Letter from the Chair

Dear Colleagues,

In our third Newsletter, I want to take the opportunity to highlight our accomplishments as a department and the many events we will be hosting in the upcoming few months.

Our faculty continues to publish and present top scholarly work on a range of diverse topics while maintaining a strong commitment to teaching, mentoring, and performing clinical duties. I invite you to read about some of this exciting research, and I am also proud to share some of the significant recognitions our young investigators have received:

- **Dr. Pucella** in the Reizis lab was awarded with a NIH F32 fellowship
- **Dr. Witkowski** in my lab received a prestigious fellowship from the Children’s Oncology Group Foundation
- **Drs. Schwartz, Allison, Hernandez, and Parini**, residents and fellows in our department, were invited to present their research at the USCAP (United States and Canadian Academy of Pathology) Annual Meeting at National Harbor, Maryland, last March

These are only a few examples of our trainees’ many achievements. These exceptional young scientists come to us around the world to receive world-class training, which we are proud to offer; with them, they each bring a unique perspective that adds tremendous value to our research and clinical programs. It is truly a tremendous responsibility and honor for our faculty to help guide them towards becoming the leading pathologists and researchers of tomorrow.

As the Department is expanding its footprint, we are providing our faculty, trainees and staff with state-of-the-art, collaborative spaces and facilities to conduct their important work. In the last year, we have been working with RED+F and OSR to renovate and utilize space in the Smilow Research Building. The **Feske, Koralov, and Papagiannakopoulos** labs have already moved to the building’s 5th floor, and the **Possemato and Park** labs will move to the 6th floor in the summer. The lab of Dr. **Reizis** will move to the 4th floor of the new Science Building this summer, joining Dr. **Naik** in that space.

Finally, let me briefly highlight some of the events we will be hosting this summer as examples of the department’s efforts to implement our vision of a world-class integrated research and clinical community:

- **Residents day** will take place on Thursday, June 13, 4-5pm, Science Building 103, and our guest speaker will be Dr. Montgomery from Johns Hopkins University
- The **7th Annual Pathology Retreat** will be held on Friday, June 14, 8 am to 7 pm, in the Smilow Seminar room; this is our department’s premier event to showcase some of our best clinical and basic research, and I invite everyone to come and hear about the amazing work done in our labs, interact with our trainees and faculty, exchange and generate new ideas, and foster collaborations within the Department; the two keynote speakers will be: **Aravinda Chakravarty, PhD**, Director of the Center for Human Genetics and Genomics at NYU Langone Health, and **Timothy Chan, MD PhD**, Director of Immunogenomics and Precision Oncology Platform at Memorial Sloan Kettering Cancer Center—needless to say, we expect the day to be exciting and we would like to see all of you there!
- The **Annual Immunology and Inflammation Retreat** will be held on Wednesday, June 19, 9:30 am to 7 pm, in Alumni Hall B, and will feature presentations by faculty and trainees
- Our **Welcome Breakfast** for new residents and fellows who will join the department will take place on Monday, July 1st, in Smilow 13th floor, room1301

I hope that you will enjoy reading more about our department’s events and activities in this newsletter. Please feel free to contact us with any questions or comments—we would love to hear from you.

Best regards,

Iannis
Selected Publications

In Chronological Order

Tikhonova, Anastasia N; Dolgalev, Igor; Hu, Hai; Sivaraj, Kishor K; Hoxha, Edilira; Cuesta-Domínguez, Álvaro; Pinho, Sandra; Akhmetzhanova, Ilseyar; Gao, Jie; Witkowski, Matthew; Guillamot, Maria; Gutkin, Michael C; Zhang, Yutong; Marier, Christian; Diefenbach, Catherine; Kousteni, Stavroula; Heguy, Adriana; Zhong, Hua; Fookman, David R; Butler, Jason M; Economides, Aris; Frenette, Paul S; Adams, Ralf H; Satija, Rahul; Tsirigos, Aristotelis; Aifantis, Iannis. 'The bone marrow microenvironment at single-cell resolution'. Nature. 2019 (4); (# 3809302) Impact Factor: 41.577 ; RCR:null | NIH %:null May


Mimitou, Eleni P; Cheng, Anthony; Montalbano, Antonino; Hao, Stephanie; Stoeckius, Marlton; Legut, Mateusz; Roush, Timothy; Herrera, Alberto; Papalex, Efthymia; Ouyang, Zhengqing; Satija, Rahul; Sanjana, Neville E; Koralov, Sergei B; Smibert, Peter. 'Multiplexed detection of proteins, transcriptomes, clonotypes and CRISPR perturbations in single cells'. Nature methods. 2019 16(5):409-412 (# 3821452) Impact Factor: 26.919 ; RCR:null | NIH %:null May 2019


Banin, Andrew N; Tuen, Michael; Bimela, Jude S; Tongo, Marcel; Zappile, Paul; Khodadadi-Jamyran, Alireza; Nanfack, Aubin J; Meli, Josephine; Wang, Xiaohong; Mbanya, Dora; Ngogang, Jeanne; Heguy, Adriana; Nyambi, Phillipe N; Fokunang, Charles; Duerr, Ralf. 'Development of a Versatile, Near Full Genome Amplification and Sequencing Approach for a Broad Variety of HIV-1 Group M Variants'. Viruses. 2019 11(4); (# 3784052) Impact Factor: 3.761 ; RCR:null | NIH %:null April 2019

