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University of California, San Francisco

CURRICULUM VITAE

Name: Alexis Jeremie Pierre Combes

Position: Assistant Professor In Residence, Step 2
Pathology
School of Medicine

Address: Box 0511
Location Required, 001
University of California, San Francisco
Varies, CA 00000
Email: alexis.combes@ucsf.edu

EDUCATION

2007 - 2010	Aix-Marseille University France	Licence	Cell biology	
2010 - 2012	Aix-Marseille University France	Master	Development and Immmunology	
2012 - 2016	Aix-Marseille University	PhD	Immunology	Philippe Pierre & Evelina Gatti
2016 - 2017	INSERM France	Post doctocal Associate		Philippe Pierre
2017 - 2019	University of California San Francisco	Post-doctoral Associate		Matthew Krummel

PRINCIPAL POSITIONS HELD

2019 - present	UCSF	Director of Disease to Biology CoLab	CoLabs/EVCP
2022 - present	UCSF	Assistant professor	Pathology and Medicine GI division

HONORS AND AWARDS

2023	Stuart Lindsay Endowed Chair in Experimental Pathology,	UCSF
2015	PhD student award	ARC Foundation France

KEYWORDS/AREAS OF INTEREST

System immunology
Tumor Immunology
Metabolism
Anti-viral response
Transcription and Translation control

PROFESSIONAL ACTIVITIES

MEMBERSHIPS

2012 - 2016	Treasurer of LABO'M (society of Scientist from Luminy Campus) Marseille France
2013 - 2016	Representative Graduate student at Laboratory council for CIML institue Marseille France
2017 - present	Member, ImmunoX Scientific Outreach Committee
2019 - present	Member of UCSF Immunoprofiler Consortium leadership
2020 - present	Scientific lead of UCSF COMET consortium
2020 - present	Member,UCSF CoLabs PostBac Research Program
2021 - present	Member of American Association of Cancer Research
2021 - present	Member of French Society of Immunology
2021 - present	Member,ImmunoX Media Outreach Team
2022 - present	Faculty Member, The Benioff Center for Microbiome Medicine
2022 - present	Faculty Member, Bakar ImmunoX

SERVICE TO PROFESSIONAL PUBLICATIONS

2021 - present	Guest Editor for Frontiers in Immunology
2021 - present	Reviewer for Frontiers in Immunology
2022 - present	Reviewer for BMC medicine
2022 - present	Reviewer for Cancer Cell
2023 - present	Editorial board member BMC medicine journal, Nature publishing group

INVITED PRESENTATIONS - INTERNATIONAL

2013	International workshop on Plasmacytoid dendritic cells, Pasteur Institute Paris France	Poster
2013	Second International Graduate students in Immunology conference, Marseille France	Talk
2014	Harvard Medical School retreat Immunology department	Poster

2014	International dendritic cells symposium,Tours France	Poster
2016	International congress of Immunology, Melbourne Australia	Talk
2019	Midwinter conference of Immunologist, Asilomar California USA	Poster
2020	Federation of Clinical Immunology Societies (FOCIS), On-line conference	Poster
2021	AARDA Noel R. Rose Scientific Colloquium	Talk
2021	Invited Talk in Human immune monitoring Center in Immunonology institute at Mt Sinai	Talk
2021	Invited Talk for the Global Immunology Symposium organized by 10X genomics	Talk
2021	Invited Talk for ImmunoX Seminar Series UCSF	Talk
2022	Invited talk for Federation of Clinical Immunology Societies San Francisco	Talk
2022	Invited Oral presentation Congress of European Society of Macrophage and Dendritic cells	Talk
2023	Keystone symposium	Poster
2023	Invited Speaker for Human immune monitoring Conference, Standford	Talk
2023	Invited speaker for Immuno US 2023 Conference, San Diego	Talk

INVITED PRESENTATIONS - NATIONAL

2012	Annual meeting club exocytose endocytose, Sorgues France	Poster
2013	Annual meeting Doctoral school Aix-Marseille University, France	Talk

UNIVERSITY AND PUBLIC SERVICE

SERVICE ACTIVITIES SUMMARY

In August 2022 i served as Faculty organizer and judge for the ImmunoX Computational Biology Initiative Hackathon organized every year by the UCSF Data Science CoLab. The ImmunoX Computational Biology Initiative seeks to promote data science participation and innovation in the biological space. Made possible by generous philanthropic support, funding will be invested into bridging biology and data science through the computer scientist sabbatical program, support for the UCSF Data Library platform, and investment in researchers at the post-baccalaureate and PhD level. The overarching goal of the program is to leverage data collected by the entire UCSF ImmunoX research community, taken from a cross-section of health and disease, to discover treatments for human disease.

The Hackathon is a 48hr event where teams with diverse skills worked together to process, annotate, and analyze single-cell RNA sequencing data and gain immunological insights into patient data. This years focus was on Cancer Immunology by analyzing single cell RNA sequencing data that were generated by my lab through the immunoprofiler consortium. I have overseen the preparation of the dataset and coordinate with the Data science group to set up the challenges. I was also part of the jury of Faculty who evaluated and grade the different teams.

UCSF CAMPUSWIDE

2020 - present	UCSF CoLabs Postbac Research Program	Member
2021 - present	UCSF COVID vaccination team	Volunteer
2021 - present	ImmunoX Media Outreach team	Member
2022 - present	ImmunoX Computational Biology Initiative Hackathon	Faculty organizer and Judge
2023 - present	Biomedical Sciences (BMS) Graduate Program	Admission committee

COMMUNITY AND PUBLIC SERVICE

2017 - 2017	Discovery day (AT&T Park)	Volunteer
2018 - 2018	Discovery day (AT&T Park)	Volunteer
2018 - 2018	Cal Academy NightLife	Volunteer
2022 - 2022	Discovery day (Oracle Park)	

CONTRIBUTIONS TO DIVERSITY

CONTRIBUTIONS TO DIVERSITY Contributions to Diversity, Equity & Inclusion Guidance

The UCSF CoLabs Postbac Research Program is a 2-year program that provides mentoring and training opportunities for recent college graduates who are planning to pursue a future in biomedical research. My group, the Disease to Biology CoLab, is actively part of this program and offer post graduate position to underrepresented communities in STEM. As part of this program, the participant will be in a series of activities designed to promote your scientific development, including educational seminars and workshops, individual research projects, journal clubs, one-on-one mentoring, graduate school resource sessions, lab and project meetings, and other community-building activities. This program serves as an excellent stepping stone to prepare for admission to graduate or professional schools.

