BIOGRAPHICAL SKETCH

NAME **Bouchra GHAZI**	POSITION TITLE **Associate professor in Immunology**
eRA COMMONS USER NAME B.Ghazi	

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
Ibn Abdoune College, Khouribga, Morocco	**Baccalaureate**	2003	Experimental Biology
Chouaib Doukkali University, El Jadida, Morocco	**Licence**	2006	Cellular and Molecular Biology
Paris-Est University (UPEC), Creteil, France	**MSc**	2008	Immunology
Paris-Est University (UPEC), Creteil, France	**PhD**	2012	Immunology/ Physiopathology

A. Personal Statement

I have built my career on a series of rich experiences by taking on greater responsibilities to evolve professionally. It began with my first research in the immunology, dermatology and oncology lab under the supervision of Dr Armand BENSUSSAN. I have worked on minimal/critical promoter region identification and dissecting of human CD160 gene. CD160 is tightly associated with peripheral blood NK cells and CD8 T lymphocytes with cytolytic effector activity and interestingly this CD160+ cells are found in cutaneous inflammatory lesions of atopic dermatitis and psoriasis. We have identified and analysed the minimal promoter region which leads as to highlight the implication of AML-1 transcription factor in promoter activation (Schmitt C, Ghazi B, et al. Identification and analysis of the human CD160 promoter: implication of a potential AML-1 binding site in promoter activation. Genes Immun. 2009). A second part of my research, in collaboration with Pr. Philippe Gaulard team, focuses on the molecular pathogenesis of nasal T/NK-cell lymphomas (Huang Y, de Reyniès A, de Leval L, Ghazi B, et al. Gene expression profiling identifies emerging oncogenic pathways operating in extranodal NK/Tcell lymphoma, nasal type. Blood. 2010). As a MSc student, I have participated in transcriptomic study of a collection of T-NK extra-ganglionic lymphoma. This study has provided us a more comprehensive understanding of T/NK-cell lymphomas specific molecular signature which includes survival/apoptosis genes, granzyme H gene and EBV-associated genes. Abnormal constitutive activation of many signaling pathways like Jak/STAT3, AKT, PDGFR and VEGF was confirmed by immunohistochemistry.

Reasonably satisfied with the results of this experience, i chose to do a thesis in order to confirm or not my passion for academic research. Thus, i have worked on expression and function of KIR3DL2, a specific marker of tumoral Sézary T CD4+ cells, to investigate the possible influence of this receptor on mechanisms regulating the tumoral cells outgrowth and apoptosis process. To this aim, two axes were developed. The first axis aimed to highlight the function of KIR3DL2 on the malignant T lymphocyte population and to elucidate the intracellular signaling mechanisms initiated by engagement of the receptor with the monoclonal antibody AZ158. Our results have shown that KIR3DL2 can exert an inhibitory co-receptor function in malignant Sezary cells. Indeed, triggering of KIR3DL2 inhibits the CD3-mediated proliferation and cell death of the CD4+ KIR3DL2+ cells, this inhibition being correlated to a down-modulation of the TCR-mediated signals. Thus, KIR3DL2 does not behave as an independent signaling unit in Sezary cells, unlike NK cells. The second axis aimed to evaluate a new function of KIR3DL2 as CpG ODN receptor. We have shown for the first time a direct effect of CpG ODN on tumoral CD4+ T Sezary cells. Thus, we observed a caspase-dependent apoptotic effect of CpG ODN-C on Sezary cell lines and circulating malignant T cells. This process of cellular death is correlated to a dephosphorylation of the transcription factor STAT3, which is found constitutively phosphorylated and activated in Sezary cells (Ghazi B et al., KIR3DL2/CpG ODN Interaction Mediates Sézary Syndrome Malignant T Cell Apoptosis. J Invest Dermatol 135: 229).