Eckstein, Miriam; Vaeth, Martin; Aulestia, Francisco J; Cl ostiniti, Veronica; Kassam, Serena N; Bromage, Timothy G; Pedersen, Pal; Isseikut, Thomas; Idaghdour, Youssif; Moursi, Amr M; Feske, Stefan; Lacruz, Rodrigo S. 'Differential regulation of Ca²⁺ influx by ORAI channels mediates enamel mineralization'. Science signaling. 2019 12(578); (# 3821202) Impact Factor: 6.378 ; RCR:null | NIH %:null April 2019

Ng, Charles; Aichinger, Martin; Nguyen, Tung; Au, Christy; Najar, Tariq; Wu, Lin; Mesa, Kai R; Liao, Will; Quivy, Jean-Pierre; Hubert, Benjamin; Almouzni, Genevieve; Zuber, Johannes; Littman, Dan R. 'The histone chaperone CAF-1 cooperates with the DNA methyltransferases to maintainCd4 silencing in cytotoxic T cells'. Genes & development. 2019 (4); (# 3809382) Impact Factor: 9.462 ; RCR:null | NIH %:null April 2019


Basu, Atreyee; Moreira, Andre L; Simms, Anthony; Brandler, Tamar C. 'Sarcomatoid carcinoma in cytology: Report of a rare entity presenting in pleural and pericardial fluid preparations'. Diagnostic
Feske, Stefan. 'CRAC channels and disease - From human CRAC channelopathies and animal models to novel drugs'. Cell calcium. 2019 80():112-116 (#3821362) Impact Factor: 3.718; RCR:null | NIH %:null March 2019


Targeting Mitochondrial Structure Sensitizes Acute Myeloid Leukemia to Venetoclax Treatment


The BCL-2 family plays important roles in acute myeloid leukemia (AML), and upregulation of the anti-apoptotic protein BCL-2 is a poor-risk factor in AML and is associated with poor response to intensive chemotherapy. Thus, Venetoclax, a selective BCL-2 inhibitor, has received breakthrough therapy designation and FDA approval for the treatment of AML. However, the resistance to Venetoclax monotherapy rapidly ensues, highlighting the need for a greater mechanistic understanding of Venetoclax resistance.

To shed light on the mechanisms of resistance to Venetoclax, and to propose novel Venetoclax treatment combinations, we performed a genome-wide CRISPR/Cas9 loss-of-function screen in human AML cells in the presence or absence of Venetoclax. Genes involved in mitochondrial organization and function were significantly depleted throughout our screen. Consistently, we observed mitochondrial structure changes both after Venetoclax treatment and upon acquisition of resistance, highlighting the importance of mitochondrial structural regulators in regulating Venetoclax resistance.

Therefore, we hypothesized that targeting proteins regulating mitochondrial cristae maintenance and function might open up potential synthetic lethal vulnerabilities for Venetoclax treatment. After filtering, we focused on CLPB, a mitochondrial AAA+ ATPase chaperonin, whose ablation sensitizes AML cells to the drug treatment. We showed that the mitochondrial protein CLPB is upregulated in AML patients and protects AML cells against caspase-dependent apoptosis and mitochondrial dysfunction. Mechanistically, we demonstrated that CLPB is essential for sustaining the correct mitochondrial cristae morphology by its direct interaction with OPA1, the master regulator of mitochondrial dynamics. Moreover, CLPB deficiency leads to mitochondrial dysfunction which causes ATF4-mediated mitochondrial stress responses and alterations at the cell transcriptome and metabolome. Furthermore, we confirmed that CLPB ablation synergizes with Venetoclax and Venetoclax/Azacitidine combination in AML in a p53-independent manner. Hence, depleting CLPB sensitizes AML cells to Venetoclax-induced programmed cell death.

Our work suggests that targeting mitochondrial structure could be a promising strategy to overcome Venetoclax resistance in AML patients.

The Bone Marrow Microenvironment at Single-Cell Resolution


Molecular cross-talk between hematopoietic stem cells and their microenvironment is impossible to discern without a clear understanding of the molecular and functional diversity of the bone marrow niche. Therefore, to define the functional interactions that mediate hematopoiesis at steady state and after chemotherapy-induced stress, we mapped the transcriptional landscape of the bone marrow vascular, perivascular, and osteoblast niche populations at single-cell resolution in homeostasis and following chemotherapy treatment. To reliably label the major bone marrow niche subsets, we generated lineage-specific transgenic reporter animal models that fluorescently labeled vascular, mesenchymal or osteogenic cell populations with fluorescent reporter. To refine the
understanding of the transcriptomic diversity within the bone marrow niche, we examined the transcriptional landscape of these cellular subset at single-cell resolution. Here, by profiling 17,374 single bone marrow niche cells, we identify previously unrecognized heterogeneity within the bone marrow microenvironment and demonstrate how the microenvironment responds to acute bone marrow stress at a single-cell level. This analysis identified two clusters specific to vascular endothelial cells, four mesenchymal clusters, and three osteo populations, indicating that niche populations were indeed highly heterogeneous. Biomarkers for niche subpopulations were identified, and patterns of various pro-hematopoietic factors examined. Under conditions of stress, our studies revealed a significant transcriptional remodeling of these niche elements accompanying the myeloid skewing that characterizes emergency hematopoiesis. Among the stress-induced changes, vascular Notch ligand delta-like 4 (Dll4) was significantly downregulated and its vascular-specific deletion was sufficient to recapitulate the shift from lymphoid to myeloid output. In the absence of vascular Dll4, the myeloid transcriptional program was prematurely induced at the hematopoietic stem cell (HSC) stage. This work revealed a previously unappreciated level of cellular heterogeneity in the niche, enabled the identification of novel cellular fractions, and resolved cellular sources of pro-hematopoietic growth factors, chemokines, and membrane-bound ligands. This study has provided a fascinating glimpse into the myriad of changes that occur in bone marrow niche populations following chemotherapy treatment. Changes in molecular architecture of bone marrow niche are likely to cause aberrant alterations in HSC differentiation that underlie malignant hematopoiesis.