TEACHING AND MENTORING

TEACHING SUMMARY

BMS Graduate Program Service: I have served in several capacities in the BMS Graduate Program, including (1) faculty reader of the Admission Committee (2022 □ present), (2) member of the Admission Committee (starting from 2021 □ 2022 admission cycle), (3) faculty interviewer for BMS Admission (20022 □ present), and (4) faculty advisor for the 1st and 2nd

year graduate students (2022 □ present). I also lead discussion for BMS260 Cell Biology and BMS 255 genetic.

FORMAL TEACHING

	Academic Yr	Course No. & Title	Teaching Contribution	School	Class Size
	2021 - 2021	BMS 225A selective workshop: Approaches for Immune Monitoring	Instructor	Grad	20

MENTORING SUMMARY

During the Summer 2022 I have hosted a summer student in the lab for three weeks. Iris Tholke is an incoming sophomore year at Northeastern University with a focus on science in Behavioral neuroscience. Iris had her first research lab experience with us and by shadowing Brittany Davidson a SRA of my lab, she learned basic laboratory techniques as well as the multi dimensional immune monitoring techniques we are routinely performing in the lab, such as flow cytometry and single-cell genomics. I'm also part of the dissertation committee of two graduate student in the BMS program. I have regularly meet with them to help them prepare their qualifying exam and will continue to meet with them regularly during their Ph.D. project.

PREDOCTORAL STUDENTS SUPERVISED OR MENTORED

Dates	Name	Program or School	Mentor Type	Role	Current Position
2015 - 2015	Magali Guarelia	School of Medicine Marseille France	Project Mentor	Rotation student	Pediatrician Resident, Marseille Hospital France
2016 - 2017	Diego Urbina	School of Medicine Marseille France	Project Mentor	Rotation Student	Pediatrician Resident, Marseille Hospital France
2017 - 2018	Joy HSU	UCSF	Research/Scholarly Mentor	SRA	Graduate student SK cancer institute New york
2017 - 2018	Arun Bura	UCSF	Project Mentor	SRA	Med School Student UCSF

Dates	Name	Program or School	Mentor Type	Role	Current Position
2018 - present	Jessica TSUI	UCSF	Research/Scholarly Mentor,Project Mentor	SRA	Lab Manager at UCSF in Disease to Biology CoLab
2018 - 2020	Gabriella Reeder	UCSF	Research/Scholarly Mentor,Project Mentor	SRA	Graduate Student at UCSF
2018 - present	Nayvin Chew	UCSF	Research/Scholarly Mentor,Project Mentor	SRA	SRA UCSF
2018 - 2020	Peter Yan	UCSF	Research/Scholarly Mentor,Project Mentor	SRA	Med School student at UCLA
2019 - present	Alan Shen	UCSF	Research/Scholarly Mentor,Project Mentor	SRA	SRA accepted in Med School at UCSD
2019 - present	Divyashree Kushnoor	UCSF	Research/Scholarly Mentor,Project Mentor	SRA	SRA
2020 - present	Brittany Davidson	UCSF	Research/Scholarly Mentor,Project Mentor	SRA	SRA
2021 - present	Vrinda Johiri	UCSF	Research/Scholarly Mentor,Project Mentor	SRA	SRA
2021 - present	Christina Ericksen	UCSF	Research/Scholarly Mentor,Project Mentor	SRA	SRA
2022 - present	Liz Rurangwa,	UCSF	Research/Scholarly Mentor	SRA	SRA

Dates	Name	Program or School	Mentor Type	Role	Current Position
2022 - 2022	Iris Tholke	UCSF	Research/Scholarly Mentor	Visiting Student	Incoming Sophomore year at Northeastern University
2022 - present	Nicholas Carey	UCSF	Research/Scholarly Mentor	Graduate student	
2022 - present	Laura Dwyer	UCSF	Research/Scholarly Mentor	Graduate student	
2022 - present	Molly Bassette	UCSF	Research/Scholarly Mentor	Graduate Student	
2023 - present	Tammie Tam	UCSF	Research/Scholarly Mentor,Project Mentor	SRA	SRA
2023 - present	Saba Shaik	UCSF	Research/Scholarly Mentor,Project Mentor	SRA	SRA
2023 - present	Isabel Shen	UCSF	Research/Scholarly Mentor,Project Mentor	BMS Graduate student	

POSTDOCTORAL FELLOWS AND RESIDENTS MENTORED

Dates	Name	Fellow	Mentor Role	Faculty Role	Current Position
2019 - present	Tristan Courau	Post doctoral fellow	Project Mentor		Post doctoral fellow
2020 - present	Justine Levan	Post-doctoral fellow	Project Mentor		Post doctoral fellow
2020 - present	Im Kwok	Post-doctoral fellow	Project Mentor		Post doctoral fellow

