Michal Tal

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EDUCATION

Yale University, Ph.D , Viral Immunology 2012
Ben Gurion University, Israel, B.Sc , Life Sciences 2006

EXPERIENCE

10+ years expertise in innate immune pathogen recognition and the intersection of metabolism and immune responses. 4+ years expertise in chronic infection

Passionate about and involved in medical innovation to impact public health

Postdoctoral Fellow/Team Lead

February 2013 - PRESENT

Stanford University School of Medicine, Stanford, CA

- Led the infectious disease team research projects in the lab of Irving Weissman, a unique environment with both independent research and 3 research teams, over 100 million dollars in non-federal funding, clinical trials, 100s of patents, startup spinoffs
- Identified a conserved host defense mechanism activated by pathogen detection which facilitates adaptive immune responses, validated in clinical HCV samples.
- Discovered the expression of a novel inhibitory receptor on exhausted T cells.
- Initiated and drove multiple collaborations across the country investigating this receptor in multiple mouse chronic infection models and HIV patient samples.

Entrepreneurial experience

- Founding member in a multidisciplinary team of domain experts (C.S., E.E., M.D.) coming together out of Lean Launchpad to make a non-invasive Celiac diagnostic.
- Founded a multidisciplinary team (M.E., M.B.A) centered on developing a rapid home diagnostic for Strep infection that was selected for Startup Garage.

Graduate Student/Research Assistant

September 2006 – August 2012

Yale University, New Haven, CT

- Expert in host mediated pathogen detection and pattern recognition signaling - written multiple primary and review articles on this topic.
- Discovered how the process of cytosolic antiviral signaling is impacted by multiple physiological processes including autophagy, reactive oxygen species production and how the mitochondria servers as an integrator of multiple stress signaling pathways.
- Investigated how these signaling pathways are impacted by aging in a mouse and human study of Flu resistance and disease severity with age.
- Broadly trained in immunology, molecular biology, virology, biochemistry, cell biology, pathology, and genetics with interests in climate change and public health.

Teaching experience

Stanford: Teacher for Stanford Splash "A Shot in the Dark" and Guest lecturer for Translational Immunology 209

Designed and taught a high school level class on the history of vaccines, and a grad/med level class on innate host recognition of pathogens and mitochondrial stress signaling.

Yale: Teaching assistant (TA) then Head TA "Introduction to the Immune System"

After high evaluations as a TA, brought back as Head TA to restructure the TA led sections. Designed new interactive learning modules for diverse learning styles.

Communication

- Lead author on 4 refereed publications, co-author on 3 refereed publications
- Advanced courses in Science Communication, Team Science Management, Building functional Teams, Conflict Resolution and Stress Management.
- Presented research results at over a dozen scientific conferences and symposia
- Co-founder of and VP of communications for Yale Science Diplomats

SKILLS

Infectious diseases
Worked with diverse infection models including Flu, VSV, HSV, HIV, HCV, LCMV, Friend Virus, VZV, Borrelia, Salmonella, Toxoplasma and Malaria

Diagnostic Assays
over 500hrs of flow cytometry (LSRII, Fortessa, CytoFLEX), trained sorting operator on FACS ARIA I and II, ELISA, qPCR, CYTOF, Confocal and fluorescent microscopy, Western blotting, IHC

Data Analysis
Expert in FlowJo analysis with advanced training, PRISM, Boolean relations, GEXC, Genespring, and Ingenuity

Immune assays:
Functional T and NK assays (cytotoxicity and cytokine), phagocytosis assays, DC:T priming assays, stimulating and assessing different pathogen recognition pathways in diverse cell types, mitochondrial assays

FDA regulation of Medical Devices
40+ hours of training by UCSF-Stanford CERSI, 5 certificates of completion

MANAGEMENT

Stanford: Managed the infectious disease team within the laboratory with 5 direct reports. Hired, conducted safety training, hands-on technique instruction and guided their progress and development with daily or weekly meetings depending on the context and career stage. Designed multi-year thesis projects for three graduate students.

Yale: Mentored three rotation students; Responsible for project design, skills, safety training, direct supervision and guidance.

AWARDS

Kleberg Foundation I wrote the research grant awarded $750,000 and led a team conducting Lyme Disease research.