Targeting an RNA-Binding Protein Network in Acute Myeloid Leukemia


RNA-binding proteins (RBPs) regulate many aspects of transcription and translation and, as such, are thought to play cell- and tissue-type specific functions. Recently, aberrant expression of RBPs has been linked to tumorigenesis and mutations impacting RBPs involved in RNA splicing have been found to be common in leukemias and other cancers. These discoveries have led to the identification of a number of RBPs that are preferentially required for the survival of cancer cells over non-malignant counterpart cells. To systematically identify RBPs preferentially required in acute myeloid leukemia (AML) over other forms of cancer or normal hematopoietic cells we performed a CRISPR/Cas9 domain-based, loss-of-function screen targeting approximately 500 canonical RBPs. This screen was performed in cells lines representing AML, T-cell acute lymphoblastic leukemia (T-ALL), and lung adenocarcinoma (LUAD) and revealed multiple RBPs uniquely required for AML survival compared to other cancer lineages. These included RBPs that were significantly overexpressed in AML patient samples versus normal adult CD34+ cells. Amongst these RBPs was RBM39, an RBP described to be involved in a number of cellular processes previously, including interacting with key RNA splicing proteins. Genetic ablation as well as pharmacologic degradation of RBM39 using the small molecules, E7820 or indisulam, conferred significant anti-leukemia effects in vivo with surprisingly minimal effects on normal hematopoietic cells. Proteomic analysis of RBM39 in AML cells identified that RBM39 physically interacts with the core RNA splicing machinery, as well as with several of the RBPs identified in our screen as preferentially required in AML. Analysis of RNA physically interacting with RBM39 in AML through eCLIP-Seq identified that RBM39 physically binds to exonic regions of RNA near exon/intron borders and RBM39 loss results in impaired splicing similar to the effects seen with inhibition of the core splicing machinery. Currently, a regimen that includes indisulam in combination with standard chemotherapy is being investigated in phase II trials in patients with refractory or relapsed myeloid malignancies. The present study supports further clinical investigation of E7820 in patients with myeloid malignancies. The data presented here also provides the mechanistic support for expanded use of sulfonamides in clinical trials, as it identifies RBM39 as a key non-oncogenic addiction in AML, describes its mechanism of action, and offers valuable potential biomarkers and genetic predictors of response.
Microglandular Adenosis is an Advanced Precursor Breast Lesion with Evidence of Molecular Progression to Matrix-Producing Metaplastic Carcinoma


Microglandular adenosis (MGA) is a borderline lesion of the breast characterized by a proliferation of small glands within adipose or fibrous tissue. MGA lacks myoepithelial cells but retains the basement membrane around the infiltrating glands. There is morphologic evidence of MGA progression to atypical MGA (AMGA), carcinoma in situ (CIS) and invasive carcinoma. There is also molecular evidence that MGA can be a non-obligate precursor to breast cancer particularly the triple negative breast cancer. We identified a case, which demonstrated the morphologic evidence of MGA progression harboring four distinct components of MGA, AMGA, CIS and triple negative matrix-producing metaplastic carcinoma (MPMC) in juxtaposition. We macrodissected each component and applied whole exome sequencing to analyze the clonal relationship between the four components of the tumor. Using Pyclone, which selects genes with similar variant allele frequency, we identified three distinct gene clusters, containing 29, 4 and 1 unique genes that were shared by all four foci, namely MGA, AMGA, CIS and MPMC. The cluster with 29 genes constituted the predominant clone with the highest prevalence score with the other two clusters constituting the subclones. In addition, all four foci shared discrete high amplification in the CCND1 locus (cyclin D1 protein), which was confirmed by immunohistochemistry for cyclin D1 diffusely labeling the lesional cells in all four foci. Of note, among an expansive repertoire of non-synonymous somatic mutations, MGA, AMGA, CIS and MPMC harbored recurrent TP53 mutation (R213X; confirmed by Sanger) and ZNF862 stop-gain mutation. Interestingly, a unique and hitherto undescribed mutation in ADAMTS16 gene involving the acceptor splice site at the boundaries of intron 4 and exon 5, was detected only in the MPMC component (confirmed by Sanger). Overall, these findings strongly point to the clonal relatedness of the four morphologic components representing MGA and its transitional phases. Moreover, the above findings shed light on the early mutational events underpinning the pathogenesis of MGA-related breast cancer. Finally, the findings of ADAMTS16 mutation in the MPMC component gives an insight to the late events in transitioning from a non-invasive lesion to full-blown malignant invasive carcinoma. To our knowledge, this is the first clonality study of MGA using whole exome sequencing.
Calcium Signaling Controls Pathogenic Th17 Cell-Mediated Inflammation by Regulating Mitochondrial Function