RESEARCH AND CREATIVE ACTIVITIES

RESEARCH AND CREATIVE ACTIVITIES SUMMARY

Early this year, two of my main project focusing on defining the immune states across solids tumors have been published. First We processed 364 individual tumors across 12 cancer types using standardized protocols. Computational clustering of flow cytometry and

transcriptomic data obtained from cell sub-compartments uncovered twelve conserved, dominant patterns of immune composition across cancers of diverse origins. These compositional archetypes also corresponded to distinct transcriptional patterns of chemokine-receptor pairs as well as unique patterns in the tumor cells themselves, suggesting mechanisms that may generate and reinforce these archetypes. While further refinement and discovery of these dominant archetypes are inevitable, our work provides a template for understanding cancer immunity as a collection of dominant patterns of immune organization (Combes et al Cell 2022). Using a similar approach we refined the relationship between Treg and monocytes to macrophage differentiation in tumors. We found that, monocyte-to-macrophage differentiation is tied to the abundance of regulatory T cell (Treg) which in return influenced the composition of the whole tumor immune microenvironment including the quality of the intratumoral CD8+ T cells. Assessing the connections between these cell types stratified patients with renal cell carcinoma by outcome, highlighting how patient immune archetype can provide clinically important information (Mujal AM*,Combes AJ* et al Cancer immunology research 2022). During this year, i have also joined the faculty in the department of Pathology, as assistant professor in residence and officially opened my independent research lab in January 2022. In the last six month my focus has been on recruiting post doctoral and graduate student in the lab to be able to pursue my independent research program. In parallel, my group through the disease to biology CoLab has been supporting a variety of immune profiling accros the campus. Including, a deep immune profiling of women with endometriosis which has been recently published in BMC medicine (Juanico-Valve et al 2022) , a study that i co-lead with Dr Guidice and that is now leading to a R-01 submission in the fall

RESEARCH AWARDS - CURRENT

1. ImmunoX CoPilot Cycle 1 Co-PI	10 % effort	Krummel MF and Arguello RJ (PI)
Bakar ImmunoX initiative	06/01/2019	12/01/2023
Metabolomic profiling of Acute Myeloid Leukemia		$ 135k total

The energetic metabolism (EM) profile describes the main sources of energy and biochemical pathways from which cells depend on to produce ATP and also their potential to exploit other alternative sources of energy. EM profile also determines the competence of cells to survive in different anatomic locations and upon exposure to intrinsic and extrinsic signaling cues. This information is central to understand the physiological function and cellular state of different cell types. Among others, cancer stem cells, tumoral cells and different immune cells have an EM profile that impact on their capacity to proliferate, differentiate, and perform their physiological functions. Moreover, EM profile is also key in tumors, as it allows to determine the susceptibility of transformed cells to inhibitors of particular metabolic pathways (Wallace et al., 2010) (Connolly et al., 2014; Ganeshan and Chawla, 2014; MacIver et al., 2013). Recently, studies on immuno-metabolism indicate that immune cells have a tightly controlled and cell type-specific metabolic profile. This metabolic profile relies in the expression of particular genes cells that regulate EM and that is part of their differentiation program. Immune or cancer cell-specific EM profiles reflect the state of activation or differentiation and determine the competence of these cells to migrate, survive, or respond to different immunological challenges. Using a combination of multiparametric single-cell methods, SCENITH a technique we recently developed (Arguello RJ, Combes AJ et al Cell Metabolism 2020) combined to single-cell RNA-sequencing and single-cell DNA/-sequencing, we will determine metabolic, phenotypic, and genotypic heterogeneity in leukemic cells from blood and bone marrow. This project will be the first to study in parallel, in single cells, the transcriptomic and genetic landscape and its association with particular metabolism profiles in different anatomical locations. As the energetic metabolism profile of a cell reflect its state of activation, differentiation and determine its competence to migrate, survive, or respond to chemotherapeutic treatments. Our aim is to identify tumor heterogeneity in different tissue locations by studying it at three levels: 1) Functional (metabolic), 2) Phenotypic (SCRNAseq and CyTOF) and 3) genetic (scDNA seq) level.

Firstly, I will design and perform the initial experiment using single-cell RNA sequencing and SCENITH to profile in parallel and cell composition and their different metabolism profile. Secondly, I will train and supervise an SRA from my group to reproduce those experiments on the entire cohort of patients. Finally, I will mentor this SRA for the analysis and supervise the conclusion of the experiment in collaboration with the two principal investigators of the project.

RESEARCH AWARDS - SUBMITTED

1.	Co-investigator/Core Director	10% % effort	Lynch (PI)
NIH-U19		09/2021	09/2026
Dissecting microbial and metabolic influences on preterm infants functional immune trajectory			$ 5,000,000 total

The study proposed in this application will leverage this pre-existing BCMM-PTBi research infrastructure and samples to assess, at high-resolution, early-life nutritional-microbial-immune interactions and their effect on functional immune development, immunometabolic status, epigenetic programming, and clinical outcomes through 18-months of age.

I will oversee within-core work flows the different assays proposed. I will also coordinate this work with the other cores in collaboration with the Data Science CoLabs director, Dr Fragiadakis and Dr. Ha director of the Microbial Genomics Facility. I will oversee cellular profiling with cutting-edge technologies such as multi-parametric flow cytometry, and single-cell RNA-seq to define cellular states in both patients and healthy individuals. . As lead of Core B, I will craft the experimental strategy collaboratively for both proposed projects, oversee data generation and transfer in the Data Library. I will also work closely with the data analysis and will participate in monthly project meetings and in all resulting manuscripts.

2.	Co-investigator/Core director	15% % effort	Jones (PI)
	NIH-NIAID-NIEHS-NICHD (U54)	12/01/2021	12/01/2026
	UCSF Tissue Mapping Center (TMC) is to generate multiparametric single-cell data for human tissue-derived senescent (SenNET)		$ 5,000,000 total

The Goal of this project is to establish state-of-the-art Tissue Mapping Centers (TMCs) to work within the Cellular Senescence Network (SenNet). The goal of the SenNet consortium is to identify and functionally characterize the heterogeneity of senescent cells across multiple tissues in human health, disease, and lifespan at single-cell resolution.

