Professor Amir M. Orian (Oryan) MD/PhD
I.D. 059015750

July 2023

1. ACADEMIC DEGREES

1993	B.Sc. (Cum laude)	Medical Sciences	Faculty of Medicine, Technion-IIT
1999	M.D.	Medicine	Faculty of Medicine, Technion-IIT
2000	Ph.D.	Biochemistry	Faculty of Medicine, Technion-IIT

2. Clinical Training:

1998-1999 Clinical Rotating internship (with excellence), Rambam Medical Center, Haifa, Israel.

3. ACADEMIC APPOINTMENTS

2012- Current	**Professor**, Faculty of Medicine, Technion-IIT
2012- 2023	**Associate Professor**, Faculty of Medicine, Technion-IIT
2005-2012	**Senior Lecturer**, Faculty of Medicine, Technion-IIT.
2023-Current	**Director,** R-Technion integrative cancer center, (R-TICC) Technion-IIT
2018-Current	**Chair,** Dpt. of cancer cell biology, Faculty of Medicine -Technion IIT
2005-Current	**Member**, Rappaport Research Institute, Haifa, Israel.
2013-Current	**Member,** R-Technion integrative cancer center, (R-TICC) Technion-IIT
2012-2020	**Member,** SignGene, Helmholtz International Graduate School.

4. PROFESSIONAL EXPERIENCE

2006-2019	**Visiting Assistant Professor** Laboratory of Dr. Susan Parkhurst, Division of Basic Sciences, Fred Hutchinson Cancer Research Center, Seattle, WA, USA.
2015-2018	**Adjacent Associate Professor**, Dpt. of Biochemistry and Molecular Genetics, Feinberg School of Medicine, North Western University, Chicago, IL, USA
2000-2005	**Postdoctoral Fellow** with Dr. Robert N. Eisenman, Cancer Biology: The role of Myc in *Drosophila* development. Division of Basic Sciences, Fred Hutchinson Cancer Research Center. Seattle, WA, USA.
1995-2000	**PhD Candidate** Thesis dissertation: "The role of the ubiquitin-proteolytic system in the activation of the transcriptional factor NF-κB", Thesis advisor: Prof. Aaron Ciechanover, Faculty of Medicine, Technion-IIT.
1991-2000	**Medical Student** MD/PhD Program, Faculty of Medicine, Technion Haifa, Israel.
1991, 1993, 1995, 1998	**Visiting Scientist** with Dr. Alan L. Schwartz. Division of Hematology/Oncology, Department of Pediatrics, Children's Hospital, Washington University School of Medicine, St.-Louis, MO, USA.

5. RESEARCH INTERESTS:

1. Regulation of cell identity and aging by ubiquitin and ubiquitin-like proteins.
2. Ubiquitin-dependent oncoproteins-stabilization and addiction in cancer
3. Cell biology, *Drosophila* genetics, genomics.

6. TEACHING

2006-2014	274113	Anatomy for Medical students; Lecturer and academic head of the course
2014-Current	274150	The Molecular biology of cancer (MD course, lecturer and academic head of the course)
2015-Current	274243	Molecular biology (MD course, lecturer)

8. ACADEMIC AND PUBLIC PROFESSIONAL ACTIVITIES

2005-2015 Member, Faculty search committee, Equipment committee.
2013-2014 Coordinator, Faculty search committee.
2019- Current Head, Department of Cancer and Cell biology.
2005- Current Member, MD/PhD committee
2007-Current Evaluator MOR Faculty entry exams.
2014-Current Member, R-TICC steering committee

Ad hoc review for scientific Journals including; Dev. Cell, NCB, MCB, PNAS, *e-Life*, NAR, G&D.
Ad hoc review for granting agencies: AICR, MRC, GIF, ISF, Israel Ministry of Health, (MOH).
Ad hoc member, professional committees: University of Haifa.

