

Laetitia LARGEAUD, PharmD

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CURRENT STATUS: Assistant Professor @ Toulouse University and Toulouse Hospital (2018-present)

Research activities @ UMR1037, Pr Delabesse, Cancer Research Center of Toulouse

- ❖ PhD project: « **New approach to decipher GATA2 deficiency syndrome: focus on the recurrent GATA2 R396Q mutation** »

Manuscript in preparation, **EHA and ASH** oral presentations, French society of hematology **SFH 2020 scientific award**

- Main approaches:
 - *In vivo* characterization of hematopoietic stem cells in mice
 - Flow cytometry analyses (14 colors)
 - RNA et ATAC sequencing and bioinformatics analyses
 - Clonogenic assays, syngenic transplantations with or without treatments



- ❖ Secondary PhD project: « **Somatic genomic landscape of GATA2 deficiency patients** »

Manuscript submitted in January 2022, **Young expert in hematology award** French Innovative Leukemia Organization 2021

- Main approaches:
 - Recruitment of GATA2 deficient patients
 - Targeted sequencing of the 90 most frequent mutated genes In myeloid hemopathies
 - Management of clinical and biological data (of at least 15 hospitals in France and in Belgium)
 - Correlation analyses
 - Data base management
 - Member of French-Belgium GATA2 Club

Medical activities @ Hematology laboratory, Pr. Delabesse, Oncopole, Toulouse

- ❖ Clinico-biology projects: “Genomic atlas of patients with acute myeloid leukemia (AML) establishing one molecular profile of response”.
- Sequencing of 6 patient cohorts: 2 published (LAMSA-07 and DEXAML-00) and 4 ongoing (DEXAML-02, Epidemiology and AML, CLL and Ibrutinib, DDX41)
- ❖ Review and report of the hematological test results to medical staff with a focus on
 - Molecular biology:
 - Sequencing targeted gene panels on hematological malignancies
 - Patients chimerism follow-up
 - Fragment analyses : FLT3-ITD, CEBPA
 - Chronic lymphoid leukemia : mutational status, resistance genes
 - Validation of RNA Sequencing et WES data (France Genomique : Auragen)
 - Cytology expertise:
 - Bone marrow, lymph nodes, blood smears
 - Complete blood count
 - Training technicians for cytology



Teaching activities @ Faculty of pharmaceutical sciences, Toulouse

- Teaching for practical and theoretical courses (from the 1st to the 5th year of medical school, 120h/years)
- Co-writing of a book to prepare the internship contest (« L'ouvrage de l'ASSHIB »)
- Student tutoring for professional cursus



Student supervision @ Toulouse Hospital and Cancer Research Center of Toulouse

- MD and PharmD thesis director (1 finalized and 1 on going)
- Two master students (on « Cooperation of STAG2 and GATA2 mutations» and « Phenotypic characterization of middle aged mutated *Gata2* mice »)

SOFTWARES

Office, Flow cytometry (Fortessa BD®, Flow Jo, Umap, Trimap analyses softwares), RNA and ATAC Sequencing analyses (Galaxy, Kmeans, Heatmap, GSEA, Metascape), Prism, Adobe illustrator

LANGUAGE

French: Maternal language

English: B1

EDUCATION

- ✓ **PhD (on going) @ Centre de Recherche en Cancérologie de Toulouse (UMR1037) (since 2018)**

Subject: « New approach to decipher GATA2 deficiency syndrome: focus on the recurrent GATA2 R396Q mutation »

- ✓ **Pharmacy internship: Medical Biology specialization @ Ile-de-France (2018)**

- ✓ **Pharm.D / Diploma of Specialized Studies in medical Biology (with highest honour) @ Faculté de pharmacie de Châtenay-Malabry (2018)**

Study of STAT3 phosphorylation in chronic lymphocytic leukemia and Richter syndrome

- **MASTER 2 : Biochemistry, cell, therapeutic targets (BC2T) @ Université Paris Diderot (2017)**

Molecular and functional biology of hematopoiesis: Targeting STAT5 transcription factors in acute myeloid leukemias by PPAR gamma agonists