I will oversee within-core work flows the different assays proposed. I will also coordinate this work among the different Core with the help of Genomics CoLabs director Walter Eckalbar, Flow Cytometry CoLab director Claudia Bispo, and imaging CoLabs director Kyle Marchuk, as well as sample acquisition with the Biospecimen Core and computational analysis in collaboration with the Data Analysis Core. I will leverage my experience on cellular profiling with cutting edge technologies such as multi-parametric flow, mass cytometry, and single-cell RNA-seq and ATAC-seq to define cellular states in both patients and healthy individuals. He also developed the SCENITH method a flow cytometry-based method that will be used to profile metabolic states of senescent cells.

3.	Co-PI	10% % effort	Ye (PI)
	NIH- NIAMS NIAID NIDCR	09/01/2021	09/01/2026
	Defining systemic and tissue immune mechanisms associated with Auto-immune diseases		$ 2,345,123 total

Autoimmune and immune-mediated diseases (AIM) in aggregate affect more than 5% of the U.S. population and often have chronic systemic and organ-specific manifestations.We will use State-of-the-art single-cell and spatial genomic methods opportunities for unbiased, high-dimensional, and high-throughput cellular phenotyping.

Dr. Alexis Combes will collaborate with UCSF tissue experts Knox (salivary gland), Scharschmidt (skin), Huang (kidney), and Pelkin (tissue immunity) to develop novel and improve existing protocols for processing small biopsies and cryopreservation across tissues relevant to AIM diseases. Protocols will be developed collaboratively with the larger AMP community to enable standardized sample processing and profiling. The D2B CoLab (combes's lab) is a collaboration-based research lab that focuses on profiling the immune system across diseases including cancer, infectious disease, and autoimmunity

4.	Co-I	10% % effort	Lynch (PI)
	NIH-NIAD UM1	01/01/2023	01/01/2028

Systems Approach to the Early-Life Origins of Food Allergy and Atopic Dermatitis (SOFA)	$ 1,799,804 direct/yr 1	$ 8,994,443 total

Our goal is to apply a systems approach to understanding the developmental origins of food allergy, atopic dermatitis, and their co-expression. We propose a massively parallel inter-generational characterization of longitudinal immune endotypes using five major technologies (mass high parameter epigenetics, cytometry analysis, transcriptomics RNASeq, scRNAseq and CITEseq) and microbiomics to identify the longitudinal immune endotypes that underlie the complex clinical expression of these heterogeneous conditions during early life.

I will oversee the different. Immune monitoring assays proposed here to define the developmental trajectory of the immune system in enfant with FA and AD. His lab is specialized in using a system immunology approach combining bulk and single cell omics technologies to profile the immune system in diverse human tissues. I will leverage my experience in cellular profiling with cutting-edge technologies such as multi-parametric flow cytometry, and single-cell RNA-seq to define cellular states in both patients and healthy individuals across a diverse set of diseases. I will craft the experimental strategy collaboratively for both proposed projects, oversee data generation and transfer to the data science group. I will also work closely with the data analysis and will participate in monthly project meetings and in all resulting manuscripts.

5.	CO-I	10% % effort	Barcellos-Hoff, (PI)
NIH-NCI		01/01/2023	01/01/2028
Cross-species Credentialing of Immune Archetypes in a Preclinical Cancer Model		$ 408,006 direct/yr 1	$ 2,164,585 total

The ultimate goal of personalized medicine is to determine which patients will benefit most from a therapeutic regimen, particularly new treatment combinations of cytotoxic therapies that synergize with immunoncology drugs. Here we will translate newly defined human immune archetypes to preclinical carcinomas and generate foundational correlative data with immunotherapy response.

I will coordinate the interrogation of immune archetypes in the mouse cancer specimens, supervise immune profiling and develop the experimental plan and research approaches with Dr. Barcellos-Hoff. I will interact with the team at project meetings and informally, and report results at scientific meetings.

RESEARCH AWARDS - PAST

1. MM35, OT133-334	Post doctoral fellow	50% % effort	Krummel MF (PI)
International immuno oncology Network in partnership with Bristan Myer and Squibb		01/01/2018	01/01/2020
Evaluating the effects of CTLA-4 blockade and Fc□R interactions on tumor specific T cells of differing TCR affinities			$ 350k total

While CTLA-4 has a well-defined role as a negative regulator of T cell activity, it is unclear whether CTLA-4 inhibits high and low avidity T cells to an equal degree. Data from mouse experiments implied that CTLA-4 may preferentially inhibit high avidity T cells due to higher surface expression and T cell synapse localization of CTLA-4 on these cells after activation. Based on this data CTLA-4 was hypothesized to broaden the TCR repertoire of responding cells by restricting the expansion of high avidity clones. Recent data from patients treated with ipilimumab however contradicted this hypothesis and indicated that CTLA-4 blockade led to a more diverse TCR repertoire after treatment. Using established tumor models that express the model antigen OVA, the effect of CTLA-4 blockade on TCR transgenics with either high avidity (OT-I) or low avidity (OT-III) will be characterized.

I designed, performed, and analyzed the data from different experiments. I also trained and supervised an SRA who joined the lab for those specific projects. The results of this project have been included in a manuscript published in 2019 (Binnewies et al Cell 2019) as well as in a manuscript in preparation (Mujal AM, Combes AJ in prep)

2. 20150034	Graduate-Student	100% % effort	Pierre and Gatti (PI)
ARC: Association of Cancer Research		10/01/2015	10/01/2016
Deciphering the role Toll Like Receptor trafficking in human plasmacytoid dendritic cells			$ 60k total

3. MESR20120987	Graduate Student	100% % effort	Pierre and Gatti (PI)
French Ministry of Research		10/01/2012	10/01/2012
Understanding the role of BAD-LAMP in controlling Toll like Receptor trafficking			$ 100k total

