
BIOGRAPHICAL SKETCH

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NAME: **Ronai, Ze'ev**

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

POSITION TITLE: Professor and Director, Translation Science Institute, Cedars Sinai, Los Angeles, CA

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
The Hebrew University, Jerusalem, Israel	B.S.	06/1980	Biology
The Hebrew University, Jerusalem, Israel	M.S.	07/1982	Microbiology
The Hebrew University, Jerusalem, Israel	Ph.D.	11/1985	Immunobiology
Columbia University, New York, New York	Postdoc	12/1988	Molecular Biology

A. Personal Statement

My passion for science is reflected in my dedication to solving critical unmet clinical problems in cancer, with the focus of my research on epigenetic mechanisms that underlie tumor development, progression, and resistance. Our studies often provided new fundamental understanding for rewired signal transduction pathways in cancer, focusing on epigenetic regulators, including ubiquitin ligases, resulting in novel paradigms. In addition to the privilege of serving as a cancer researcher, I have had several administrative duties, including the establishment of the Signal Transduction Program, serving as Associate Director / Deputy Director to NCI Cancer Center, Scientific Director at Sanford Burnham Prebys Medical Discovery Institute (SBP) La Jolla. Over the past few years, parallel to serving as Chief Scientific Advisor at SBP, I have established a new cancer center at the Technion, in Israel (Technion Integrated Cancer Center, with the Nobel Laureate Aaron Ciechanover). Currently, I serve as the Director of the NCI-designated Cancer Center at SBP.

I have initiated and led several large grant initiatives, led the SAC for the Melanoma Research Foundation, and the DOD melanoma parent vision committee. In addition to serving on several editorial boards, I served as EiC for Pigment Cell Melanoma Research, the formal journal for the Melanoma Society. Among notable scientific contributions was the development of sensitive PCR enabling the detection of mutant Ras oncogene in normal-appearing tissues, defining the early days of personalized medicine; the appreciation of rewired signal transduction in cancer, and the fundamental understanding of ubiquitin ligases' role in key cellular processes (i.e., hypoxia, UPR), which define cancer development, progression, and therapy resistance.

Ongoing and pending projects include:

R35 CA197465, Ronai, Z. (PI)
02/02/2016 – 01/31/2023; (renewed 2024-2031)
Rewired Signaling at the Nexus Melanoma Metastasis and Resistance

R01 CA266973, Ronai, Z. Olson, S (MPI)
07/01/2022 – 06/31/2027
GCDH Addiction in Melanoma

B. Positions, Scientific Appointments, and Honors

2024 – present	Director, Institute Translational Science, Cedars Sinai Medical Center, Los Angeles, CA
2024 - present	Director, Melanoma Surgical Program, Cedars Sinai Medical Center, Los Angeles, CA
2024 – present	Professor, Department Surgery, Cedars Sinai Medical Center, Los Angeles, CA
2021 – 2024	Director, NCI Cancer Center, SBP Medical Discovery Inst., La Jolla, CA.
2021 – 2024	Professor, Aging Immuno-oncology Program, SBP Medical Discovery Inst., La Jolla, CA.
2021 - 2023	Chair, DOD (CDMRP) programmatic vision committee in melanoma.
2016 – 2020	Chief Scientific Advisor, Sanford Burnham Prebys Medical Discovery Institute, La Jolla, CA.
2016 – 2018	Professor & Co-Director, Technion Integrated Cancer Center, Technion, Haifa, Israel.
2013 – 2016	Scientific Director, Sanford-Burnham Medical Research Institute, La Jolla, CA.
2013 – 2020	Professor, Tumor Initiation and Maintenance Program, SBMRI, La Jolla, CA.
2008 – 2014	Associate/Deputy Director, NCI Cancer Center, SBMRI, La Jolla, CA.
2005 – 2016	Adjunct Professor, Molecular Pathology Program, UC San Diego, La Jolla, CA.
2004 – 2013	Director and Professor, Signal Transduction Prog, Sanford-Burnham Med Res Inst, CA.
1993 – 1998	Consultant, Department of Medicine, Memorial Sloan Kettering, New York, NY.
1989 – 1997	Assistant/Associate Prof. Depts Microbiology Pathology, NY Med College, Valhalla, NY.
1988 – 1998	Head, Molecular Carcinogenesis Program, American Health Foundation.
1985 – 1989	Postdoctoral Fellow, Columbia University, NY, Mentor I.B. Weinstein.
1982 – 1985	Ph.D., Lautenberg Center, Hebrew University, Jerusalem, Israel.
1999 – 2005	Professor, Rutenberg Cancer Center, MSSM, New York, NY.
1997 – 1999	Associate Professor, Rutenberg Cancer Center, Mount Sinai School of Medicine, NY.

