hematology (ASH) Annual Meeting

SELECTED PUBLICATIONS

Llaó Cid L*, Wong JKL*, Fernandez Botana I, Paul Y, Wierz M, Flörchinger A, Gonder S, Pagano G, Chazotte M, Bestak K, Schiffiers C, Iskar M, Roider T, Mallm JP, Cosma, A, Campton, DE, Rosenwald A, Colomer D, Campo E, Shapiro D, Dietrich S, Lichter P, Zapatka M#, Seiffert M#, Moussay E#, Paggetti J#. **T cell landscape definition by multi-omics identifies galectin-9 as novel immunotherapy target in chronic lymphocytic leukemia.** *BioRxiv* 2022.12.15.519719.

Pagano G*, Fernandez Botana I*, Wierz W, Roessner PM, Ioannou N, Zhou X, Al-Hity G, Borne C, Gargiulo E, Gonder S, Qu B, Stamatopoulos B, Ramsay AG, Seiffert M, Largeot A, Moussay E#, Paggetti J#. **Ebi3/IL-27 depleted microenvironment favors leukemia progression in CLL by impairing CD8⁺ T-cell-mediated anti-tumor immunity** (in revision at *Haematologica*).

Largeot A, Klapp V, Viry E*, Gonder S*, Fernandez Botana I*, Blomme A*, Benzarti M*, Pierson S, Duculty C, Marttila P, Wierz M, Gargiulo E, Pagano G, An N, El Hachem N, Perez Hernandez D, Chakraborty S, Ysebaert L, François JH, Cortez S, Berchem G, Efremov DG, Dittmar G, Szpakowska M, Chevigne A, Nazarov PV, Helleday T, Close P, Meiser J, Stamatopoulos B, Desaubry L, Moussay E*, Paggetti J* (2023) **Inhibition of MYC translation through targeting of the newly identified PHB-eIF4F complex as therapeutic strategy in CLL.** *Blood* (in press). Selected for the cover.

Green AL*, Martilla P*, Kiweler N*, Chalkiadaki C, Wiita E, Cookson V, Lesur A, Eiden K, Bernhardin F, Vallin KSA, Borhade S, Long M, Kamali Ghahe E, Jiménez-Alonso JJ, Jemth AS, Loseva O, Mortusewicz O, Meyers M, Viry E, Johansson A, Hodek O, Homan E, Bonagas N, Ramos L, Sandberg L, Frödin M, Moussay E, Letellier E, Paggetti J, Storgaard Sørensen C, Helleday T#, Henriksson M#, Meiser J# (2023) **Formate overflow drives toxic folate trapping in MTHFD1 inhibited cancer cells.** *Nature Metabolism* 5(4):642-659.

Gargiulo E, Viry E, Morande PE, Largeot A, Gonder S, Xian F, Ioannou N, Benzarti M, Kleine Borgmann FB, Mittelbronn M, Dittmar G, Nazarov PV, Meiser J, Stamatopoulos B, Ramsay AG, Moussay E*, Paggetti J* (2023) **Extracellular vesicles secretion by leukemia cells *in vivo* promotes CLL progression by hampering antitumor T-cell responses.** *Blood Cancer Discovery* 4(1):54-77. Selected for the cover of the January issue.

Góral A, Firczuk M, Fidyt K, Sledz M, Simoncello F, Siudakowska K, Pagano G, Moussay E, Paggetti J, Nowakowska P, Gobessi S, Barankiewicz J, Saloman-Perzynski A, Benvenuti F, Efremov DG, Juszczynski P, Lech-Maranda E, Muchowicz A (2022) **A specific CD44^{lo} CD25^{lo} subpopulation of regulatory T cells inhibits anti-leukemic immune response and promotes the progression in a mouse model of chronic lymphocytic leukemia.** *Frontiers in Immunology* 13:781364.

Paggetti J, Seiffert M, Moussay E (2021) **Editorial: New Insights Into the Complexity of Tumor Immunology in B-Cell Malignancies: Disease Biology and Signaling.** *Frontiers in Oncology* 11:820984.

Gonder S, Largeot A, Gargiulo E, Pierson S, Fernandez Botana I, Pagano G, Moussay E*, Paggetti J* (2021) **The Tumor Microenvironment-Dependent Transcription Factors AHR and HIF-1alpha Are Dispensable for Leukemogenesis in the Emicro-TCL1 Mouse Model of Chronic Lymphocytic Leukemia.** *Cancers* 13(18):4518.

Wurzer H, Filali L, Hoffmann C, Krecke M, Biolato AM, Mastio J, Dewilde S, François JH, Largeot A, Berchem G, Paggetti J, Moussay E, Thomas C (2021) **Intrinsic resistance of chronic lymphocytic leukemia cells to NK cell-mediated lysis can be overcome *in vitro* by pharmacological inhibition of Cdc42-induced actin cytoskeleton remodeling.** *Frontiers in Immunology*. 12:619069.