COST-Proteostasis network -Member and Israeli vice-president

Editorial board member:

Cells ISSN 2073-4409
Science-open (http://about.scienceopen.com/editorial-board/)

10. HONORS AND FELLOWSHIPS

2007 Krill award Wolf-Foundation (www.wolffund.org)
2005 Alon Fellowship -Young Israeli scientist-ISF
2005-2007 Technion Horev Fellow
2005-2007 Human Frontier Science Program (HFSP) -Career Development Award
2004-2006 Leukemia Lymphoma Special Fellow (LLS-USA)
2000-2003 Human Frontier Science Program (HFSP) Postdoctoral Fellowship
2000 EMBO-Postdoctoral Fellowship-Declined
1997-1999 "Clore" Fellowship for academic excellence (The Clore Scholars Program, the Charles Clore Israel Foundation)
Rambam Intern Excellence Award 1998-9, Rambam Medical Center, Haifa, Israel
1996 Wolf Foundation Prize for M.Sc. Research.
1995-1997 "Alon" a 3-year PhD scholarship.
1995-1998 The "Foulkes" Foundation Fellowship for MD/PhD. students (The Foulkes Foundation, United Kingdom, and the Israeli Academy of Science and Humanities).
1993 Dean's list
1992 The Faculty of Medicine Award for M.D. Student in Basic Research.

11. GRADUATE STUDENTS AND FELLOWS

Former Postdoctoral Researchers and MD Fellows 2.
Graduate students**:** Completed theses: 11 PhD; 4 M.SC. Former MD students 2.
Current Postdoctoral Researchers and MD Fellows 1
Current PhD students 3; Current M.Sc. students 1, Current MD students 1

HONORS, FELLOWSHIPS AND AWARDS TO MY STUDENTS AND LAB FELLOWS:

2005-2008 Dr. Dorit Kenyagin –"Lady Davis" Postdoctoral fellowship
2007 Ms. Mona Abed-Fulbright Fellowship (short term)
2008 Ms. Mona Abed-Vattat Excellene PhD Fellowship
2010 Dr. Yaniv Zohar-American Physicains for Israel- Grant Award
2011 Dr. Yaniv Zohar-"Atidim" Fellow program, Rambam Medical Center
2011 Ms. Mona Abed-Lendue Meeting Award
2011 Dr. Yaniv Zohar-Dalia Gredinger Fellowship
2014 Dr. Rossti Novak MD/PhD -"Atidim" Fellow program, Rambam Medical Center
2016 Dr. Emily Hersh-Avitan- "Wolf flundation prize for PhD student"
2018 Dr. Rossti Novak MD/PhD ICA- "Non oncogene addiction in osteosarcoma"

2019 Ms. Salwa Daniel-Arab minority excellence scholarship.
2022 Ms. Avital-Oknin Wiesamann-Rubinstein PhD fellow.

12. COMPETITIVE RESEARCH GRANTS (not including Technion internal grants)

2004-2007 Senior Leukemia and Lymphoma Fellow –Leukemia and Lymphoma Society of America (162,000$)
2005-2007 HFSP -Career Developments Award (180,000$)
2005-2006 "Alon" Young Scientist Fellowship (29,000$)
2006-2008 Rappaport Research Grant (75,000$)
2009-2011 Rappaport Research Grant (90,000$)
2008-2010 GIF-German-Israeli Foundation (With Prof. Martin Eilers Marburg 196,000Euro [50%])
2008-2010 Bikura ISF- (With Prof. Zee'v Paroush HUJI 128,000$ [50%]).
2009-2013 ISF- Research Grant; Role of STUbL in transcription (120,000$).
2010 Maria Ascoli Research Grant: "Role of RNF4 in melanoma" (20,000$;
2011-2012 Israel Cancer Association project grant (75,000 NIS).
2011-2012 ICRF- Project Grant: "Targeting the SUMO Pathway and RNF4 in Myeloma" (60,000$)
2011-2012 "Atidim", together with Dr. Yaniv Zhoar (Rambam Medical Center- 40,000$)
2012- 2013 MOI "Nofar" project grant: Targeting RNF4 in multiple myeloma (110,000$)
2012-2014 Rappaport Research Grant (120,000$)
2013-2014 ICRF Project Grant (60,000$)
2014-2015 "Atidim" together with Dr. Rosti Novak (Rambam Medical Center- 40,000$)
2015-2018 Rappaport Research Grant (75,000$)
2015-2019 ISF-Research Grant; Molecular mechanisms that are required for maintaining a differentiated identity (386,890$).
2018-2019 ISF-INCPM Grant: Genomic studies regrading of cell identity 45,000 NIS.
2018-2019 ICRF Project Grant (100,000$).
2018-2020 GIF-German-Israeli Foundation (With Dr. Markus Diefenbacher Würzburg). 200,000 Euro [50%])
2020-2023 ISF-Research Grant 318/20 Regulation of cell identity by de-ubiquitination (210,000 USD)
2021-2024 MOI-KAMIN: Development of degradation inducing PROTAC in therapy resistant cancers ; 410,000$ (together with Prof. Ashraf Brik, Chemistry Technion)
2022-2023 Rappaport research institute translation STS grant (30,000$)