Lay summary of the research study

SF: T cells play important roles in fighting infections but can also cause autoimmune disease. A subset of T cells, T helper 17 (Th17) cells, so named because they produce interleukin 17 (IL-17) are effector cells that exemplify this duality. On one hand, Th17 cells provide immunity to fungal and bacterial pathogens. On the other hand, Th17 cells can promote tissue inflammation and destruction in autoimmune and inflammatory diseases such as multiple sclerosis (MS), colitis, psoriasis and asthma. The identification of the molecular mechanisms that control the differentiation and function of pathogenic Th17 cells has profound clinical implications for the development of new molecular targets to treat autoimmune diseases. In this study, which is a collaboration between the Feske and Koralov labs in the Department of Pathology, we demonstrated that calcium uptake by T cells through the CRAC calcium channel is required for the pathogenic function of Th17 cells. CD4 T cells that express a hyperactive form of the transcription factor STAT3 spontaneously develop into proinflammatory Th17 cells and cause severe multiorgan inflammation in mice as shown by Dr. Koralov’s lab. Surprisingly, deletion of the CRAC channel subunit STIM1 (stromal interaction molecule 1) in T cells completely reversed the effects of hyperactive STAT3 in mice, which did not show signs of pulmonary or skin inflammation. At the molecular level, we found that potentially proinflammatory Th17 cells lacking STIM1 failed to produce IL-17, had a gene signature resembling non-pathogenic Th17 cells and lacked expression of many mitochondrial genes. As a result, STIM1-deficient Th17 cells had strongly impaired mitochondrial function and defective oxidative phosphorylation (OXPHOS), whereas their ability to produce reactive oxygen species (ROS) was increased. These factors together interfere with the capacity of STIM1-deficient Th17 cells to cause inflammation and tissue damage. CRAC channel inhibition may be a potent new approach for the treatment of Th17 cell mediated diseases.

Current position
UK/SK: Ulrike Kaufmann is a Senior Scientific Researcher in Tumor Immunology at Genentech. Sascha Kahlffuss is a postdoctoral fellow in the Feske Lab.

What is the novelty of your study?

SF: The Feske lab previously showed that calcium influx through CRAC channels is crucial for the function of pathogenic Th17 cells in mouse models of autoimmune disease. Deletion of one of the two main subunits of the CRAC channel, ORAI1 or STIM1, attenuated the severity of CNS and intestinal inflammation in mouse models of colitis and multiple sclerosis. The underlying calcium-
dependent mechanisms that control pathogenic Th17 cell function, however, are incompletely understood. The novelty of the current study is that we identified a critical role of CRAC channels in regulating mitochondrial respiration and oxidative phosphorylation (OXPHOS), which enables Th17 cells to cause multiorgan inflammation and autoimmunity. These findings are surprising because the function of Th17 cells, like that of other proinflammatory effector CD4+ T cell subsets, was typically considered to depend on another metabolic pathway, aerobic glycolysis. By contrast, we did not observe a defect in glycolysis in STIM1-deficient Th17 cells that could account for their abolished pathogenicity. Our findings demonstrate that the function of pathogenic Th17 cells that develop under the influence of strong STAT3 signaling depends on mitochondrial function and in particular OXPHOS.

Can you give us the key results of the paper in a paragraph?
SF: For the current study we used mice that express a hyperactive form of signal transducer and activator of transcription 3 (STAT3) in T cells (S3CD4 mice), which limits the lifespan of S3CD4 mice by inducing severe Th17 cell-mediated skin, intestinal and pulmonary inflammation. We crossed S3CD4 mice to mice lacking the SOCE-activating protein STIM1 in T cells (S1CD4 mice). Our data show that the resulting S1-S3CD4 mice are protected from severe multiorgan inflammation. The reason for this protection is that potential pathogenic Th17 cells from S1-S3CD4 mice preferentially upregulate genes that were previously shown to belong to a non-pathogenic Th17 cell gene signature. Furthermore, Th17 cells of S1-S3CD4 mice showed downregulation of genes regulating mitochondrial function including many subunits of the electron transport chain (ETC) resulting in impaired OXPHOS. Inhibition of OXPHOS in pathogenic Th17 cells of wildtype mice altered their gene expression profile to one resembling non-pathogenic Th17 cells and attenuated their proinflammatory function. Despite reduced ETC function, mitochondria in STIM1-deficient Th17 cells produced more reactive oxygen species (ROS), resulting in increased DNA damage and cell death. Taken together, we think that CRAC channel inhibition mitigates the pathogenicity of Th17 cells by suppressing OXPHOS, changing their gene expression profile and by reducing their viability through enhanced mitochondrial ROS production.