- **MASTER 1 : Immunology @ Faculté de Médecine Paris Descartes (2016)**

With specialization in **Cellular biology, Physiology, Pathology and Pharmacology and toxicology**

PAST MEDICAL EXPERIENCES

2013 – 2018: Medical biology internship @ Paris (Assistance Publique des Hôpitaux de Paris)



Semester 8: **Haematology**, in Pr. Delhommeau department @ Hôpital Saint-Antoine Paris

Semester 7: **Haematology**, in Pr. Delhommeau department @ Hôpital Saint-Antoine Paris

Master 2: in Pr. Bardet department (UMR1173) @ Faculté de Médecine de Saint-Quentin en Yvelines *Montigny-le-Bretonneux*

Semester 6: **Haematology - immunology** in Pr. Bardet department @ CHU Ambroise Paré, *Boulogne-Billancourt*

Semester 5: **Haematology**, in Pr. Macintyre-Davi department @ CHU Necker Enfants Malades Paris

Semester 4: **Bacteriology – Virology**, in Dr. Fortineau department @ CHU Bicêtre/Paul Brousse *Le Kremlin-Bicêtre*

Semester 3: **Immunology**, in Pr. Tartour department @ Hôpital Européen Georges Pompidou Paris

Semester 2: **Haematology**, in Pr. Macintyre-Davi department @ CHU Ambroise Paré *Boulogne-Billancourt*

Semester 1: **Biochemistry**, in Pr. Bonnefont-Rousselot department @ CHU Pitié-Salpêtrière Paris

SCIENTIFIC PUBLICATIONS (25 INCLUDING 5 AS FIRST OR CO-FIRST AUTHOR), CITATIONS: 71, H-INDEX: 5

- **Largeaud L**, Bertoli S, Bérard E, Tavitian S, Picard M, Dufrechou S, Prade N, Vergez F, Rieu JB, Luquet I, Sarry A, Huguet F, Ruiz J, De Mas V, Delabesse E, Récher C. Genomic landscape of hyperleukocytic acute myeloid leukemia. *Blood Cancer J.* 2022 Jan 5;12(1):4. doi: 10.1038/s41408-021-00601-5. PMID: 34987148.
- Singh P, Heer M, Resteu A, Mikulasova A, Reza M, **Largeaud L**, Dufrechou S, Prade N, Dickinson RE, Bustamante J, Neven B, Bigley V, Delabesse E, Rico D, Pasquet M, Collin M. GATA2 deficiency phenotype associated with tandem duplication GATA2 and over-expression of GATA2-AS1. *Blood Adv.* 2021 Oct 12;bloodadvances.2021005217. doi: 10.1182/bloodadvances.2021005217. Epub ahead of print. PMID: 34638133.