During my time at Paris Descartes University 2012-2013, I was working as ATER in the Pr Dominique BELLET and Salima Hacein Bey Abina teaching team to 2nd, 4th year Pharmacy and science students. The objective

was to introduce the students to the basic concepts of immunology as it relates to human health. The program has been designed to help understand the ability of our immune system to defend against invading pathogens in a logic reaction sequence. This includes our innate ability to defend against microorganisms as the first line of defense, mobilization of acquired immunity if innate immunity fail; the consequence if we react excessively (hypersensitivity) or we misdirect our defense (autoimmunity) and can we educate immune system to avoid attacks from invading pathogens (vaccination). Furthermore, I have read widely in immunobiology of cancer and related fields to keep moving toward my goal of gaining expertise in the biology of cancer, this together with my previous knowledge strengthened my academic abilities for teaching immunology and immunopathology across multidisciplinary boundaries.

At CEA of Fontenay-aux-Roses (2014-2016), I demonstrated aptitude for training with a primary emphasis in the areas of the microenvironment of cancer. My work aimed at gaining a better understanding of the nature of infiltrating specific stromal cell subsets in situ and investigate to what extent stromal cells from normal BM physically and functionally differ from that of T-ALL BM. I have been interested particularly in medullary adipocytes, which originate from mesenchymal stromal cells, as a greatest source of growth factors, cytokines, and chemokines that influence leukemia behavior and response to treatment. In this way, I have developped two mice models: (1) the aged bone marrow microenvironment with young and old mice (2) bone marrow adipocyte hyperplasia induced by chemotherapy drug (cytarabine). As a first step, i have assessed adipogenic rates in the bone marrow of this models. Next, I started looking for correlation between adipogenic rates in the bone marrow and in vivo leukemia development.

B. Positions and Honors

Positions and Employment

2012-2013 **Teaching and Research Temporary Attaché**, Paris Descartes University, Paris, France

2014-2016 **Post-Doctoral Fellow**, Atomic Energy Commission (CEA), Fontenay-aux-Roses, France

2016-2020 **Assistant Professor**, Immunology, Faculty of medicine, Mohammed VI University of Health and Sciences (UM6SS), Casablanca, Morocco

2018- 2020 **Professional Master's degree coordinator**, « Design and Monitoring of Clinical Trials », Faculty of Pharmacy, Mohammed VI University of Health Sciences (UM6SS), Casablanca, Morocco

2019- **Master's degree coordinator**, « Immunity-Infection-Inflammation », Faculty of Medicine, Mohammed VI University of Health Sciences (UM6SS), Casablanca, Morocco

2020-2021 **Head of COVID-19 Serology Platform**, Mohammed VI National Laboratory for Medical Analysis, Casablanca, Morocco

2020- **Associate Professor**, Immunology, Faculty of Medicine, Mohammed VI University of Health and Sciences (UM6SS), Casablanca, Morocco

2022- **Scientific Head of the IVF Laboratory**, Mohammed VI International University Hospital (HUIM6), Bouskoura, Morocco

2023- **Head of the Immunopathology-Immunotherapy-Immunomonitoring (3Is) Laboratory,** Faculty of Medicine, Mohammed VI University of Health and Sciences, Casablanca, Morocco

Other Experience and Professional Memberships

2008 **Master degree in Immunology**. Paris-Est University, Paris, France

2009-2011 **PhD « Immunology/Physiopathology ».** Paris-Est University, Paris, France

2010 **PhD Fellowship.** The Fondation René Touraine (FRT), Paris, France

2010 **Research Award.** Cephalon/French Society of Dermatology (SFD)

2012 **Certificate of animal experimentation training level I.** National veterinary school of Alfort (ENVA), Maisons-Alfort, France

2012 **PhD Fellowship.** French Association for Cancer Research (ARC), France

2012 **PhD Fellowship.** French Foundation for Medical Research, France

2014 **Clinical Research Associate Formation**. Médiaxe, Paris, France

2014-2016 **Postdoctoral Fellowship.** French National League against Cancer, France

2017-2018 **DU (University Diploma)** « **Immunological therapeutics: vaccines, antibodies, cytokines, immunomodulators, cell and gene therapies** ». Paris Descartes University, France

2018 **Flow Cytometry Courses**: (1) Introductory and refresher course in flow cytometry et (2) Advanced flow cytometry for hematologists and immunologists. Swiss Flow Cytometry School. Genève, Switzerland

2022 **In vitro Fertilization courses**: (1) Overview on IVF techniques, (2) ICSI techniques: How to inject in a less invasive way, et (3) Cryopreservation (oocyte, embryo and blastocyst) and Assisted Hatching. Embryotools, Spain