Where will this work take the Feske lab?
SF: We were intrigued to find that the function of pathogenic Th17 cells is very dependent on mitochondrial metabolism, which in turn is controlled by the calcium-regulated expression of mitochondrial genes. These findings suggest that pharmacological inhibition of CRAC channels, and thus mitochondrial energy metabolism, may be a strategy to attenuate Th17 cell-mediated inflammation in autoimmune diseases. As mentioned earlier, however, Th17 cells also have important roles in protective immunity to infection with bacteria and fungal pathogens. We are therefore conducting a follow-up study in which we investigate the role of CRAC channels in non-pathogenic Th17 cells in the context of local and systemic infection with the yeast Candida albicans. In particular, we are trying to understand how calcium signals contribute to the metabolic function of non-pathogenic Th17 cells. The results of our study so far indicate that CRAC channels also regulate the function of non-pathogenic Th17 cells, but have a broader impact on several metabolic pathways compared to their more singular effect on mitochondrial function in pathogenic Th17 cells.

How did you come to join the Feske lab, and what drives your research?
UK: I joined the Feske lab right after my Ph.D. graduation at the LMU Munich (Germany), where I investigated the role of T helper cells in autoimmune eye disease. My background perfectly aligned with the research interests of the Feske lab and joining the lab allowed me to expand my research to new diseases and signaling pathways. The supportive environment in the Feske lab and the scientific excellence at NYU enabled me to work on exciting research projects, obtain prestigious research fellowships and publish in high impact journals. My research is driven by scientific rigor, a passion for science and exploration and a desire to make a difference for patients. For this reason, I advanced to a research position in tumor immunology at Genentech, where I am inspired to make new discoveries and our innovative research impacts patients’ lives.
SK: I went to medical school in Magdeburg (Germany). During my studies, I conducted research for my experimental MD thesis on the role of glutamatergic ion channels in T and B cells. After completing one year residency in internal medicine, I obtained a German Research Foundation (DFG) fellowship and joined the Feske lab because it is one of the leading labs in the world that studies ion channels and their function in immune cells. Since the beginning of my experimental work in immunology, I had followed the research of the Feske lab through publications and was thrilled when Stefan provided me with the opportunity to work in his lab. During my time in his lab I have greatly expanded my immunological knowledge and experimental skills from which I will benefit throughout my scientific career. I am right now investigating how the CRAC channel pathway regulates the function of different T cell subsets including Th17, Th2 and follicular T cells. For these studies I am using a variety of conditional knockout mice and murine disease models including asthmatic airway inflammation, influenza infection and experimental autoimmune encephalomyelitis as a model of multiple sclerosis. As a trained MD, I find it particularly gratifying to be able to combine my studies in mice with the analysis of human patient samples, for instance for the analysis of T cell function and gene expression at the single cell level. For me it is fascinating to conduct research in the Feske lab, which is actively expanding the boundaries of research on ion channels in immunity, an emerging research field with much to discover and explore.

Finally, let's move outside the lab – what do you like to do in your spare time in NYC?

UK: During my time at NYU, I joined the New York Road Runners and have participated in many races, including the New York City marathon.

SK: In my spare time, I enjoy to be with my wife and daughter. We often just go outside and enjoy the people and places that make New York City unique.
Academic Achievements

Grants

Jorge A. Ghiso, PhD
NIH RO1
Relevance of Abeta N-terminal Truncations for Alzheimer Pathogenesis and Therapy

Richard Possemato, PhD
Gabrielle’s Angel Foundation for Cancer Research
Modulating Iron Metabolism to Treat Myelodysplastic Syndrome

Ioannis Aifantis, PhD
The Leukemia & Lymphoma Society
Targeting the stress response machinery in pediatric T cell acute lymphoblastic leukemia (T-ALL)

Sergei Koralov, PhD
Bristol-Myers Squibb Company (BMS)
Delineating the role of KEAP1 and STK11 resistance to checkpoint therapy in NSCLC

Research Fellowship

Joseph Pucella, PhD
Reizis lab
NHI F32
Kinetic Characterization of Hematopoietic Stem Cell Differentiation During Homeostasis and Pathological Conditions

Matthew Witkowski, PhD
Aifantis lab
The Children’s Oncology Group Foundation, Inc.
Mapping and Therapeutic Targeting of the B-ALL Bone Marrow Microenvironment

Christopher Park, MD, PhD
Barth syndrome Foundation
Characterization of Hematopoietic Stem and Progenitor Cells in Barth Syndrome
Spotlights

Thomas Scambler, PhD

And the Winner Is...

2019-2020 Postdoc Member of Pathology Seminar Series Organizational Committee

Congratulations to Tom Scambler, a postdoc in Feske lab. Tom was nominated 2019-2020 postdoc member of Pathology Seminar Series Organizational Committee!!! This is the first time the committee gives the opportunity to a postdoc member to actively participate in planning a department seminar series. This is a leadership position to act as a liaison between Pathology trainees and faculty and be part of the decision making as to who is invited to the Pathology seminar series. This is also a fantastic way for the department trainees to host a speaker who inspires them. Congratulations Tom!

Antonio Serrano, MD
Douglas Allison, MD

2019-2020 Chief Residents

Antonio Serrano, MD and Douglas Allison, MD were elected the new Chief Residents for 2019-20 academic year. Both, Antonio and Douglas are currently in their second year of Residency of the Pathology Program starting their third year in the 2019-20 cycle.