Professional Activities:

NIH grant review: 2021- 2023, DOD (CDMRP) melanoma vision committee; 2018-2020 – DOD CDMRP vision committee; 2012–present Ad Hoc NCI study sections CAMP, TCB, OIA/R35, and others; 2012 NCI Provocative Questions; 2007–2009 NIH TPM Study Section; 2001 NIH Review for PPG on Melanoma Biology; 1996–2001 Member of NCI Chemical Pathology Study Section; 1995 NIH Review Committee for Program Project on Radiation Biology; 1995–1997 NCI Multidisciplinary Special Emphasis Study Section; 1994–1999 Member Cancer Study Section Tobacco Research Program, UCSF; 1991 NIH committee for RFA in Radiation Biology.

Scientific Advisory Boards: Co-leader of the SAC for Melanoma Research Foundation (MRF); P01, University of Arizona, Tucson; P01, Wistar Institute, Philadelphia; SPORE, University of Colorado, Denver, Cancer Center, MGH, Boston. **Conference Organization:** 2016 Melanoma workshop, Israel; 2015 Melanoma workshop Iceland; 2015, Ubiquitin Workshop, Southern China; 2007 Co-organizer International Melanoma Conference; 2004, 2006, 2010 Co-organizer, Ubiquitin Workshop, Hebrew University, Jerusalem; 2000 Co-Chair, NIH workshop on Melanoma; 1996 Organizing Committee, Cancer & Biotechnology, Nice, France; Organizing committee, 4th International Cancer Biotech., Geneva, Switzerland; 1994 Chair, Int. Cell Diff. Conf Hiroshima, Japan.

Editorial: 2010–2012 Editor-in-Chief *Pigment Cell and Melanoma Research*. Frequent reviewer *Cell*, *Mol. Cell*, *Cancer Cell*, *Science*, *Science Sig*, *Nature*, *Nat. Cell Biol*, *Nat. Med*, *Nat Comm* *PNAS*, *EMBO J*, *PLoS journals*, and others; 2007–2009 Executive Editor *Pigment Cell and Melanoma Research*; 2007–2010 Associate Editor *Cancer Research*; 2002–present *Molecular and Cellular Biology*; 2002–2007 *Journal of Biological Chemistry*; 2002–present *Cancer Biology and Therapy*; 2001–present *Molecular Carcinogenesis*; 1997–2001 *Cancer Prevention and Detection*; 1999–2002 Associate Editor *Clinical Cancer Research*; 1996–98 and 2001–2003 *Carcinogenesis*.

Awards and Honors:

2023	NCI Director's Ground Rounds presentation
2023	Keynote speaker, the annual SMR meeting, Philadelphia.
2022	Osher Lifelong Learning Institute at UCSD.
2021,2023	AACI, NCI designated Cancer Center @ SBP presentation
2020	Keynote speaker, Cancer Biology & Signaling Program Retreat, UCSD, La Jolla, CA.
2020	Distinguished Scientist Seminar, University of Maryland, MD.
2019	Keynote speaker, C3 (UCSD; Salk; SBP) cancer centers symposia.
2016	Society Melanoma Research, Lifetime Achievement Award, Boston, MA.