NIH NRSA F32 Postdoctoral and F31 Predoctoral Fellowships Highly prestigious national fellowships totaling over $200,000 in support, received the highest possible score on the F31

Stanford Immunology postdoctoral fellowship and renewal Academic research funding ($90,000)

Gershon Fellowship Awarded to the top 3rd year Immuno graduate student at Yale

Publications and contributions to science

Accumulation of damaged mitochondria in absence of autophagy leads to heightened antiviral signaling:

I identified that in the absence of the physiological process of autophagy (which mediates engulfment of organelles and their lysosmal degradation), that cells were less susceptible to RNA virus infection and displayed heightened antiviral responses. I found that in the absence of autophagy mitochondria were accumulating, and by comparing mitochondrial mass to mitochondrial respiration, I was able to demonstrate that the mitochondria that were accumulating were damaged. Together with the other contributing authors, I published the first report on how mitochondrial ROS production directly modulates interferon production mediated by cytosolic viral recognition in PNAS in 2009 (my 3rd year of graduate school). This article showed a novel role for autophagy in the regulation of signaling emanating from mitochondria, has been cited over 300 times, and has since been confirmed by other articles. Additionally, the technique that I developed in that paper to monitor the ratio of damaged mitochondria by flow cytometry has since been used by multiple other articles. I wrote an in-depth review on the emerging research in the field concerning the antiviral and antibacterial signaling pathways emanating from and impacted by mitochondria.

a. Tal MC, Sasai M, Lee HK, Yordy B, Shadel GS, Iwasaki A. Absence of autophagy results in reactive oxygen species-dependent amplification of RLR signaling. Proc Natl Acad Sci U S A. 2009 Feb 24;106(8):2770-5. PubMed PMID: 19196953; PubMed Central PMCID: PMC2650341.
b. Tal MC, Iwasaki A. Autophagic control of RLR signaling. Autophagy. 2009 Jul;5(5):749-50. PubMed PMID: 19571662; NIHMSID: NIHMS468554; PubMed Central PMCID: PMC3693554.
c. Tal MC, Iwasaki A. Mitoxosome: a mitochondrial platform for cross-talk between cellular stress and antiviral signaling. Immunol Rev. 2011 Sep;243(1):215-34. PubMed PMID: 21884179; NIHMSID: NIHMS305102; PubMed Central PMCID: PMC3170140.

Dysfunctions in autophagy with age correlate with increased mitochondrial levels of ROS and cytosolic viral signaling in the elderly:

Strikingly, I found that cells obtained from elderly humans and old mice were highly resistant to influenza infection in vitro. Moreover, old mice challenged with respiratory influenza infection were highly resistant to virus infection in vivo, and were able to survive and recover from high dose respiratory influenza challenge. These data demonstrated that dysregulated hyper inflammatory responses downstream of cytosolic antiviral signaling lead to resistance against influenza infection in older hosts, and suggest that the high morbidity of elderly humans following influenza infection may be due to immune pathology from these hyper inflammatory responses to primary flu infection or secondary bacterial infection, and not due to inability to control replication of the initial infection. Intriguingly, monocytes from elderly infected in vitro, and mice infected in vivo with Flu had defective type I IFN responses. This research is summarized in my dissertation which is publicly available. The reduced IFN responses was my contribution to the Pillai et al paper.

d. Tal MC. Autophagy, ROS and aging impact cytosolic antiviral immunity. Dissertation, Yale University 2012 181; 3535395. http://pqdtopen.proquest.com/doc/1317656568.html?FMT=ABS
e. Pillai PS, Molony RD, Martinod K, Dong H, Pang IK, Tal MC, Solis AG, Bielecki P, Mohanty S, Trentalange M, Homer RJ, Flavell RA, Wagner DD, Montgomery RR, Shaw AC, Staeheli P, Iwasaki A. Mx1 reveals innate pathways to antiviral resistance and lethal influenza disease. Science. 2016 Apr 22;352(6284):463-6. doi: 10.1126/science.aaf3926. Pubmed PMID: 27102485

Mitochondrial DNA stress primes the antiviral innate immune response

As my doctoral research focused in large part on how the mitochondria can impact antiviral signaling, I was approached by a postdoc at Yale to collaborate on his project where he had done a microarray on cells that were deficient in TFAM, a transcription factor that is responsible for binding mitochondrial DNA. The absence of TFAM induces a mitochondrial DNA stress, and the microarray showed increases in select interferon stimulated genes. I infected these cells with a variety of different RNA and DNA viruses and assessed the responses to these infections to assess the antiviral signaling in these cells, and was able to characterize a significant resistance to viral infection, especially with HSV infection.

f. West AP, Khoury-Hanold W, Staron M, Tal MC, Pineda CM, Lang SM, Bestwick M, Duguay BA, Raimundo N, MacDuff DA, Kaech SM, Smiley JR, Means RE, Iwasaki A, Shadel GS. Mitochondrial DNA stress primes the antiviral innate immune response. Nature. 2015 Apr 23;520(7548):553-7. PubMed PMID: 25642965; NIHMSID: NIHMS649676; PubMed Central PMCID: PMC4409480.

Complete List of Published Work in My Bibliography:

https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/44618330/?sort=date&direction=ascending