Chief Residents are appointed by the Director of the Program and their duties usually include, but they are not limited to, acting as liaison between residents and faculty members. They help the dialogue and collaboration between the two parts of the community and support the Director of Training in different administrative tasks.

Congratulations Antonio and Douglas!
New & Notable

Our Pathologists at
USCAP Annual Meeting 2019:
Residents and Fellows Take the Stage

Residents, Fellows and Clinical Faculty members of our department attended the USCAP (United States and Canadian Academy of Pathology) Annual Meeting at National Harbor, Maryland, last March 16th-21st. The conference is a great opportunity for personalized education, mentoring and outreach for world class Pathologists. This year the meeting was particularly designed for a broad spectrum of learning and social opportunities with access to the plethora of Companion Society meetings, and pre-select short courses, interactive microscopy sessions, evening specialty conferences and special courses in genomics, quality and patient safety, and leadership.

Our Pathology department contributed many posters, platform and oral presentations. In particular, we would like to highlight the accomplishments of our Residents and Fellows. Dr. Parini, PGY4 of our Residency program, gave an oral poster presentation on the prognostic utility of Long Non-Coding RNAs in prostate cancers and their future implication in clinical trials. Dr. Schwartz, a PGY3 in our Pathology department, was invited to deliver a platform presentation on his studies on DNAH9, a protein involved in the function of cilia, that is frequently mutated in breast cancers with micropapillary and tubulopapillary morphology. A second platform presentation was given by Dr. Hernandez, one of our Fellows, whose research aims to determine the reproducibility of PD-L1 immunohistochemistry in clinical samples. Dr. Allison, a PGY2 and new Chief Resident, during his platform presentation discussed the benefit of screening for colorectal adenocarcinoma (CRAC) under the age of 50, as recently indicated by the American Cancer Society (ACS) new guidelines. Dr. Cangiarella, Associate Professor and Associate Dean for Education, Faculty and Academic Affairs and Vice Chair of Clinical Operations in our department, indicated ‘through their talks, our fellows and residents exemplified the vibrant clinical research currently ongoing at our Department. The USCAP annual meeting is a great opportunity for all our pathologists to meet and discuss their work with international colleagues. “The diverse research and outreach activities provided by USCAP Annual Meeting ensure high quality education that positively influences world class pathologists” said Dr. Moreira, Director of Center for Biospecimen Research and Development, Pulmonary Pathology and Cardiopulmonary Pathology Fellowship Program, who present at two major sessions of the meeting, the “Papanicolaou Society of Cytopathology” and at the “Pulmonary Pathology Society”. Dr. Cenaj, Anatomic Pathologist in our department, was also invited to a platform presentation where he discussed the molecular correlates of dysplasia subtypes in sessile serrated polyps and their relationship to colorectal carcinoma.
Who is New

Jozef Bossowski, PhD
Postdoctoral Fellow
Papagiannakopoulos Lab

Hongyu Ding, PhD
Postdoctoral Fellow
Papagiannakopoulos Lab

Krysten Harvey
Student Intern
Aifantis Lab/ABL

Fara Faye Regis, DVM
Associate Research Scientist
Skok Lab

Goyaert Roosen
Predoctoral Fellow
Aifantis Lab
Alumni News

Martin Vaeth, PhD
Junior Group Leader
Würzburg Institute of Systems Immunology
https://www.med.uni-wuerzburg.de/en/systemimmunologie/research/me tabolism-and-immune-cell-signalling-vaeth-lab/

1. Position in NYU/Supervisor/When position started—ended?
MV: I joined Dr. Stefan Feske's lab in October 2013 as a postdoctoral researcher supported by a fellowship of the German Research Foundation. In 2017, Stefan promoted me as Instructor in the Department of Pathology. My main research focus was to understand how Ca2+ signals regulate immune responses in the context of infection, autoimmunity and cancer. In addition, I was fortunate to participate in several other projects within the Feske lab and with external collaborators. After interesting and productive 4.5 years in Dr. Feske’s lab I left NYU in July 2018 to start my own independent research lab in Germany at the Wurzburg Institute of System Immunology.

2. Present position/when did you start?
MV: I am currently an independent research group leader at the Institute for Systems Immunology at the University of Würzburg, Germany. My position corresponds to an Assistant Professor position in the US with a tenure-track option. The Institute for Systems Immunology was founded in 2018 and is a joint venture of the Max Planck Society and the University of Würzburg. There are currently 4 different research groups at the institute working on different aspects of immunity (e.g. tissue-resident lymphocytes in infection and cancer, lymphocyte dynamics and trafficking, transcriptional and metabolic programming of immune cell function and host-microbial interaction in early life). The unifying topic of all research groups is the interaction of the immune system with other tissues and organs but each group tackle this question from a different angle. Since our institute is still developing and more research groups will be recruited it is a truly exciting time to build and establish this new research institute.