Theses:
PhD Thesis dissertation: "The role of the ubiquitin-proteolytic system in the activation of the transcriptional factor NF-κB" Thesis advisor: Research Professor Aaron Ciechanover.

Research papers:

1. Reissland M Hartmann O, Tauch S, Prieto-Garcia C, Schulte C, Solvie D, Loebbert S, Jacomin AC, Pesic M, Bugter JM, Schuelein-Voelk C, Fuss C, Pahor N, Ade C, Buck V, Potente M, Li V, Beliu G, Wiegering A, Bitman-Lotan E, Grossmann T, Rosenfeldt M, Eilers M, Maric H, Maurice MM, Greten F, Dikic I, Orian A, Gallant P, Diefenbacher ME. Stabilization of β-Catenin-WNT signaling by USP10 in APC-truncated colorectal cancer drives cancer stemness and enables super-competitor signaling (*BioRxiv*).

2. Novak R, Abu Ahmed1Y, Timaner M, Bitman-Lotan L, Oknin-Vaisman A, Nikomarov D, Diefenbacher M, Shaked Y, Orian A. (2022) RNF4-RGMb axis is required for osteogenic differentiation and cancer cell survival. Cell Death & Disease 13:820.

3 Erez, N., Israitel L., Bitman-Lotan E., Wong, W. H., Raz G., Danial S., Flint Brodsly N., Belova, E., Maksimenko, O., Georgiev P., Druley, T., Mohan R., **Orian A.** (2021) A Non-stop identity complex (NIC) supervises enterocyte identity and protects from pre-mature aging. ***e****-Life* 10:e62312.

4 Hartmann, O., Reissland M., Maier C. R. , Fischer, T., Prieto-Garcia, C., Baluapuri, A., Schwarz, J., Schmitz, W., Garrido-Rodríguez, M., Pahor, N., Davies, C. C., **Orian, A**., Wolf, E., Schulze, A., Calzado, M. A., Rosenfeldt, M. T., Diefenbacher M. (2021) Implementation of CRISPR/Cas9 genome editing to generate murine lung cancer models that depict the mutational landscape of the human disease. *Frontiers in Cell and Developmental Biology* 9: 641618.

5 Avitan-Hersh E., Feng Y., Oknin-Vaisman A., Abu-Ahmed Y., Zhang T., Zohar Y., Lazar I., Khalil S., Feiler Y., Lee S J., Kluger H., Kahana H., Brown K., Ruppin E., Ronai Z., **Orian A.** (2020) Regulation of eIF2a by RNF4 underlies melanoma development and therapy resistance. *J. Investigative Dermatology* 29:S0022-202; 31404-3114.

6 Cammarata-Mouchtouris A, Nguyen XH, Goto A, **Orian A**, Bonnay F, Fauvarque MO, Reichhart JM, Matt N. (2020) Hyd ubiquitinates the NF-κB co-factor Akirin to activate an effective immune response in Drosophila. *PLoS Pathogens* 27; 16:e1008458.