PEER REVIEWED PUBLICATIONS

1. Terawaki S, Camosseto V, Prete F, Wenger T, Papadopoulos A, Rondeau C, Combes A, Rodriguez Rodrigues C, Vu Manh TP, Fallet M, English L, Santamaria R, Soares AR, Weil T, Hammad H, Desjardins M, Gorvel JP, Santos MA, Gatti E, Pierre P. RUN and FYVE domain-containing protein 4 enhances autophagy and lysosome tethering in response to Interleukin-4. J Cell Biol. 2015 Sep 28; 210(7):1133-52. PMID: 26416964. PMCID: PMC4586740
2. Tiveron MC, Beurrier C, Céni C, Andriambao N, Combes A, Koehl M, Maurice N, Gatti E, Abrous DN, Kerkerian-Le Goff L, Pierre P, Cremer H. LAMP5 Fine-Tunes GABAergic Synaptic Transmission in Defined Circuits of the Mouse Brain. PLoS One. 2016; 11(6):e0157052. PMID: 27272053. PMCID: PMC4896627
3. Combes A, Camosseto V, N'Guessan P, Argüello RJ, Mussard J, Caux C, Bendriss-Vermare N, Pierre P, Gatti E. BAD-LAMP controls TLR9 trafficking and signalling in human plasmacytoid dendritic cells. Nat Commun. 2017 10 13; 8(1):913. PMID: 29030552. PMCID: PMC5640662

4. Dalet A, Argüello RJ, Combes A, Spinelli L, Jaeger S, Fallet M, Vu Manh TP, Mendes A, Perego J, Reverendo M, Camosseto V, Dalod M, Weil T, Santos MA, Gatti E, Pierre P. Protein synthesis inhibition and GADD34 control IFN-ß heterogeneous expression in response todsRNA. EMBO J. 2017 03 15; 36(6):761-782. PMID: 28100675. PMCID: PMC5350567

5. De Angelis Rigotti F, De Gassart A, Pforr C, Cano F, N'Guessan P, Combes A, Camossetto V, Lehner PJ, Pierre P, Gatti E. MARCH9-mediated ubiquitination regulates MHC I export from the TGN. Immunol Cell Biol. 2017 10; 95(9):753-764. PMID: 28559542

6. Barry KC, Hsu J, Broz ML, Cueto FJ, Binnewies M, Combes AJ, Nelson AE, Loo K, Kumar R, Rosenblum MD, Alvarado MD, Wolf DM, Bogunovic D, Bhardwaj N, Daud AI, Ha PK, Ryan WR, Pollack JL, Samad B, Asthana S, Chan V, Krummel MF. A natural killer-dendritic cell axis defines checkpoint therapy-responsive tumor microenvironments. Nat Med. 2018 Aug; 24(8):1178-1191. PMID: 29942093. PMCID: PMC6475503

7. Perego J, Mendes A, Bourbon C, Camosseto V, Combes A, Liu H, Manh TV, Dalet A, Chasson L, Spinelli L, Bardin N, Chiche L, Santos MAS, Gatti E, Pierre P. Guanabenz inhibits TLR9 signaling through a pathway that is independent of eIF2a dephosphorylation by the GADD34/PP1c complex. Sci Signal. 2018 01 23; 11(514). PMID: 29363586

8. Binnewies M, Mujal AM, Pollack JL, Combes AJ, Hardison EA, Barry KC, Tsui J, Ruhland MK, Kersten K, Abushawish MA, Spasic M, Giurintano JP, Chan V, Daud AI, Ha P, Ye CJ, Roberts EW, Krummel MF. Unleashing Type-2 Dendritic Cells to Drive Protective Antitumor CD4+ T Cell Immunity. Cell. 2019 Mar 12. PMID: 30955881

9. Argüello RJ, Combes AJ, Char R, Gigan JP, Baaziz AI, Bousiquot E, Camosseto V, Samad B, Tsui J, Yan P, Boissonneau S, Figarella-Branger D, Gatti E, Tabouret E, Krummel MF, Pierre P. SCENITH: A Flow Cytometry-Based Method to Functionally Profile Energy Metabolism with Single-Cell Resolution. Cell Metab. 2020 Dec 1;32(6):1063-1075.e7. doi: 10.1016/j.cmet.2020.11.007. PMID: 33264598.

10. Kratz JR, Li JZ, Tsui J, Lee JC, Ding VW, Rao AA, Mann MJ, Chan V, Combes AJ, Krummel MF, Jablons DM. Genetic and immunologic features of recurrent stage I lung adenocarcinoma. Sci Rep. 2021 12 08; 11(1):23690. PMID: 34880292. PMCID: PMC8654957

11. Combes AJ, Courau T, Kuhn NF, Hu KH, Ray A, Chen WS, Chew NW, Cleary SJ, Kushnoor D, Reeder GC, Shen A, Tsui J, Hiam-Galvez KJ, Muñoz-Sandoval P, Zhu WS, Lee DS, Sun Y, You R, Magnen M, Rodriguez L, Im KW, Serwas NK, Leligdowicz A, Zamecnik CR, Loudermilk RP, Wilson MR, Ye CJ, Fragiadakis GK, Looney MR, Chan V, Ward A, Carrillo S, UCSF COMET Consortium, Matthay M, Erle DJ, Woodruff PG, Langelier C, Kangelaris K, Hendrickson CM, Calfee C, Rao AA, Krummel MF. Publisher Correction: Global absence and targeting of protective immune states in severe COVID-19. Nature. 2021 Aug; 596(7872):E8. PMID: 34341540. PMCID: PMC8328349

12. Cueto FJ, Del Fresno C, Brandi P, Combes AJ, Hernández-García E, Sánchez-Paulete AR, Enamorado M, Bromley CP, Gomez MJ, Conde-Garrosa R, Mañes S, Zelenay S, Melero I, Iborra S, Krummel MF, Sancho D. DNGR-1 limits Flt3L-mediated antitumor immunity by restraining tumor-infiltrating type I conventional dendritic cells. J Immunother Cancer. 2021 05; 9(5). PMID: 33980589. PMCID: PMC8118081