- Lafage-Pochitaloff M, Gerby B, Baccini V, **Largeaud L**, Fregona V, Prade N, Juvin PY, Jamrog LA, Bories P, Hébrard S, Lagarde S, Mansat-De Mas V, Dovey OM, Yusa K, Vassiliou GS, Jansen JH, Tekath T, Rombaut D, Ameye G, Barin C, Bidet A, Boudjarane J, Collonge-Rame MA, Gervais C, Ittel A, Lefebvre C, Luquet I, Michaux L, Nadal N, Antoine-Poirel H, Radford-Weiss I, Ribourtout B, Richebourg S, Struski S, Terré C, Tigaud I, Penther D, Eclache V, Fontenay M, Broccardo C, Delabesse E. The CADM1 tumor suppressor gene is a major candidate gene in MDS with deletion of the long arm of chromosome 11. *Blood Adv.* 2021 Oct 12;bloodadvances.2021005311. doi: 10.1182/bloodadvances.2021005311. Epub ahead of print. PMID: 34638130.
- Kassir AE, **Largeaud L**, Vergnolle I, Oberic L, Schavgoulidze A, Rieu JB. How to diagnose lymphoplasmacytic lymphoma without infiltration of plasmacytoid lymphocytes? *Blood Res.* 2021 Sep 30;56(3):125. doi: 10.5045/br.2021.2021098. PMID: 34349043; PMCID: PMC8478622.
- Rieu JB, **Largeaud L**. Diet of neutrophils by bone marrow macrophages in autoimmune neutropenia. *Blood.* 2021 Aug 19;138(7):584. doi: 10.1182/blood.2021011947. PMID: 34410357.
- Rieu JB, El Kassir A, **Largeaud L**, Dion J, Comont T, Mansat-De Mas V. Characteristic vacuolisation of granulocytic and erythroid precursors associated with VEXAS syndrome. *Br J Haematol.* 2021 Jul;194(1):8. doi: 10.1111/bjh.17381. Epub 2021 Mar 2. PMID: 33651376.
- Luquet I, El Kassir A, Sailler L, **Largeaud L**, Mansat-De Mas V. Characteristic vacuolization of myeloid precursors and UBA1 mutation in a woman with monosomy X. *Int J Lab Hematol.* 2021 Jun 10. doi: 10.1111/ijlh.13617. Epub ahead of print. PMID: 34111334.
- **Largeaud L**, Cornillet-Lefebvre P, Hamel JF, Dumas PY, Prade N, Dufrechou S, Plenecassagnes J, Luquet I, Blanchet O, Banos A, Béné MC, Bernard M, Bertoli S, Bonmati C, Fornecker LM, Guièze R, Haddaoui L, Hunault M, Ianotto JC, Jourdan E, Ojeda M, Peterlin P, Vey N, Zerazhi H, Yosr H, Mineur A, Cahn JY, Ifrah N, Récher C, Pigneux A, Delabesse E; French Innovative Leukemia Organization (FILO). Lomustine is beneficial to older AML with ELN2017 adverse risk profile and intermediate karyotype: a FILO study. *Leukemia.* 2021 May;35(5):1291-1300. doi: 10.1038/s41375-020-01031-1. Epub 2020 Sep 18. PMID: 32943750.
- **Largeaud L**, Ribes A, Dubois-Galopin F, Mémier V, Rolland Y, Gaudin C, Rousset D, Geeraerts T, Noel-Savina E, Rieu JB, Vergez F. Major rise of a chronic lymphoid leukemia clone during the course of COVID-19. *Int J Lab Hematol.* 2021 Apr;43(2):e82-e83. doi: 10.1111/ijlh.13383. Epub 2020 Nov 8. PMID: 33161639.
- Duployez N, Jamrog LA, Fregona V, Hamelle C, Fenwarth L, Lejeune S, Helevaut N, Geffroy S, Caillault A, Marceau-Renaut A, Poulain S, Roche-Lestienne C, **Largeaud L**, Prade N, Dufrechou S, Hébrard S, Berthon C, Nelken B, Fernandes J, Villenet C, Figeac M, Gerby B, Delabesse E, Preudhomme C, Broccardo C. Germline PAX5 mutation predisposes to familial B-cell precursor acute lymphoblastic leukemia. *Blood.* 2021 Mar 11;137(10):1424-1428. doi: 10.1182/blood.2020005756. PMID: 33036026.
- Rieu JB, Vergnolle I, Oberic L, **Largeaud L**, Vergez F. CD5+CD200- B-cell neoplasms deserve an extra look. *Ann Biol Clin (Paris).* 2021 Feb 1;79(1):90-91. doi: 10.1684/abc.2020.1610. PMID: 33258458.
- Cadot S, Valle C, Tosolini M, Pont F, **Largeaud L**, Laurent C, Fournie JJ, Ysebaert L, Quillet-Mary A. Longitudinal CITE-Seq profiling of chronic lymphocytic leukemia during ibrutinib treatment: evolution of leukemic and immune cells at relapse. *Biomark Res.* 2020 Dec 9;8(1):72. doi: 10.1186/s40364-020-00253-w. PMID: 33298182; PMCID: PMC7724843.
- Rieu JB, Tavitian S, Vergez F, **Largeaud L**. Do not forget megakaryocytes morphology when you deal with chronic myeloid leukaemia. *Ann Biol Clin (Paris).* 2020 Dec 1;78(6):691-692. doi: 10.1684/abc.2020.1595. PMID: 33079062.
- Ricard L, Hirsch P, **Largeaud L**, Deswarte C, Jachiet V, Mohty M, Rivière S, Malard F, Tenon M, de Vassoigne F, Fain O, Gaugler B, Rossignol J, Delhommeau F, Mekinian A; on behalf MINHEMON (French Network of dysimmune disorders associated with hemopathies). Clonal haematopoiesis is increased in early onset in systemic sclerosis. *Rheumatology (Oxford).* 2020 Nov 1;59(11):3499-3504. doi: 10.1093/rheumatology/keaa282. PMID: 32757002.
- Bories P, Prade N, Lagarde S, Cabarrou B, **Largeaud L**, Plenecassagnes J, Luquet I, De Mas V, Filleron T, Cassou M, Sarry A, Fornecker LM, Simand C, Bertoli S, Recher C, Delabesse E. Impact of TP53 mutations in acute myeloid leukemia patients treated with azacitidine. *PLoS One.* 2020 Oct 1;15(10):e0238795. doi: 10.1371/journal.pone.0238795. PMID: 33001991; PMCID: PMC7529302.
- Rieu JB, **Largeaud L**, Vergez F, Evrard S. Acute myeloid leukemia with myelodysplasia-related changes and basophilic differentiation. *Blood Res.* 2020 Sep 30;55(3):130. doi: 10.5045/br.2020.2020095. PMID: 32792469; PMCID: PMC7536570.
- Beziat G, Tavitian S, Bertoli S, Huguet F, **Largeaud L**, Luquet I, Vergez F, Rieu JB, Bories P, Delabesse E, Récher C. Dactinomycin in acute myeloid leukemia with NPM1 mutations. *Eur J Haematol.* 2020 Sep;105(3):302-307. doi: 10.1111/ejh.13438. Epub 2020 May 25. PMID: 32452083.