7 Prieto-Garcia C, Hartmann O, Reissland M, Braun F, Fischer T, Walz S, Schülein-Völk C, Eilers U, Ade CP, Calzado MA, **Orian A**, Maric HM, Münch C, Rosenfeldt M, Eilers M, Diefenbacher ME (2020) Maintaining protein stability of ΔNp63 via SP28 is required by squamous cancer cells. *EMBO Mol Med.* 12:e11101.

8 Lotan-Bitman E, Raz G, Rincon H, and **Orian A**. (2019) Determination of Chromatin Accessibility of Drosophila Midgut Enterocytes by In Situ 5mC Labeling *Bio-Protocol* Vol 9, Iss 22. DOI: 10.21769/BioProtoc.3435

9 Flint-Brodsly, N. Bitman-Lotan E, Boico O, Shafat A, Monastirioti M, Gessler M, Delidakis C, Rincon-Arano H, **Orian A**. (2019) The transcription factor Hey and nuclear lamins specify and maintain cell identity, e-Life pii: e44745. doi: 10.7554/eLife.44745.

10 Yan Li, Roberto Tinoco, Lisa Elmén, Igor Segota, Yibo Xian, Yu Fujita, Avinash Sahu, Raphy Zarecki, Kerrie Marie, Yongmei Feng, Ali Khateb, Dennie T. Frederick, Shiri K Ashkenazi, Hyungsoo Kim, Eva Guijarro Perez, Chi-Ping Day, Rafael S. Muñoz, Robert Schmaltz, Shibu Yooseph, Miguel A. Tam, Tongwu Zhang, Emily Avitan-Hersh, Lihi Tzur, Shoshana Roizman, Ilanit Boyango, Gil Bar-Sela, **Amir Orian**, Randal J. Kaufman, Marcus Bosenberg, Colin R Goding, Bas Baaten, Mitchell P. Levesque, Reinhard Dummer, Kevin Brown, Glenn Merlino, Eytan Ruppin, Keith Flaherty, Amanda Ramer-Tait, Tao Long, Scott N. Peterson, Linda M. Bradley, Ze'ev A. Ronai (2019). Regulation of Gut Microbiota and Anti-Tumor Immunity by Host ER-stress in RNF5 $^{-/-}$ mice Restricts Melanoma Growth. *Nature communication* 10:1492. doi: 10.1038/s41467-019-09525-y.

11 Yanku, Y, Bitman-Lotan E, Zohar Y, Kurant E, Zilke N, Eilers M, and **Orian A** (2018) *Drosophila* HUWE1 ubiquitin ligase regulates endoreplication and antagonizes JNK signaling during salivary gland development *Cells* **7,** 151; doi:10.3390/cells7100151

12 Koltun B, Shackelford E, Bonnay F, Matt N, Reichhart JM, **Orian A**. (2017) Dgrn, a SUMO-targeted ubiquitin ligase, is essential for *Drosophila* innate immunity *J. Int. Dev. Biol.* **1**:319-327.

13 Thomas JJ, Abed M, Heuberger J, Novak R, Zohar Y, Beltran Lopez AP, Trausch-Azar JS, Ilgan M, Benhamou D, Dittmar G, Kopan R Birchmeier W, Schwartz AL, and **Orian A.** (2016) RNF4-dependent oncogene activation by protein stabilization *Cell Reports* **16**, 3388-3400.