Gargiulo E, Morande PE, Largeot A, Moussay E*, Paggetti J* (2020) **Diagnostic and Therapeutic Potential of Extracellular Vesicles in B-Cell Malignancies.** *Front Oncol.* 10:580874.

Gonder S, Fernandez Botana I, Wierz M, Pagano G, Gargiulo E, Cosma A, Moussay E*, Largeot A*, Paggetti J* (2020) **Method for the Analysis of the Tumor Microenvironment by Mass Cytometry: Application to Chronic Lymphocytic Leukemia.** *Frontiers in Immunology* 11:578176.

Largeot A, Pagano G, Gonder S, Moussay E*, Paggetti J* (2019) **The B-side of Cancer Immunity: The Underrated Tune.** *Cells* 8(5):E449. IF:5.656

Causse SZ, Marcion G, Chanteloup G, Uyanik B, Boudesco C, Grigorash BB, Douhard R, Dias AMM, Dumetier B, Dondaine L, Gozzi GJ, Moussay E, Paggetti J, Mirjolet C, de Thonel A, Dubrez L, Demidov ON, Gobbo J, Garrido C (2019) **HSP110 translocates to the nucleus upon genotoxic chemotherapy and promotes DNA repair in colorectal cancer cells.** *Oncogene* 38(15):2767-2777.

Wierz M, Pierson S, Gargiulo E, Guerin C, Moussay E*, Paggetti J* (2019) **Purification of leukemia-derived exosomes to study microenvironment modulation.** Book "Cancer Immunosurveillance". *Methods Mol Biol.* 1884:231-245.

Wierz M, Pierson S, Guyonnet L, Viry E, Lequeux A, Oudin A, Niclou SP, Ollert M, Berchem G, Janji B, Guerin C, Moussay E*, Paggetti J* (2018) **Dual PD1/LAG3 immune checkpoint blockade limits tumor development in a murine model of chronic lymphocytic leukemia.** *Blood* 131(14):1617-1621.

Wierz M, Pierson S, Chouha N, Desaubry L, François JH, Berchem G, Moussay E*, Paggetti J* (2018) **The prohibitin-binding compound fluorizoline induces apoptosis in chronic lymphocytic leukemia cells *ex vivo* but fails to prevent leukemia development in a murine model.** *Haematologica* 103(4):e154-e157.

Mgrditchian T, Arakelian T, Paggetti J, Noman MZ, Viry E, Moussay E, Van Moer K, Kreis S, Guerin C, Buart S, Robert C, Borg C, Vielh P, Chouaib S, Berchem G, Janji B (2017) **Targeting autophagy inhibits melanoma growth by enhancing NK cells infiltration in a CCL5-dependent manner.** *Proc Natl Acad Sci U S A.* 114(44):E9271-E9279.

Haderk F, Schulz R, Iskar M, Cid LL, Worst T, Willmund KV, Schulz A, Warnken U, Seiler J, Benner A, Nessling M, Zenz T, Gobel M, Durig J, Diederichs S, Paggetti J, Moussay E, Stilgenbauer S, Zapata M, Lichter P, Seiffert M (2017) **Tumor-derived exosomes modulate PD-L1 expression in monocytes.** *Science Immunology* 28(213).

Paggetti J and Moussay E (2016) **BCR engagement in CLL: when translation goes wrong.** *Blood* 127(4):378-80. IF:13.164

Berchem G, Noman MZ, Bosseler M, Paggetti J, Baconnais S, Le Cam E, Nanbakhsh A, Moussay E, Mami-Chouaib F, Janji B and Chouaib S. (2016) **Hypoxic tumor-derived microvesicles negatively regulate NK cell function by a mechanism involving TGF-beta and miR23a transfer.** *Oncolimmunology* 5(4):e1062968.

Paggetti J*, Haderk F, Seiffert M, Janji B, Distler U, Ammerlaan W, Kim YJ, Lichter P, Solary E, Berchem G, and Moussay E* (2015) **Exosomes released by chronic lymphocytic leukemia cells induce cancer-associated fibroblast formation.** *Blood* 126(9):1106-17.

Viry E, Paggetti J, Baginska J, Mgrditchian T, Berchem G, Moussay E and Janji B. (2014) **Autophagy: An adaptive metabolic response to stress shaping the antitumor immunity.** *Biochemical Pharmacology* 92(1):31-42.

Baginska J, Viry E, Paggetti J, Medves S, Berchem G, Moussay E and Janji B. (2013) **The critical role of the tumor microenvironment in shaping natural killer cell-mediated anti-tumor immunity.** *Frontiers in Immunology* 4:490.

Paggetti J, Berchem G and Moussay E. (2013) **Stromal cell-induced miRNA alteration in chronic lymphocytic leukaemia: how a minute and unavoidable cell contamination impairs miRNA profiling.** *Leukemia* 27(8):1773-6.