13. van der Wijst MGP, Vazquez SE, Hartoularos GC, Bastard P, Grant T, Bueno R, Lee DS, Greenland JR, Sun Y, Perez R, Ogorodnikov A, Ward A, Mann SA, Lynch KL, Yun C,

Havlir DV, Chamie G, Marquez C, Greenhouse B, Lionakis MS, Norris PJ, Dumont LJ, Kelly K, Zhang P, Zhang Q, Gervais A, Le Voyer T, Whatley A, Si Y, Byrne A, Combes AJ, Rao AA, Song YS, Fragiadakis GK, Kangelaris K, Calfee CS, Erle DJ, Hendrickson C, Krummel MF, Woodruff PG, Langelier CR, Casanova JL, Derisi JL, Anderson MS, Ye CJ, UCSF COMET consortium . Type I interferon autoantibodies are associated with systemic immune alterations in patients with COVID-19. Sci Transl Med. 2021 09 22; 13(612):eabh2624. PMID: 34429372

14. Seed RI, Kobayashi K, Ito S, Takasaka N, Cormier A, Jespersen JM, Publicover J, Trilok S, Combes AJ, Chew NW, Chapman J, Krummel MF, Lou J, Marks J, Cheng Y, Baron JL, Nishimura SL. A tumor-specific mechanism of Treg enrichment mediated by the integrin αvβ8. Sci Immunol. 2021 Mar 26; 6(57). PMID: 33771888

15. Transcriptomic analysis of immune cells in a multi-ethnic cohort of systemic lupus erythematosus patients identifies ethnicity- and disease-specific expression signatures. Commun Biol. 2021 Apr 21; 4(1):488. PMID: 33883687. PMCID: PMC8060402

16. You R, Artichoker J, Fries A, Edwards AW, Combes AJ, Reeder GC, Samad B, Krummel MF. Active surveillance characterizes human intratumoral T cell exhaustion. J Clin Invest. 2021 Jul 22:144353. doi: 10.1172/JCI144353. Epub ahead of print. PMID: 34292884.

17. Combes AJ, Samad B, Tsui J, Chew NW, Yan P, Reeder GC, Kushnoor D, Shen A, Davidson B, Barczak AJ, Adkisson M, Edwards A, Naser M, Barry KC, Courau T, Hammoudi T, Argüello RJ, Rao AA, Olshen AB, Immunoprofiler Consortium, Cai C, Zhan J, Davis KC, Kelley RK, Chapman JS, Atreya CE, Patel A, Daud AI, Ha P, Diaz AA, Kratz JR, Collisson EA, Fragiadakis GK, Erle DJ, Boissonnas A, Asthana S, Chan V, Krummel MF. Discovering dominant tumor immune archetypes in a pan-cancer census. Cell. 2022 01 06; 185(1):184-203.e19. PMID: 34963056. PMCID: PMC8862608

18. Adamik J, Munson PV, Hartmann FJ, Combes AJ, Pierre P, Krummel MF, Bendall SC, Argüello RJ, Butterfield LH. Distinct metabolic states guide maturation of inflammatory and tolerogenic dendritic cells. Nat Commun. 2022 09 02; 13(1):5184. PMID: 36056019. PMCID: PMC9440236

19. Vallvé-Juanico J, George AF, Sen S, Thomas R, Shin MG, Kushnoor D, Vásquez JJ, Vo KC, Irwin JC, Roan NR, Combes AJ, Giudice LC. Deep immunophenotyping reveals endometriosis is marked by dysregulation of the mononuclear phagocytic system in endometrium and peripheral blood. BMC Med. 2022 04 15; 20(1):158. PMID: 35421980. PMCID: PMC9011995

20. Mujal AM, Combes AJ, Rao AA, Binnewies M, Samad B, Tsui J, Boissonnas A, Pollack JL, Argüello RJ, Meng MV, Porten SP, Ruhland MK, Barry KC, Chan V, Krummel MF. Holistic Characterization of Tumor Monocyte-to-Macrophage Differentiation Integrates Distinct Immune Phenotypes in Kidney Cancer. Cancer Immunol Res. 2022 Feb 18. PMID: 35181780. PMCID: PMC8982148

21. Laviron M, Petit M, Weber-Delacroix E, Combes AJ, Arkal AR, Barthélémy S, Courau T, Hume DA, Combadière C, Krummel MF, Boissonnas A. Tumor-associated macrophage heterogeneity is driven by tissue territories in breast cancer. Cell Rep. 2022 May 24; 39(8):110865. PMID: 35613577

22. Kersten K, Hu KH, Combes AJ, Samad B, Harwin T, Ray A, Rao AA, Cai E, Marchuk K, Artichoker J, Courau T, Shi Q, Belk J, Satpathy AT, Krummel MF. Spatiotemporal co-

dependency between macrophages and exhausted CD8+ Tcells in cancer. Cancer Cell. 2022 06 13; 40(6):624-638.e9. PMID: 35623342. PMCID: PMC9197962

23. Hysenaj L, Little S, Kulhanek K, Magnen M, Bahl K, Gbenedio OM, Prinz M, Rodriguez L, Andersen C, Rao AA, Shen A, Lone JC, Lupin-Jimenez LC, Bonser LR, Serwas NK, Mick E, Khalid MM, Taha TY, Kumar R, Li JZ, Ding VW, Matsumoto S, Maishan M, Sreekumar B, Simoneau C, Nazarenko I, Tomlinson MG, Khan K, von Gottberg A, Sigal A, Looney MR, Fragiadakis GK, Jablons DM, Langelier CR, Matthay M, Krummel M, Erle DJ, Combes AJ, Sil A, Ott M, Kratz JR, Roose JP. SARS-CoV-2 infection of airway organoids reveals conserved use of Tetraspanin-8 by Ancestral, Delta, and Omicron variants. Stem Cell Reports. 2023 03 14; 18(3):636-653. PMID: 36827975. PMCID: PMC9948283