14 Wang M, Sang J, Ren Y, Liu K, Liu X, Zhang J, Wang H, Wang J, **Orian A**, Yang J, Yi J. (2015) SENP3 regulates the global protein turnover and the Sp1 level via antagonizing SUMO2/3-targeted ubiquitination and degradation. *Protein Cell*. DOI 10.1007/s13238-015-0216-7

15 Trausch-Azar JS, Abed M, **Orian A,** Schwartz AL. (2014) Differential regulation of PGC-1α by

isoform-specific SCF^{Fbw7}ubiquitylayion. *J. Cell Physiol. doi: 10.1002/jcp.24812.*

16 Singer R, Shimshi A, Atias O, Oron E, Segal D, Hirch JA, Tuller T, **Orian A**, Chamovitz DA. (2014) *Drosophila* COP9 Signalosome Subunit 7 interacts with multiple genomic loci to regulate development. *Nuc. Acid. Research* **42**: 9761-9770

17 Fuchs Y, Brunwasser M, Haif S, Hadad J, Shneyer B, Goldshmidt-Tran O, Korsensky L, Abed M, Zisman-Rosen S, Lilach Koren, Carmi Y, Apte R, **Orian A**, Bejar J, and Dina Ron. (2012) Sef is a novel inhibitor of pro-inflammatory cytokine signaling, acting by cytoplasmic sequestration of NF-κB. *Dev. Cell* **23**: 611-623.

18 Helman A, Cinnamon E, Mezuman S, Von Ohlen T, **Orian A**, Jiménez G, and Parous Z. (2011) Phosphorylation of Groucho mediates RTK feedback inhibition and spatiotemporal maintenance of pathway target gene expression *Curr. Biol,* **21**:1102-1110.

19 Barry KC, Abed M, Kenyagin D, Werwie TR, Boiko O, **Orian A*,** Parkhurst SM*.(2011) Degringolade a Drosophila STUbL is required for cellularization, sex determination, and early embryonic patterning. *Development* **138**: 1759-1769. (*Corresponding author)

20 Abed M, Barry KC, Kenyagin D, Koltun B, Phippen TP, Delrow JJ, Parkhurst SM, and **Orian, A.** (2011) The STUbL protein Degringolade is a negative regulator of Hairy-mediated Groucho dependent repression. *EMBO J.* **30**: 1289 - 1301.

21 Herkert B, Dwertmann A, Herold H, Abed M, Naud JF, Finkernagel F, Harms GS, **Orian A,** Wanzel M, and Eilers M. (2010) The Arf tumor suppressor protein inhibits Miz1 to suppress cell adhesion and induce apoptosis. *J. Cell Biol.* **188**: 905-918.

22 Cinnamon E, Helman, A, **Orian, A,** Jiménez G, and Paroush, Z. (2008) Multiple RTK pathways down-regulate Groucho-mediated repression in Drosophila embryogenesis *Development* **135**: 829-37.

23 **Orian A***, Delrow, J, Rosales-Nieves, E, Abed M, Paroush Z, Eisenman, RN & Parkhurst SM.* (2007) A Myc–Groucho complex integrates EGF and Notch signaling to regulate neural development *PNAS* **104**: 15771-1576 (*Corresponding author)

24 **Orian A,** Grewal S, Knoepfler PS, Edgar BA, Parkhurts SM, Eisnman RN. (2005) Genomic Binding and Transcriptional Regulation by the *Drosophila* Myc and Mnt *Cold Spring Harbor Symp. Quant. Biol* **70:** 1-10.

25 Grewal SS, Li L, **Orian A**, Edgar BA (2004) Myc-dependent regulation of ribosomal RNA synthesis during *Drosophila* development. *Nat. Cell. Biol*. **7**: 295-302.

26 Welcker M*, **Orian A*,** Eisenman RN, Clurman BE. (2004) Regulation of Cell Growth and c-Myc by a Nucleolar Fbw7 Isoform. *Cur. Biol.* **14**: 1852-1857. (*equal contributors).

27 Bianchi-Frais D**, Orian A,** Delrow J, Vazquez J, Rosales-Nieves AE, and Parkhurst S. M, (2004). Hairy-mediated transcriptional repression, and cofactor recruitment in *Drosophila. PloS Biol.* **2**: 975-986.

28 Welcker M. *, **Orian A. ***, Jin J, Harper WJ, Eisenman RN, and Clurman BE. (2004) The FbW7 F-box protein Regulates GSK3 phosphorylation dependent c-Myc protein degradation. *Proc. Natl. Acad. Sci. USA* **101:** 9085-9090 (*equal contributors).