Aucagne R, Droin N, Paggetti J, Lagrange B, Largeot A, Hammann A, Bataille A, Martin L, Yan K, Fenaux P, Losson R, Solary E, Bastie JN and Delva L. (2011) **Transcription Intermediary Factor 1 gamma is a tumor suppressor in mouse and human chronic myelomonocytic leukemia.** *Journal of Clinical Investigation* 121(6):2361-70.

Moussay E, Wang K, Cho JH, van Moer K, Pierson S, Paggetti J, Nazarov P, Palissot V, Hood L, Berchem G and Galas DJ. (2011) **MicroRNA as biomarkers and regulators in B-cell chronic lymphocytic leukemia.** *Proc Natl Acad Sci U S A* 108(16):6573-8. IF:9.681

Paggetti J, Largeot A, Aucagne R, Jacquelin A, Lagrange B, Yang XJ, Solary E, Bastie JN, and Delva L. (2010) **Cross-talk between leukemia-associated proteins MOZ and MLL regulates HOX genes expression in human cord blood CD34+ cells.** *Oncogene* 29(36):5019-31.

Jacquel A, Benikhlef N, Paggetti J, Lalaoui N, Guery L, Dufour EK, Ciudad M, Racoeur C, Micheau O, Delva L, Droin N and Solary E (2009) **CSF-1-induced oscillations in PI3K/AKT are required for caspase activation in monocytes undergoing differentiation into macrophages.** *Blood* 114(17): 3633-3641.

Zhuravleva J, Paggetti J, Martin L, Hammann A, Solary E, Bastie JN, and Delva L (2008). **MOZ/TIF2-induced acute myeloid leukaemia in transgenic fish.** *British journal of haematology* 143(3): 378-382.

PHD STUDENT SUPERVISION/JURY

- **Chloe Duculty** (member of the supervision committee), TSI group at LIH, University of Luxembourg, Luxembourg, since October 2022.
- **Vanessa Klapp** (supervisor), TSI group at LIH, University of Luxembourg, Luxembourg, since October 2022.
- Amandine Boeckx (member of the defense jury), Université de Liège, Belgium, June 2022
- Feriel Bekkal (member of the defense jury), Université de Paris, France, November 2021.
- Sura Atatri (member of the supervision committee), University of Luxembourg, Luxembourg, since May 2021.
- Christie Palmer (member of the supervision committee), University of Luxembourg, Luxembourg, since October 2020.
- **Iria Carmen Botana** (supervisor), TSI group at LIH, University of Luxembourg, Luxembourg, since October 2019.
- **Susanne Gonder** (member of the supervision committee), TSI group at LIH, University of Luxembourg, Luxembourg, since October 2019.
- Nathan Dubois (member of the supervision committee), Université Libre de Bruxelles (ULB) / Institut Bordet, Belgium, since October 2019.
- **Giulia Pagano** (supervisor), TSI group at LIH, University of Luxembourg, Luxembourg, 2018-2023.
- Marie Bordas (member of the supervision committee), Heidelberg University / DKFZ, Germany, 2018-2022.
- Malina Xiao (member of the supervision committee) FNR PRIDE Program DTU Canbio, University of Paris-Saclay, Paris, France, 2017-2021.
- **Ernesto Gargiulo** (co-supervisor), TSI group at LIH, FNR PRIDE Program DTU Canbio, University of Paris-Saclay, Paris, France, 2017-2021.
- **Marina Wierz** (co-supervisor), TSI group at LIH, University of Paris-Saclay, Paris, France, 2016-2020.
- **17 Master students since 2011**

EDITOR/REVIEWER/SCIENTIFIC EXPERTISE

- **Chairman of the Scientific Coordination Council** of the Luxembourg Institute of Health (2021-2025)
- **Animal experimentation FELASA C** (since 2009)
- **Member of the Animal Welfare Structure (AWS)** of the Luxembourg Institute for Health (2013-2017 and from 2020)
- **Expert reviewer** for abstracts of the EHA2022 Congress (Topic: Chronic lymphocytic leukemia and related disorders - Biology & Translational Research).
- **Reviewer** for Blood, Nature Communications, Molecular Cancer, Leukemia, Haematologica, Journal of Hematology & Oncology, Trends in Pharmacological Sciences, Clinical and Translational Medicine, Scientific Reports, JEV, IJMS, Cancers, Cells, Molecules, Molecular Cancer, Pharmacology & Therapeutics, Theranostics, JLB, Cancer Investigation, Cancer Immunology Immunotherapy, British Journal of Cancer, Frontiers in Oncology, Frontiers in Immunology, Metabolites.
- **Grant reviewer** for UK Research and Innovation, Czech Science Foundation, Paracelsus Medical University Salzburg (Austria), SiRIC Curamus (France), Sorbonne Université - Emergence.
- **Guest Associate Editor** for Frontiers in Oncology/Frontiers in Immunology, Topic “New Insights into the Complexity of Tumor Immunology in B-cell Malignancies” – 3 special issues with a total of 35 articles edited, with leading experts in the field.
- **Associate Editor** of Frontiers in Oncology, section Hematological Malignancies.