24. Rahim MK, Okholm TLH, Jones KB, McCarthy EE, Liu CC, Yee JL, Tamaki SJ, Marquez DM, Tenvooren I, Wai K, Cheung A, Davidson BR, Johri V, Samad B, O'Gorman WE, Krummel MF, van Zante A, Combes AJ, Angelo M, Fong L, Algazi AP, Ha P, Spitzer MH. Dynamic CD8+ T cell responses to cancer immunotherapy in human regional lymph nodes are disrupted in metastatic lymph nodes. Cell. 2023 03 16; 186(6):1127-1143.e18. PMID: 36931243. PMCID: PMC10348701

25. Im KW, Huppert LA, Malevanchik L, Rugo HS, Combes AJ, Campbell MJ, Krummel MF, Melisko ME. High-dimensional immune cell profiling of cerebrospinal fluid from patients with metastatic breast cancer and leptomeningeal disease. NPJ Breast Cancer. 2023 Apr 07; 9(1):22. PMID: 37029150. PMCID: PMC10082042

26. Munson PV, Adamik J, Hartmann FJ, Favaro PMB, Ho D, Bendall SC, Combes AJ, Krummel MF, Zhang K, Kelley RK, Butterfield LH. Polyunsaturated Fatty Acid-Bound α-Fetoprotein Promotes Immune Suppression by Altering Human Dendritic Cell Metabolism. Cancer Res. 2023 05 02; 83(9):1543-1557. PMID: 36847613. PMCID: PMC10152238

27. Hu KH, Kuhn NF, Courau T, Tsui J, Samad B, Ha P, Kratz JR, Combes AJ, Krummel MF. Transcriptional space-time mapping identifies concerted immune and stromal cell patterns and gene programs in wound healing and cancer. Cell Stem Cell. 2023 06 01; 30(6):885-903.e10. PMID: 37267918

NON-PEER REVIEWED PUBLICATIONS

1. Freedman TS, Headley MB, Serwas N, Ruhland M, Castellanos CA, Combes AJ, Krummel MF. Lessons of COVID-19: A roadmap for post-pandemic science. J Exp Med. 2020 Sep 7;217(9):e20201276. doi: 10.1084/jem.20201276. PMID: 32735669; PMCID: PMC7392636.

2. Patel RK, Jaszczak RG, Kwok I, Carey ND, Courau T, Bunis D, Samad B, Avanesyan L, Chew NW, Stenske S, Jespersen JM, Publicover J, Edwards A, Naser M, Rao AA, Lupin-Jimenez L, Krummel MF, Cooper S, Baron J, Combes AJ, Fragiadakis GK. Cyclone: an accessible pipeline to analyze, evaluate and optimize multiparametric cytometry data. bioRxiv. 2023 Mar 11. PMID: 36945648. PMCID: PMC10028883

3. Mennillo E, Kim YJ, Rusu I, Lee G, Dorman LC, Bernard-Vazquez F, Bain JL, Patel R, Andersen C, Rao A, Tamaki S, Tsui J, Shen A, Naser M, Eckalbar W, Cho SJ, Beck K, El-Nachef N, Lewin S, Selvig DR, Terdiman JP, Mahadevan U, Oh D, Fragiadakis GK, Pisco A, Combes A, Kattah MG. Single-cell and spatial multi-omics identify innate and stromal modules targeted by anti-integrin therapy in ulcerative colitis. bioRxiv. 2023 Jul 15. PMID: 36711576. PMCID: PMC9882264

4. Tanaka M, Lum L, Hu K, Ledezma-Soto C, Samad B, Superville D, Ng K, Adams Z, Kersten K, Fong L, Combes AJ, Krummel M, Reeves M. Tumor cell heterogeneity drives spatial organization of the intratumoral immune response in squamous cell skin carcinoma. bioRxiv. 2023 Jun 21. PMID: 37162860. PMCID: PMC10168251

REVIEW ARTICLES

1. Im K, Combes AJ, Spitzer MH, Satpathy AT, Krummel MF. Archetypes of checkpoint-responsive immunity. Trends Immunol. 2021 Oct 09. PMID: 34642094
2. Knight JS, Caricchio R, Casanova JL, Combes AJ, Diamond B, Fox SE, Hanauer DA, James JA, Kanthi Y, Ladd V, Mehta P, Ring AM, Sanz I, Selmi C, Tracy RP, Utz PJ, Wagner CA, Wang JY, McCune WJ. The intersection of COVID-19 and autoimmunity. J Clin Invest. 2021 Oct 28. PMID: 34710063
3. Combes AJ, Samad B, Krummel MF. Defining and using immune archetypes to classify and treat cancer. Nat Rev Cancer. 2023 07; 23(7):491-505. PMID: 37277485

SIGNIFICANT PUBLICATIONS

1. Argüello RJ, Combes AJ, Char R, Gigan JP, Baaziz AI, Bousiquot E, Camosseto V, Samad B, Tsui J, Yan P, Boissonneau S, Figarella-Branger D, Gatti E, Tabouret E, Krummel MF, Pierre P. SCENITH: A Flow Cytometry-Based Method to Functionally Profile Energy Metabolism with Single-Cell Resolution. Cell Metab. 2020 Dec 1;32(6):1063-1075.e7. doi: 10.1016/j.cmet.2020.11.007. PMID: 33264598.