29 **Orian A,** van Steensel B, Delrow J, Bussemaker HJ, Li L, Tomoyuki S, Williams E, Loo, LM, Cowley SM, Yost C, Pierce S, Edgar BA, Parkhurst SM, Eisenman RN. (2003) Genomic binding by the *Drosophila* Myc, Max, Mad/Mnt transcription factor network. *Genes & Dev.* **17**: 1101-1114.

30 Hook S, **Orian A**, Cowley SM, and Eisenman RN. (2002) Histone deacetylase 6 binds polyubiquitin through its zinc finger (PAZ domain) and co-purifies with deubiquitinating enzymes *Proc. Natl. Acad. Sci.* USA **99**: 13425-13430.

31 Cohen S*, **Orian A*,** Ciechanover A. (2001) Processing of p105 is inhibited by docking of p50 active subunits to the ankyrin repeat domain, and inhibition is alleviated by signaling via the carboxyl-terminal phosphorylation/ ubiquitin-ligase binding domain. *J. Biol. Chem*. **276**: 26769-26776 (*equal contributors).

32 Ciechanover A, Gonen H, Bercovich B, Cohen S, Fajerman I, Israel A, Mercurio F, Kahana C, Schwartz AL, Iwai K, **Orian A.** (2001) Mechanisms of ubiquitin-mediated, limited processing of the NF-kappaB1 precursor protein p105. *Biochimie* **83**: 341-349.

33 **Orian A,** Gonen H, Bercovich B, Fajerman I, Eytan E, Israel A, Mercurio F, Iwai K, Schwartz AL, Ciechanover A. (2000) SCF (β-TrCP) ubiquitin ligase-mediated processing of NF- kappaB p105 requires phosphorylation of its C-terminus by IκB kinase. *EMBO J.* **19:** 2580-2591.

34 Gonen H, Bercovich B, **Orian A,** Carrano A, Takizawa C, Yamanaka K, Pagano M, Iwai K, Ciechanover A. (1999) Identification of the ubiquitin carrier proteins, E2s, involved in signal induced conjugation and subsequent degradation of IκBα. *J. Biol Chem.* **274:** 14823-14830.

35 **Orian A,** Whiteside S, Israël A, Schwartz AL, Kahana C, and Ciechanover AC. (1999) Structural motifs involved in ubiquitin-mediated limited processing of the NF-κB1 precursor protein p105. *Mol. Cell. Biol* **19:** 3664-3673.

36 Alkali I, Yarom A, Htzubay A, **Orian A,** Ciechanover A, and Ben-Neria Y. (1995) Stimulation-dependent IκB phosphorylation marks the NF-κB inhibitor for degradation via the ubiquitin-proteasome pathway. *Proc. Natl. Acad. Sci. USA* **92**: 10599-10603.

37 Stankovsky I, Gonen H, **Orian A,** Schwartz AL, and Ciechanover A. (1995) Degradation of the proto-oncogene product c-Fos by the ubiquitin proteolytic system in vivo and in vitro: identification and characterization of the conjugating enzymes. *Mol. Cell. Biol.* **15:**7106-7116.

38 **Orian, A,** Whiteside, S, Israel A., Stankovsky I, Schwartz AL, and Ciechanover A. (1995) Ubiquitin-mediated processing of NF-κB transcriptional activator precursor p105: reconstitution of a cell-free system and identification of the ubiquitin-carrier protein, E2, and a novel ubiquitin-protein ligase, E3, involved in conjugation. *J. Biol. Chem.* **270**: 21707-21714.

39 Ciechanover A, DiGiuseppe JA, Bercovich B, **Orian, A**, Richter JD, Schwartz AL, and Broduer, GM (1991) Degradation of nuclear oncoproteins by the ubiquitin system in vitro. *Proc. Natl. Acad. Sci. USA* 88:139-143.

