BIOGRAPHICAL SKETCH

NAME: Yael Ema David Shternberg

eRA COMMONS USER NAME (credential, e.g., agency login): YAELDAVID

POSITION TITLE: Assistant Member, Chemical Biology Program, Memorial Sloan Kettering Cancer Center

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
SUNY Stony Brook (*Summa cum laude*)	B.Sc.	01/2004	Biology
SUNY Stony Brook (Lonnie Wollmuth Laboratory)	N/A	01/2004	Molecular Neurobiology
The Weizmann Institute of Science (Ami Navon Laboratory)	Ph.D.	05/2011	Biochemistry
Princeton University (Tom Muir Laboratory)	Postdoctoral	08/2016	Chemical Biology and Epigenetics

A. Personal Statement

I started my independent position as an assistant member at the Chemical Biology Program at Memorial Sloan Kettering Cancer Center in September 2016. My laboratory is predominantly interested in understanding signaling cascades linking histone modifications and transcription regulation. For that, we develop and apply chemical tools to manipulate histones *in vitro* and in *in vivo*. Together with advanced protein engineering, cell biology, proteomics, biophysics and high throughput sequencing methods, we investigate the causal role non-canonical histone marks play in DNA-templated processes in healthy and disease states. Before starting at MSKCC, I received my Ph.D. from The Weizmann Institute in Israel, where I was trained as a biochemist, applying my knowledge to address key questions in the mechanism and regulation of polyubiquitin chain assembly. Realizing the power of interdisciplinary research, I moved to the chemistry department at Princeton University where I performed my post-doctoral research under the supervision of Prof. Tom Muir. Combining my experience in cell biology and protein biochemistry with Prof. Muir's expertise in peptide chemistry I developed several tools to address the regulatory role histone modifications play in transcription. Importantly, I was able to utilize ultra-fast split inteins to chemically modify histones in live cells. This pioneering technique opened the door to performing research with a chemical precision, at a biochemical resolution but in a physiological context. My extensive practice in the fields of chromatin biology, ubiquitin enzymology, biochemistry and chemical biology developed during my research training perfectly positions me to address these unique interdisciplinary problems at the forefront of protein modifications and transcription regulation.

B. Positions and Employment

09/2016-present — Assistant Member, Chemical Biology Program, Sloan Kettering Institute, Memorial Sloan Kettering Cancer Center; Tenure track position.

Other Experience and Professional Memberships

1998-2000	Sargent in the IDF
2004-present	Golden Key International Honor Society, *member*
2012-present	American Society of Mass Spectrometry, *member*
2016-present	New York Academy of Sciences, *member*

Selected honors and awards

2002-2004	Dean's award for academic excellence
2003	Howard Hughes Medical Institute undergraduate research fellowship
2004	Phi Beta Kappa
2004	*Summa cum laude*, Stony Brook University
2007	Selected for Horizons in Molecular Biology graduate program (Max Plank)
2012	Selected for the LSRF post-doctoral fellowship
2016-2021	Josie Robertson Young Investigator's award
2017	NIH Mentoring Workshop - Diversity Travel Award
2018	CEBRA award

Selected invited talks

2013	American Society of Mass Spectrometry (MN, USA)
2015	University of Pennsylvania (PA, USA)
2015	Mount Sinai School of Medicine (NY, USA)
2016	NYAS Protein Engineering (NY, USA)
2016	Weizmann Institute of Science (Rehovot, Israel)
2016	Harvard Medical School (Boston, MA)
2016	University of Utah (UT, USA)
2017	Keystone symposia Epigenetics and Human Disease (WA, USA)
2018	CRC 992 Symposium on Medical Epigenetics (Freiburg, Germany)
2018	EPFL (Lausanne, Switzerland)
2018	Max Planck Institute (Munich, Germany)
2018	SignGene symposium (Jerusalem, Israel)