3. How did you get where you are today and how did the experience in the pathology department and Feske lab help you get there?
MV: After my undergraduate and master studies in biochemistry and toxicology I earned a PhD in molecular immunology. To broaden my research interests and to experience a different scientific environment I accepted the invitation of Dr. Stefan Feske to join his laboratory as a postdoctoral fellow in 2013. Joining a new research lab in city like New York is certainly an exciting and sometimes exhausting experience but the fantastic research community and the positive vibe in the NYU Department of Pathology helped me to integrate quickly. I really appreciated the collegial atmosphere in the Department of Pathology (especially in the 3rd floor of Smilow) and the collaborative interaction of different research labs within NYU. In addition, the unique postdoctoral training program established by Dr. Keith Micoli and his team was extremely helpful to build both a scientific and personal base within the NYU research community. My personal and professional development during my time at NYU would not have been possible without the great support of my mentor Stefan Feske. Stefan is an experienced scientist, a brilliant mind and has an impressive discipline. He truly inspired me to pursue a career as an independent researcher. His mentorship was instrumental to prepare me well for my new position and I cannot appreciate enough Stefan's investments in me. In addition to his scientific mentorship he also taught me how to write successful grant applications. This is especially important as I am applying to different grants at the moment and the lessons I learned from Stefan are now extremely valuable. I am still in regular contact with Stefan and my (former) colleagues and I am pleased to see that their research projects and careers develop well.

4. What was the most difficult moment in your scientific career and how were you able to bypass it and succeed?
MV: Personally, I think the most difficult task to pursue a career in science is to stay motivated, curious and critical. There are always times in which experiments fail or hypotheses are wrong. Because the pressure is immense in science to be productive and eventually publish papers in order to find a permanent position it is sometimes hard to maintain our scientific curiosity and motivation. I had to learn to stay patient and to avoid that failing experiments, non-funded applications and other unsettling situations drag me down. Another important lesson is to establish a healthy work-life balance. Academic research is often stressful and sometimes not-rewarding, thus it is important to counteract these situations outside of the lab to stay motivated and maintain an open and curious mindset.

5. What advice would you give postdocs to find their way?
MV: The most important task as a postdoc is to find out if a career in academic research suits you well. There are plenty of alternative options besides staying in academia and becoming an independent group leader. It is always valuable to talk to your (former) colleagues in and outside of the institution about career options, go to career development sessions and probe yourself if you are happy with what you are doing. Building a network of colleagues and (scientific) friends will help you either way to find a position that fits you best. Another advice is to apply early to career development awards that promote your scientific career path and help you to become (more) independent. There are plenty of opportunities such as the NIH K99 awards and similar funding instruments. Even if these applications are not funded, writing such an application is always a good training that will help you to identify interesting research directions and to focus on the most important questions.

6. How do you compare the NYU experience with other institutions you have been in?
MV: My experience in the Department of Pathology at NYU was certainly a unique experience for me personally that is hard to compare to other institutions. I will use my time in the Feske Lab and apply the lessons learned in my own independent lab. The collegial vibe and the positive attitude in the department was especially inspiring and I will promote a similar atmosphere in my new institute.
Peter B Illei, MD
Associate Professor of Pathology and Oncology, Division of Cytopathology
Johns Hopkins Medical Institutions, Baltimore, MD
https://www.hopkinsmedicine.org/profiles/results/directory/profile/0020089/peter-illei

1. Position in NYU/Supervisor/When position started – ended?
   2. Present position/when did you start?

PI: I first joined NYU Medical Center as pathology resident (July 1993 – June 1998) and served as chief resident between 1997-1998. In July 2002, following my fellowship training and research at MSKCC, I returned to NYU as assistant professor of Pathology in the division of Surgical Pathology. In July 2005 I moved to Johns Hopkins University where I am currently an associate professor of Pathology.

3. How did you get where you are today and how did the experience in pathology department help you get there?

PI: I received my medical degree in Hungary where I also started my training in Pathology. In 1991, I moved to the Sir William Dunn School of Pathology at the University of Oxford, where I joined a group investigating the molecular genetics and infectious properties of HIV. The years I spent in Oxford helped solidify my desire to do research. After arriving at NYU I realized how lucky I was to have been accepted to the pathology residency program. The department was lead by Dr. Vittorio Defendi who strongly encouraged and supported residents to stay engaged in research. The residency program was under the direction of Dr. Gloria Gallo who ensured that residents not only had excellent training but also enjoyed the program. We had a faculty of great teachers including Drs. Jerry Waisman, Helen Feiner, Glauco Frizzera, Gurdip Sidhu, and Alba Greco in anatomic pathology and Philip Tierno, Bruce Hanna and John Gorman in clinical pathology. This is not a complete list by far and I hope I am not offending anyone but not mentioning by name. Dr. Waisman with his love of aspiration cytology greatly influenced my choice of becoming a cytopathologist, while Dr. Feiner taught me how to be a good surgical pathologist and communicate with clinicians effectively. Dr. Frizzera taught me how to diagnose lymphomas, an area where I had a great deal of confusion before I met him. Dr. Sidhu was a great source of electron microscopy knowledge and an exceptional teacher. Pediatric pathology wouldn’t have been the same without Dr. Greco, a wonderful teacher and the greatest champion of resident’s welfare. While I chose anatomic pathology as career, I have great memories of clinical pathology rotations, as well. I also would like to mention Dr. Jonathan Melamed who started his career as a junior faculty at NYU the same year I started my residency. Jonathan was an enthusiastic teacher an advocate of residents. Jonathan is still at NYU and had trained a generation of excellent pathologist. I was also lucky to have Patricia Heller and Joan Cangiarella as my chief residents. My internship year was the best year of all my training years and that was in large part because of them. During my third year of residency I chose to do a research project in cytogenetics under the supervision of Dr. Mary Ann Perle. I learned how to do fluorescent in situ hybridization and applied the technique to tissue smears and tissue sections. My project was to study chromosomal copy number alterations in precursor lesions of invasive ductal carcinoma of the breast that was supported by an intramural cancer center grant. I presented my work at several national and international conferences and won a poster award. By mastering this technique I again got lucky since I was able to use these skills to expand my research into malignant mesothelioma and sarcomas during my time at Memorial Sloan-Kettering Cancer Center that lead to highly cited original research articles. I will be forever grateful for the opportunities that NYU provided and enabled me to get where I am today.