- Dumas PY, Bertoli S, Bérard E, **Largeaud L**, Bidet A, Delabesse E, Leguay T, Leroy H, Gadaud N, Rieu JB, Vial JP, Vergez F, Lechevalier N, Luquet I, Klein E, Sarry A, de Grande AC, Pigneux A, Récher C. Real-World Outcomes of Patients with Refractory or Relapsed *FLT3*-ITD Acute Myeloid Leukemia: A Toulouse- Bordeaux DATAML Registry Study. *Cancers (Basel)*. 2020 Jul 24;12(8):2044. doi: 10.3390/cancers12082044. PMID: 32722211; PMCID: PMC7465142.
- Serhan N, Mouchel PL, Medina P, Segala G, Mougel A, Saland E, Rives A, Lamaziere A, Despres G, Sarry JE, Larrue C, Vergez F, **Largeaud L**, Record M, Récher C, Silvente-Poirot S, Poirot M. Dendrogenin A synergizes with Cytarabine to Kill Acute Myeloid Leukemia Cells In Vitro and In Vivo. *Cancers (Basel)*. 2020 Jun 29;12(7):1725. doi: 10.3390/cancers12071725. PMID: 32610562; PMCID: PMC7407291.
- Vergez F, Nicolau-Travers ML, Bertoli S, Rieu JB, Tavitian S, Bories P, Luquet I, Mas V, **Largeaud L**, Sarry A, Huguet F, Delabesse E, Bérard E, Récher C. CD34⁺CD38⁺CD123⁺ Leukemic Stem Cell Frequency Predicts Outcome in Older Acute Myeloid Leukemia Patients Treated by Intensive Chemotherapy but Not Hypomethylating Agents. *Cancers (Basel)*. 2020 May 6;12(5):1174. doi: 10.3390/cancers12051174. PMID: 32384744; PMCID: PMC7281486.
- Bertoli S, Tavitian S, Bérard E, Mansat-De Mas V, **Largeaud L**, Gadaud N, Rieu JB, Vergez F, Luquet I, Huguet F, Sarry A, Delabesse E, Récher C. More than ten percent of relapses occur after five years in AML patients with *NPM1* mutation. *Leuk Lymphoma*. 2020 May;61(5):1226-1229. doi: 10.1080/10428194.2019.1706733. Epub 2020 Feb 5. PMID: 32022605.
- Bertoli S, Dumas PY, Bérard E, **Largeaud L**, Bidet A, Delabesse E, Tavitian S, Gadaud N, Leguay T, Leroy H, Rieu JB, Vial JP, Vergez F, Lechevalier N, Luquet I, Klein E, Sarry A, Grande AC, Récher C, Pigneux A. Outcome of Relapsed or Refractory *FLT3*-Mutated Acute Myeloid Leukemia Before Second-Generation *FLT3* Tyrosine Kinase Inhibitors: A Toulouse-Bordeaux DATAML Registry Study. *Cancers (Basel)*. 2020 Mar 25;12(4):773. doi: 10.3390/cancers12040773. PMID: 32218221; PMCID: PMC7226007.
- **Largeaud L**, Bertoli S, Bérard E, Dufrechou S, Prade N, Gadaud N, Tavitian S, Bories P, Luquet I, Sarry A, Mas V, Huguet F, Delabesse E, Récher C. Outcome of relapsed/refractory AML patients with *IDH1*^{R132} mutations in real life before the era of *IDH1* inhibitors. *Leuk Lymphoma*. 2020 Feb;61(2):473-476. doi: 10.1080/10428194.2019.1668937. Epub 2019 Sep 30. PMID: 31566052.
- Vergez F, **Largeaud L**, Oberic L, Rieu JB. Do not jump to hasty conclusions: all gamma delta T-cells neoplasms are not aggressive! *Blood Res*. 2019 Dec;54(4):243. doi: 10.5045/br.2019.54.4.243. Epub 2019 Dec 20. PMID: 31915649; PMCID: PMC6942139.
- **Largeaud L**, Bérard E, Bertoli S, Dufrechou S, Prade N, Gadaud N, Tavitian S, Bories P, Luquet I, Sarry A, De Mas V, Huguet F, Delabesse E, Récher C. Outcome of AML patients with *IDH2* mutations in real world before the era of *IDH2* inhibitors. *Leuk Res*. 2019 Jun;81:82-87. doi: 10.1016/j.leukres.2019.04.010. Epub 2019 Apr 27. PMID: 31055247.