2016 Frontiers in Cancer Research at the Nobel Forum, Karolinska Institutet, Stockholm, Sweden.
 2014 UCI Cancer Center Retreat, Keynote speaker.
 2013 UCSD Cancer Center Director's Seminar Series, speaker.
 2012 NCI Director Lecture Series.
 2008 Keynote speaker, Melanoma Symposium, Penn State University.
 2004 Karolinska Nobel Conference on Hypoxia, Stockholm, Sweden.
 2002, 2005 Banbury Conference CSH, Melanoma biology.
 2001 Karolinska Nobel Conference on Ubiquitin, Stockholm, Sweden.
 2000 Dean lecture series – Mount Sinai School of Medicine.
 1995 Princess Takamatsu Symposium, Tokyo; Hiroshima Cancer Symposium.
 1992 JPCR Fellowship from National Cancer Center, Tokyo.
 1984 Awarded the Golda Meir Fellowship.
 1982 Prize from the Hebrew University for MS. Outstanding Thesis.

C. Contributions to Science (~30,000 citations; H-index >96; i10 index >227; >300 publications)

Among the Significant discoveries from my lab are:

Rewired signaling in cancer. *Demonstrated cross talk between ERK and JNK, STAT3 and c-Jun, RACK1 and JNK signaling in melanoma, and rewired metabolic signaling in melanoma.*

- Ivanov VN, Bhoumik A, Krasilnikov M, Raz R, Owen-Schaub LB, Levy D, Horvath CM, Ronai Z. Cooperation between STAT3 and c-jun suppresses Fas transcription. *Mol Cell*. 2001; 7(3):517-28. PMID: 11463377.
- Lopez-Bergami P, Huang C, Goydos JS, Yip D, Bar-Eli M, Herlyn M, Smalley KS, Mahale A, Eroshkin A, Aaronson S, Ronai Z. Rewired ERK-JNK signaling pathways in melanoma. *Cancer Cell*. 2007; 11(5):447-60. PMC1978100.
- Lau E, Kluger H, Varsano T, Lee K, Scheffler I, Rimm DL, Ideker T, Ronai ZA. PKC ϵ promotes oncogenic functions of ATF2 in the nucleus while blocking its apoptotic function at mitochondria. *Cell*. 2012; 148(3):543-55. PMC3615433.
- Pathria, G., Lee, JS., Hasnis, E., Tandoc, K., Scott, DA., Verma, S., Feng, Y., Larue, Lionel., Sahu, AD., Topisirovic, I., Ruppin, Ronai, ZA. Translational Reprogramming Marks Adaptation to Asparagine Restriction in Cancer. *Nat. Cell Biol*. 2019; 21(12):1590-1603. PMC7307327.

Ubiquitin ligases control fundamental cellular processes. *The role of Siah2 in hypoxia, in UPR (unfolded protein response), in the control of mitochondrial fission, and the duration of stress signaling (TRAF2/JNK). Discovered the regulation of I κ B and β -catenin stability by β -TRCP ubiquitin ligase.*

- Fuchs SY, Chen A, Xiong Y, Pan ZQ, Ronai Z. HOS, a human homolog of Slimb, forms an SCF complex with Skp1 and Cullin1 and targets the phosphorylation-dependent degradation of I κ B and β -catenin. *Oncogene*. 1999; 18(12):2039-46. PMID: 10321728.
- Nakayama K, Frew IJ, Hagensen M, Skals M, Habelhah H, Bhoumik A, Kadoya T, Erdjument-Bromage H, Tempst P, Frappell PB, Bowtell DD, Ronai Z. Siah2 regulates stability of prolyl-hydroxylases, controls HIF1 α abundance, and modulates physiological responses to hypoxia. *Cell*. 2004; 117(7):941-52. PMID: 15210114.
- Scortegagna M, Kim H, Li JL, Yao H, Brill LM, Han J, Lau E, Bowtell D, Haddad G, Kaufman RJ, Ronai ZA. Fine-tuning of the UPR by the ubiquitin ligases Siah1/2. *PLoS Genet*. 2014; 10(5):e1004348. PMC4014425.
- Kim H, Scimia MC, Wilkinson D, Trelles RD, Wood MR, Bowtell D, Dillin A, Mercola M, Ronai ZA. Fine-tuning of Drp1/Fis1 availability by AKAP121/Siah2 regulates mitochondrial adaptation to hypoxia. *Mol Cell*. 2011; 44(4):532-44. PMC3360955.