4. What was the most difficult moment in your scientific career and how were you able to bypass it and succeed?
   PI: My most difficult point in my scientific career came after finishing my fellowships. I was offered a position as a Visiting Investigator at the Kettering Institute at MSKCC, however, due to uncertainty in my immigration status I faced the possibility of not being able to stay. Fortunately, everything worked out in great part because of the support I received from my former mentors at NYU.

5. What advice would you give a postdoc to find their way?
   PI: It is often said that if you do what you love for a living you will never work a day in your life. Keeping that in mind my advice to today’s trainees (both residents and graduate students) is that they need to figure out what they like to do and then stick to it, but they have to keep an open mind while they figuring it out.

6. How do you compare the NYU experience with other institutions you have been in?
   PI: I consider myself lucky to have worked in three of the best medical centers (NYU, MSKCC and JHU) in the United States. There are differences between these institutions, but all three share strong commitment to clinical care, research and education, and therefore it is easy to succeed in any of these institutions if coming from one the other ones.
Upcoming Events

'Spotlight on Faculty'
June 3
4:00pm
Alumni Hall B
Featuring Shruti Naik, PhD, from Pathology Department

Pathology Residents’ Day Lecture
June 13, 2019
4:00pm - 5:00pm
Science Building, Room 103

6th Annual Pathology Retreat
June 14, 2019
8:00am - 6:30pm
Smilow Multipurpose & Seminar room

Immunology and Inflammation Retreat
June 19, 2019
9:30am - 7:00pm
Alumni Hall B & Farkas Hallway

Also Coming Up

Welcome Breakfast for New Residents and Fellows
July 1, 2019
8:00am - 9:00am
Smilow 1301

Pathology Welcome BBQ
July 18th
4:00pm - 6:00pm

Immunology and Inflammation Open House
August 20, 2019
Alumni Hall B and Farkas Hallway

MOTI Open House
August 21, 2019
5:00pm - 7:00pm
Smilow Multipurpose Room
Suggested by You

What is preLights?
As the number of preprints grows, it will become increasingly difficult to find and filter relevant/interesting preprints. preLights does some of that work for you. Our dedicated team of scientists from the community select, highlight and comment on preprints they feel are of particular interest to the biological community. You’ll find a summary of each preprint, the reasons it was selected and the selector’s thoughts on its significance. You might also see relevant comments from the preprints’ authors. And we’d really welcome your thoughts and comments too.

An Interview with Cassandra Extavour
Cassandra Extavour is Professor of Organismic and Evolutionary Biology and of Molecular and Cellular Biology at Harvard University (www.extavourlab.com). Recently appointed an editor at Development, her lab works on the evolution and development of germ cells in animals, the genetic control of reproductive capacity, and the evolution of the arthropod body plan. We met with Cassandra at the 2018 Santa Cruz Developmental Biology meeting and heard about her scientific history, her thoughts on the future of research at the intersection of evolution and development, and her lifelong passion for music.

Career Trends: Work and Wellbeing
Every Monday at 8 pm, Tal Maizel-Zilpa leaves her husband in charge of their three children and pulls on her running shoes. For the next hour—and for this one hour every week—she pounds the pavements where she lives in Holon, Israel, with a group of fellow women runners.

A Cure for Burnout
Top employers embrace change based on a stable foundation
By Chris Tachibana

Upcoming Symposia & Conferences
Meet the Team

Caterina Berti
Manager Research Laboratory Operations
Caterina.Berti@nyumc.org

Jennifer Molde
Residency & Fellowship Program Coordinator
Jennifer.Molde@nyumc.org

Stefanie Castanza
Administrative Supervisor
stefanie.castanza@nyumc.org

Michelle Wicinski
Project Coordinator
Michelle.Wicinski@nyumc.org

Adrienne Dolginko
Program Manager, Education Division
adrienne.dolginko@nyumc.org

Ben Zapp
Webmaster
Ben.Zapp@nyulangone.org

Lyllian Mundo
Research Submissions Coordinator
Lyllian.Mundo@nyulangone.org
Amendments & Corrections

HDAC stimulates gene expression through BRD4 availability in response to IFN and in interferonopathies
Marie, Isabelle J; Chang, Hao-Ming (pictured left); Levy, David E.
Journal of Experimental Medicine Dec 2018
Fun

Orthopedic Surgery
Pathology
Pediatrics
Radiology
Genetics