INVITED REVIEWS

Guest Editor (2021): Special Issue "Ubiquitin and Ubiquitin-Like Pathways in Development and Disease". *Cells* (ISSN 2073-4409). This special issue belongs to the section "Cell Signaling and Regulated Cell Death". (https://www.mdpi.com/journal/cells/special_issues/ubiquitin_development_disease).

R1. Abu Ahmad Y., Oknin-Vaisman A., Lotan-Bitman E. and **Orian A.** (2021) From the evasion of degradation to ubiquitin-dependent protein stabilization *Cells*, 10 :2374.

R2. Bitman-Lotan E, **Orian A.** (2021) Nuclear organization and regulation of the differentiated state. *Cellular and Molecular Life Sciences* 0.1007/s00018-020-03731-4.

R3. Bitman-Lotan E, **Orian A.** (2018) Chromatin, Nuclear Lamins, and maintenance of the differentiated identity. *Current Opinion in System Biology* 8: 1-8.

R4 Abed M, Bitman-Lotan E, **Orian A.** (2018) The biology of SUMO-targeted ubiquitin ligases in Drosophila development, immunity, and cancer. J. Dev. Biol. doi:10.3390/jdb6010002

R5. Avitan-Hersh E**, Orian A** (2017) Targeting the Ubiquitin-Dependent Epigenetic Landscape in Cancer**.** *Curr Pharmacol Rep* DOI **10.1007**/s40495-017-0102-5**.**

R6. Diefenbacher M, Orian A. Stabilization of nuclear oncoproteins by RNF4 and the ubiquitin system in cancer. (2016) Molecular &Cellular oncology doi: 10.1080/23723556.2016.1260671.

R7**.** Abed M, Bitman-Lotan E, **Orian A**. (2011) A fly View of a SUMO-Targeted Ubiquitin Ligase "*Fly"***5***: 1-5*, PMID 21857164.

R8. **Orian A.** (2006) Chromatin profiling, DamID and the emerging landscape of gene expression *Curr. Op. in Genetics and Development* **16:** 157-164.

R9. **Orian A,** Eisenman RN. (2001) TGF-ß Flips the Myc Switch Science's STKE: 88 DOI: 10.1126/stke.2001.88.pe1]

R10. Ciechanover A, **Orian A,** Schwartz AL. (2000) Ubiquitin-mediated proteolysis: biological regulation via destruction *Bioassays* **22:** 442-451.

R11. Ciechanover, A, **Orian A,** and Schwartz AL (2000) The Ubiquitin Proteolytic pathway: mode of action and clinical implications. *J. Cell. Biochem.* **77:** 40-51.

BOOKS AND BOOK CHAPTERS

B1. Ubiquitin Ligase: New Insights, Emerging Roles and Clinical Implications. "Paving the Notch pathway with ubiquitin ligases". Erez N. and **Orian A,** (2017) (Nova Science Publishers, Inc.)

B2. Protein Interaction/Book 1", Editor: Jianfeng Cai. Yanku Y, **Orian A.** (2012) "Regulation of protein-protein interactions by the SUMO and Ubiquitin pathways". InTech ISBN 979-953-307-577.

B3. "Chromatin Immunoprecipitation assays"; Editor: Philippe Collas chapter 11: Abed M, Kenyagin-Karsenti D, Boico O, **Orian A.** (2009) DamID: a Methylation Based Chromatin Profiling Approach. MiMB **567:**155-169.

B4. "Proteasomes: The World of Regulatory Proteolysis" editors: Wolfgang Hilt and Dieter H. Wolf, RG Landes Co; ISBN 1570596212 Chapter 13: Ciechanover A, **Orian** A, Schwartz AL. The ubiquitin-proteasome pathway in mammals: Mechanisms of action and involvement in pathogenesis of diseases.

B5. Ubiquitin-Proteasome Proteolytic System: From Classical Biochemistry to Human Diseases, Recent Advances in Human Biology Vol. 9 World scientific ISBN 981231007 2003 Ed. Ciechanover AJ, Masucci MG, Chapter 5: Ciechanover A, Gonen H, Bercovich B, Cohen S, **Orian A.** Mechanisms and Regulation of Ubiquitin-Mediated, Limited Processing of the NF-kB Precursor Protein p105.