Ubiquitin ligases in cancer development, therapy-resistance. *Established the role of Siah2 in: melanoma development and metastasis; development of neuroendocrine prostate cancers; hormone-refractory prostate*

cancer. Discovered the importance of RNF5 in the control of glutamine carrier proteins, for BCa responsiveness taxenes, basis for clinical trials. RNF125 in melanoma resistance to BRAF inhibitor.

- Qi J, Nakayama K, Cardiff RD, Borowsky AD, Kaul K, Williams R, Krajewski S, Mercola D, Carpenter PM, Bowtell D, Ronai ZA. Siah2-dependent concerted activity of HIF and FoxA2 regulates formation of neuroendocrine phenotype and neuroendocrine prostate tumors. **Cancer Cell**. 2010; 18(1):23-38. PMC2919332.
- Qi J, Tripathi M, Mishra R, Sahgal N, Fazli L, Ettinger S, Placzek WJ, Claps G, Chung LW, Bowtell D, Gleave M, Bhowmick N, Ronai ZA. The E3 ubiquitin ligase Siah2 contributes to castration-resistant prostate cancer by regulation of androgen receptor transcriptional activity. **Cancer Cell**. 2013; 23(3):332-46. PMC3750989.
- Jeon YJ, Khelifa S, Ratnikov B, Scott DA, Feng Y, Parisi F, Ruller C, Lau E, Kim H, Brill LM, Jiang T, Rimm DL, Cardiff RD, Mills GB, Smith JW, Osterman AL, Kluger Y, Ronai ZA. Regulation of glutamine carrier proteins by RNF5 determines breast cancer response to ER stress-inducing chemotherapies. **Cancer Cell**. 2015; 27(3):354-69. PMC4356903.
- Scortegagna M, Hockemeyer K, Dolgalev I, Poźniak J, Rambow F, Li Y, Feng Y, Tinoco R, Otero DC, Zhang T, Brown K, Bosenberg M, Bradley LM, Marine JC, Aifantis I, Ronai ZA. Siah2 control of T regulatory cells limits anti-tumor immunity. **Nat Comm**. 2020 Jan 7;11(1):99. doi: 10.1038/s41467-019-13826-7. PMC6946684.

Ubiquitin ligase in the interplay between autoimmunity and anti-tumor immunity. *Demonstrated that RNF5 defines the gut microbiota's ability to induce anti-tumor immunity and tumor inhibition while the same ubiquitin ligase defines susceptibility to intestinal inflammation (IBD-like phenotypes).*