SCIENTIFIC COMMUNICATIONS

International meetings

2021

- New approach to decipher *GATA2* deficiency syndrome: focus on the recurrent *GATA2* R396Q mutation. *American Society of Hematology (ASH)* Oral communication
- Genomics of hyperleukocytic acute myeloid leukemia. *American Society of Hematology (ASH)* Poster highlight
- New approach to decipher *GATA2* deficiency syndrome: focus on the recurrent *GATA2* R396Q mutation. *Club Hématopoïèse et Oncogénèse (CHO)* Oral communication

2020

- The germline *GATA2* R396Q missense mutation alters functionally and qualitatively hematopoietic stem cell compartment in mice. *European Hematology Association (EHA)* Oral communication

2019

- Are missense germline *GATA2* mutations really loss of function? *Club Hématopoïèse et Oncogénèse (CHO)* - Poster
- How should we study *GATA2* deficiency functionally? *Collaborative network on research for children and teenagers with AML*

National meetings

2021

- Why do *GATA2* deficiency patients develop myeloid neoplasms? *French Innovative Leukemia Organisation (FILO)*

-> **Young expert in hematology award**

- New approach to decipher GATA2 deficiency syndrome : focus on the recurrent GATA2 R396Q mutation *French Society of hematology (SFH) - Poster highlight*
- Acute myeloid leukemia with germline DDX41 mutations : an unique entity of familial AML. *French Society of hematology (SFH) Poster*

2020

- The germline GATA2 R396Q missense mutation alters functionally and qualitatively hematopoietic stem cell compartment in mice. *French Society of hematology (SFH) Oral presentation*
-> **Best presentation award**
- Lomustine is beneficial to older AML with ELN2017 adverse risk profile and intermediate karyotype: FILO study. *French Society of hematology (SFH) Oral presentation*

2019

- Characterization of a missense germline GATA2 mutation in mice. *National Day of chronic neutropenia reference center Oral presentation*

AWARDS

- **Young expert in hematology award** *French Innovative Leukemia Organization 2021*
- **SFH Scientific award** *French Society of hematology 2020*