   As Co-First authors of this study, I lead the adaptation of SCENITH method to assess metabolic profiles in the Tumor microenvironment both from human biopsies and tumour mouse model. I also lead the work combining SCENITH functional assays using flow cytometry and Single cell RNA sequencing to associate it to a transcriptomic profile. We especially, were able to correlate for the first time the energetic profile of tumor associated myeloid cells and RNA expression of specific genes that

2. Combes AJ, Samad B, Tsui J, Chew NW, Yan P, Reeder GC, Kushnoor D, Shen A, Davidson B, Barczak AJ, Adkisson M, Edwards A, Naser M, Barry KC, Courau T, Hammoudi T, Argüello RJ, Rao AA, Olshen AB, Immunoprofiler Consortium, Cai C, Zhan J, Davis KC, Kelley RK, Chapman JS, Atreya CE, Patel A, Daud AI, Ha P, Diaz AA, Kratz JR, Collisson EA, Fragiadakis GK, Erle DJ, Boissonnas A, Asthana S, Chan V, Krummel MF. Discovering dominant tumor immune archetypes in a pan-cancer census. Cell. 2022 01 06; 185(1):184-203.e19. PMID: 34963056. PMCID: PMC8862608

   Some tumor microenvironments can provide tumors a pathway to tap into immune responses that are promoting for tumor tolerance due to an accommodation between the immune system and the tumor. These archetypes we term □dominant tumor archetypes□ which can vary across different tumor types resulting in □suppressed□ immunity. To discover these dominant tumor archetypes, I led an interdisciplinary team of staff research associates and computational scientists part of the UCSF Immunoprofiler Initiative (IPI). We processed 364 individual tumors across 12 cancer types using standardized protocols. Computational clustering of flow cytometry and transcriptomic data obtained from cell sub-compartments uncovered twelve conserved, dominant patterns of immune composition across cancers of diverse origins. These compositional archetypes also corresponded to distinct transcriptional patterns of chemokine-receptor pairs as well as unique patterns in the tumor cells themselves, suggesting mechanisms that may generate and reinforce these archetypes. While further refinement and discovery of these dominant archetypes are inevitable, my work provides a template for understanding cancer immunity as a collection of dominant patterns of immune organization.

3. Mujal AM, Combes AJ, Rao AA, Binnewies M, Samad B, Tsui J, Boissonnas A, Pollack JL, Argüello RJ, Meng MV, Porten SP, Ruhland MK, Barry KC, Chan V, Krummel MF. Holistic Characterization of Tumor Monocyte-to-Macrophage Differentiation Integrates Distinct Immune Phenotypes in Kidney Cancer. Cancer Immunol Res. 2022 Feb 18. PMID: 35181780. PMCID: PMC8982148

   As the Co-first author of this study, I designed and performed the experiment to characterize the transcriptomic states of the monocytes and macrophages in tumors using single-cell RNA sequencing. We identified lineage- and activation-induced programs that characterize monocyte-to-macrophage differentiation across multiple mouse models of cancer and human tumors. Further multiparametric immune-monitoring analysis shows monocyte-to-macrophage differentiation is tied to the abundance of regulatory T cell (Treg) which in return influenced the composition of the whole tumor immune microenvironment including the quality of the intratumoral CD8+ T cells. Assessing the connections between these cell types stratified patients with renal cell carcinoma by outcome, highlighting how patient immune archetype can provide clinically important information.

4. Combes AJ, Courau T, Kuhn NF, Hu KH, Ray A, Chen WS, Chew NW, Cleary SJ, Kushnoor D, Reeder GC, Shen A, Tsui J, Hiam-Galvez KJ, Muñoz-Sandoval P, Zhu WS, Lee DS, Sun Y, You R, Magnen M, Rodriguez L, Im KW, Serwas NK, Leligdowicz A, Zamecnik CR, Loudermilk RP, Wilson MR, Ye CJ, Fragiadakis GK, Looney MR, Chan V, Ward A, Carrillo S, UCSF COMET Consortium, Matthay M, Erle DJ, Woodruff PG, Langelier C, Kangelaris K, Hendrickson CM, Calfee C, Rao AA, Krummel MF. Publisher Correction: Global absence and targeting of protective immune states in severe COVID-19. Nature. 2021 Aug; 596(7872):E8. PMID: 34341540. PMCID: PMC8328349

   of As Co-First and Co-Corresponding authors of this study, I first designed and performed the initial experiment to profile peripheral blood immune cells. I then both trained and coordinated a team of 15 volunteers to perform whole-blood single-RNA sequencing on blood samples collected from UCSF inpatient with respiratory syndromes. To understand immune biology amongst COVID-19 patients, we compared them to patients presenting with similar respiratory symptoms but who were not infected with the SARS-CoV-2 virus. I also lead the analysis of single-cell RNA sequencing and designed and performed the following in vitro experiments that demonstrate that in severe COVID-19 patients, the immune system fails to generate cells that define mild disease; antibodies in their serum actively prevent the successful production of those cells. Our study defines the antibody receptor FCRyIIb as the potential for immunotherapies in severe patients to re-engage viral defense.

PATENTS ISSUED OR PENDING

1. The ability to monitor translation level in single cell give us non-only the possibility to assess translation but also to investigate any process that is tightly couple to translation. Translation is one of the most metabolically expensive and regulated processes in cells of all life kingdoms. Indeed, most of the energy that the cell obtain from degrading glucose, amino acids or lipids is constantly consumed by the protein synthesis machinery. Using this powerful concept, we generated and optimized a method that rapidly and efficiently measure the impact on the level of protein synthesis in single cells after blocking each and all the possible sources of energy. We recently patented this method called □ZeNITH□ (EP18305110.1, Arguello RJ, Combes A et al; 2018 Inserm-Transfert). Conversely to the current techniques used to profile metabolism ZeNITH needs few starting materials and can be couple to classical flow cytometry. This allow to simultaneously determine the cellular composition, phenotype and metabolism of heterogenous cells populations cells directly ex-vivo. This method is fully in line with the current race to develop analytical methods to classify cancers and define survival and treatment response profiles in patients.
2. The ability to target the antibody receptor FCRyIIb in patient with severe COVID-19 to rescue production of Interferon responding cells which are likely to be protective. This patent is based on findings from Combes AJ et al Nature 2021.
3. The ability to use an antibody against integrin beta 8 to promote anti tumor immune response

OTHER CREATIVE ACTIVITIES

1. Science vulgarisation and dissemination about COVID-19 and about COVID-19 Vaccine on Facebook and Twitter both in French and in english.