- Li Y, Tinoco R, Elmén L, Segota I, Xian Y, Fujita Y, Sahu A, Zarecki R, Marie K, Feng Y, Khateb A, Frederick DT, Ashkenazi SK, Kim H, Perez EG, Day CP, Segura Muñoz RS, Schmaltz R, Yooseph S, Tam MA, Zhang T, Avitan-Hersh E, Tzur L, Roizman S, Boyango I, Bar-Sela G, Orian A, Kaufman RJ, Bosenberg M, Goding CR, Baaten B, Levesque MP, Dummer R, Brown K, Merlino G, Ruppin E, Flaherty K, Ramer-Tait A, Long T, Peterson SN, Bradley LM, Ronai ZA. Gut microbiota-dependent anti-tumor immunity restricts melanoma growth in Rnf5^{-/-} mice. **Nat Commun**. 2019; 10(1):1492. PMC6445090.
- Fujita Y, Khateb A, Li Y, Tinoco R, Zhang T, Bar-Yoseph H, Tam MA, Chowders Y, Sabo E, Gerassy-Vainberg S, Starosvetsky E, James B, Brown K, Shen-Orr SS, Bradley LM, Tessier PA, Ronai ZA. Regulation of S100A8 stability by RNF5 in intestinal epithelial cells determines intestinal inflammation and severity of colitis. **Cell Rep**. 2018; 24(12):3296-3311.e6. PMC6185744.
- Li Y, Elmén L, Segota I, Xian Y, Tinoco R, Feng Y, Fujita Y, Segura Muñoz RR, Schmaltz R, Bradley LM, Ramer-Tait A, Zarecki R, Long T, Peterson SN, Ronai ZA. Prebiotic-Induced Anti-tumor Immunity Attenuates Tumor Growth. **Cell Rep**. 2020 Feb 11;30(6):1753-1766. PMC7053418.
- Kim H, Kim H, Feng Y, Li Y, Tamiya H, Tocci S, Ronai ZA. PRMT5 control of cGAS/STING and NLRC5 pathways defines melanoma response to antitumor immunity. **Sci Transl Med**. 2020 8;12(551): eaaz5683. PMC7508354.

Targeting cancer by novel therapeutics. *Targeting the eIF4F – translation initiation complex using SBI-756, provided a new paradigm for cancer treatment, exemplified for melanoma and DLBCL. Targeting ASNS in pancreatic cancer and melanoma with MEKi provided the basis for an ongoing clinical trial at OHSU. Targeting AML with a low level of RNF5 expression using HDAC inhibitors provides the basis for clinical evaluation currently developed at Scripps.*

- Feng Y, Pinkerton AB, Hulea L, Zhang T, Davies MA, Grotegut S, Cheli Y, Yin H, Lau E, Kim H, De SK, Barile E, Pellecchia M, Bosenberg M, Li JL, James B, Hassig CA, Brown KM, Topisirovic I, Ronai ZA. SBI-0640756 Attenuates the Growth of Clinically Unresponsive Melanomas by Disrupting the eIF4F Translation Initiation Complex. **Cancer Res**. 2015; 75(24):5211-8. doi: 10.1158/0008-5472.CAN-15-0885. PMC4681635.
- Pathria G, Lee JS, Hasnis E, Tandoc K, Scott DA, Verma S, Feng Y, Larue L, Sahu AD, Topisirovic I, Ruppin E, Ronai ZA. Translational reprogramming marks adaptation to asparagine restriction in cancer. **Nat Cell Biol**. 2019; (12):1590-1603. doi: 10.1038/s41556-019-0415-1. PMC7307327.

- Khateb A, Deshpande A, Feng Y, Finlay D, Lee JS, Lazar I, Fabre B, Li Y, Fujita Y, Zhang T, Yin J, Pass I, Livneh I, Jeremias I, Burian C, Mason JR, Almog R, Horesh N, Ofran Y, Brown K, Vuori K, Jackson M, Ruppin E, Deshpande AJ, Ronai ZA. The ubiquitin ligase RNF5 determines acute myeloid leukemia growth and susceptibility to histone deacetylase inhibitors. **Nat Commun**. 2021; 12(1):5397. doi: 10.1038/s41467-021-25664-7. PMC8437979.
- Verma S, Crawford D, Khateb A, Feng Y, Sergienko E, Pathria G, Ma CT, Olson SH, Scott D, Murad R, Ruppin E, Jackson M, Ronai ZA. NRF2 mediates melanoma addiction to GCDH by modulating apoptotic signaling. **Nat Cell Biol**. 2022; 24(9):1422-1432. doi: 10.1038/s41556-022-00985-x PMC9977532.

Complete List of Published Work in My Bibliography:

<https://www.ncbi.nlm.nih.gov/sites/myncbi/ze'ev.ronai.1/bibliography/47757767/public/?sort=date&direction=descending>

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