2022 **Reproductive Biology practitioner Certification**. The Moroccan Society for Endometriosis and Reproductive Medicine (MSERM), Morocco

2023 **Basic Diploma in Reproductive Medicine and Embryology**. Kiel School of Reproductive Medicine. Germany

2024- **Master Degree in the Biotechnology of Human Assisted Reproduction and Embryology.** IVIRMA-University of Valencia. Spain

Teaching Classes and qualification

2012-2013 I participated in the update and organisation of courses under the supervision of Professor Dominique BELLET and Professor Salima Hacein-Bey-Abina.
I taught Fundamental Immunology and ImmunoPathology to pharmacy students (2nd and 4th years) and Licence 3 students (Undergrad, third year).

2015 Qualified by the CNU (National Universities Council, French Ministry of Higher Education and Research) for the position of Maître de conférences in French universities (section 65: cell biology and section 87: basic and clinical biological sciences).

C. peer-reviewed publications (in chronological order)

2008 Schmitt C, **Ghazi B** et al., NK cells and surveillance in humans, Reprod Biomed Online 16: 192

2009 Schmitt C, **Ghazi B** et al., Identification and analysis of the human CD160 promoter: implication of a potential AML-1 binding site in promoter activation, Genes Immun 10: 616

2010 Huang Y, de Reyniès A, de Leval L, **Ghazi B** et al., Gene expression profiling identifies emerging oncogenic pathways operating in extranodal NK/T-cell lymphoma, nasal type, Blood 115 : 1226

2015 **Ghazi B** et al., KIR3DL2/CpG ODN Interaction Mediates Sézary Syndrome Malignant T Cell Apoptosis. J Invest Dermatol 135: 229

2018 El Bairi K, Tariq K, Himri I, Jaafari A, Smaili W, Kandhro AH, Gouri A, **Ghazi B**. Decoding colorectal cancer epigenomics. Cancer Genet. 2018 Jan;220 :49-76.

2020 K Fichtali, A Bititi, A Elghanmi, **Ghazi B**. Serum Lipidomic Profiling in Breast Cancer to Identify Screening, Diagnostic, and Prognostic Biomarkers. BioResearch Open Access. Jan 2020.1-6.

2020 **Ghazi B**, Elghanmi A. Why Do We Need Serological Tests for Severe Acute Respiratory Syndrome Coronavirus-2 Diagnosis? Biores Open Access. 2020 Dec 2;9(1):255-257.

2020 Aguennouz M, Polito F, Visalli M, Vita G, Raffa G, Oteri R, **Ghazi B**, Scalia G, Angileri FF, Barresi V, Caffo M, Cardali S, Conti A, Macaione V, Bartolotta M, Giorgio RD, Germanò A. microRNA-10 and -221 modulate differential expression of Hippo signaling pathway in human astroglial tumors. Cancer Treat Res Commun. 2020;24:100203.

2022 **Ghazi B** et al., CAR T-cells for colorectal cancer immunotherapy: Ready to go? Front. Immunol., 15 November 2022. Sec. Vaccines and Molecular Therapeutics Volume 13 – 2022

2024 Harmak Z, Kone AS, Ghouzlani A, **Ghazi B**, Badou A. Beyond Tumor Borders: Intratumoral Microbiome Effects on Tumor Behavior and Therapeutic Responses. Immune Netw. 2024 Dec 9;24(6):e40.

2024 Azil S, Mbaye MM, Louanjli N, **Ghazi B**, Benkhalifa M. Phospholipase C zeta: a hidden face of sperm for oocyte activation and early embryonic development. Obstet Gynecol Sci. 2024 Nov;67(6):588.

2024 **Ghazi B**, Harmak Z, Rghioui M, Kone AS, El Ghanmi A, Badou A. Decoding the secret of extracellular vesicles in the immune tumor microenvironment of the glioblastoma: on the border of kingdoms. Front Immunol. 2024 Aug 29;15:1423232.

2024 Kouhen F, **Ghazi B**, Nasser S, Sehouli J, El Ghanmi A. PARSGO and UM6SS: spearheading excellence in gynecological oncology in Morocco. Int J Gynecol Cancer. 2024 Oct 7;34(10):1647-1648.