C. Contribution to Science

1. **Identifying the inherited selectivity of E2 ubiquitin conjugating enzymes.** My early work concentrated on studying the biochemical principles of protein ubiquitination. Ubiquitination is a key protein post-translational modification involved in multiple cellular cascades including proteasomal degradation. Ubiquitination is performed by concerted action of three enzymes: E1, E2 and E3 although the precise role each of these enzymes plays is still an active area of research. I initially focused on investigated the role E2 conjugating enzymes play in determining the site and ubiquitin chain type added onto a target protein. I identified the inherent preference of the human E2 enzymes in generating specific ubiquitin chain topologies, as well as the mechanistic details underlying this polymerization reaction. To accomplish this, I used a systematic in vitro screen approach involving the cloning, expression and purification of all the E2-conjugating enzymes. I then tested their ability to polymerize ubiquitin though each of the seven ubiquitin lysines using mutational analysis and mass-spectrometry.

a. **David Y**, Ziv T, Admon A, Navon A. The E2 Ubiquitin Conjugating Enzymes Direct Polyubiquitination to Preferred Lysines. J Biol Chem. 2010 Mar 19;285(12):8595-604. PMCID: PMC2838281
b. Shahar-Pomerantz Y, Elbaz J, Kirenberg I, Reizel Y, **David Y**, Galiani D, Nevo N, Navon A, Dekel N. From Ubiquitin-Proteasomal Degradation to CDK1 Inactivation: Requirements for the First Polar Body Extrusion in Mouse Oocytes. FASEB J. 2012 Nov;26(11):4495-505. PMID: 22859367

2. **Determining the work division between E2 and E3 enzymes during substrate ubiquitination.** Next, I turned to study the role E3 ligases play in enforcing selectivity on the E2 conjugating enzymes on native substrates. To address this question I first engineered an artificial substrate that recruits the E2 in an E3-independent manner. By comparing E3-dependent and -independent ubiquitination products I determined that the E3 ligases govern the selection of ubiquitin chain type by narrowing down the inherit specificity presented by the E2 enzymes. Moreover, I identified that this selectivity can be further narrowed down by the presence of auxiliary factors, which associate with the E3 ligase. This was demonstrated by the oncogenic protein p53 and its cognate E3/auxiliary complex MDM2/MDMX.

a. **David Y***, Ternette N*, Edelmann M, Ziv T, Gayer B, Sertchook R, Dadon Y, Kessler BM, Navon A. E3 Ligases Determine the Ubiquitination Site and Chain Type by Enforcing Specificity on E2 Enzymes. JBC. 2011 Dec 23;286(51):44104-15. PMCID: PMC3243545

3. **Developing a method to modify chromatin in live cells.** Next I turned to investigate the role monoubiquitinatination plays in epigenetic transcription regulation. In the process, I developed an innovative method to generate semi-synthetic histones bearing site-specific chemical modifications on chromatin using a protein *trans*-splicing. I was able to introduce these chemically modified proteins into live cells as a potential means to study their biological function. I used this method to incorporate chemical probes such as fluorophores as well as install monoubiquitinated histones into native chromatin. I then applied the method to illustrate, for the first time in a native context, the role specific ubiquitin residues play in the Dot1-dependent crosstalk between monoubiquitination and Histone H3 methylation. To further study the role of histone monoubiquitination in human cells I synthesized these modified histones using expressed protein ligation and developed a mass spectrometry based method to identify their cross talk with other PTMs.

a. **Yael David**, Miquel Vila-Perello, Shivam Verma and Tom Muir. Chemical Tagging and Customizing of Cellular Chromatin States using Ultrafast Trans-Splicing Inteins. Nature Chemistry. 2015 May;7(5):394-402. PMCID: PMC4617616
b. Liszczak GP, Brown ZZ, Kim SH, Oslund RC, **David Y**, Muir TW. Genomic targeting of epigenetic probes using a chemically tailored Cas9 system. PNAS. 2017 Jan 24;114(4):681-686
c. Matthew Holt, **Yael David**, Sam Pollock, Zhanyun Tang, Jongcheol Jeon, Jaehoon Kim, Robert G. Roeder and Tom W. Muir. Identification of a Functional Hotspot on Ubiquitin Required for Stimulation of Methyltransferase Activity on Chromatin. Proc Natl Acad Sci U S A. 2015 Aug 18;112(33):10365-70. PMCID: PMC4547310

Complete list of publications

https://www.ncbi.nlm.nih.gov/pubmed/?term=David%20Y%5BAuthor%5D&cauthor=true&cauthor_uid=21965653