14. PATENTS:

1. Tech-P-0139-USP mAb as prognostic marker in cancer (3/2018 PCT)
2. Tech-P-0134-USP RNF4-selective inhibitors in cancer (3/2018-terminated)
3. Tech-P-0254-USP RNF4 Targeting compounds and uses. (3/2021)

15. CONFERENC ES

Plenary invited talks in meetings and conferences - International

1995 Regulation of the Cell Cycle and Cancer, Hebrew University, Jerusalem.
"Ubiquitin mediated processing of the transcriptional Activator p105/NFkB1"

2002 Human Frontier Science Program (HFSP) meeting Ottawa Canada. "Genomic Targets of the Myc/Max/Mad Transcriptional network in *Drosophila".*

2003 43rd Annual *Drosophila* Research Conference Chicago, USA. "Global Analysis of genome binding by the Myc/Max/Mad transcriptional network in *Drosophila".*

2005 Human Frontier Science Program (HFSP) meeting Washington D.C. "Integration of Transcriptional Networks During Development and Their Effects on *Drosophila* Progenitors".

2007 Transregio-17 Rothenberg-ob-der-Tauber, Germany. "Regulation of Stem cell development by EGF/Notch Myc and Groucho".

2008 Zome5 The Fifth international Meeting on the COP9 Signalosome, RIKEN, Yokohama, Japan. **"**Degringolade encodes a SUMO targeted E3 ubiquitin ligase required for Notch-mediated HES family repression".

2009 SUMO, Ubiquitin and UBL proteins; implications for human disease; MD Anderson Center, Texas: "Role of STUbL proteins in *Drosophila* development "

2010 Hebrew University Advanced studies International Meeting: Biology of the Ubiquitin and the Ubiquitin-Like Systems - "Role of STUbL proteins in transcriptional-repression".

2010 "Notch and Stem cells" International meeting Athens, Greece; "Regulation of Notch pathway by STUbL"

2010 Israel-German Symposia, MDC, Berlin: "Molecular Selectors".

2011 The UK-Israeli seminar of human genetics. Technion-Haifa, Israel. "molecular selectors in development and cancer"

2011 Gemini workshop; Periconceptional developmental programming, Hebrew University, Jerusalem "A fly view on SUMO-targeted ubiquitin ligases in early development"

2011 EMBO conference, Ubiquitin and ubiquitin like modifiers from functional modules to system biology, Caveat, Croatia. "A fly view on SUMO-targeted ubiquitin ligase."

2012 6th SUMO, Ubiquitin and UBL proteins; implications for human disease; MD Anderson Center, Texas: "Role of STUbL proteins in transcriptional activation "

2012 Frontiers in Cell Signaling and Gene Regulation: From molecular structures to cellular networks, MDC-Berlin "Decision making at the tissue/molecular level.

2012 FEBS Special meeting Pine Bay Turkey; "Activation of oncogenic pathways by SUMO-targeted ubiquitin ligase".

2013 SignGene 1st International seminar , Berlin "A genetic networks that maintain the differentiated state".

2013 1st Annual Broad-Israel Cell Circuits Symposia, Jerusalem : "Maintaining the differentiated state; lessons from flies"

2013 Notch 7th International meeting Athens, Greece: "Notch-dependent and independent functions of dHey in gut homeostasis.

2014 SignGene International Winter School, Haifa: "Maintaining the differentiated state",

2014 Biomedical engineering 2014, Haifa: *Drosophila* models in cancer drug development.

2015 SignGene International Winter School, Jerusalem: "Oncogene activation by STUbL"

2015 International Symposium on Ubiquitin and Diseases Zhangjiajie City, Hunan, China: "Oncogene activation by RNF4 a SUMO-Targeted Ubiquitin ligase.

2015 1st international meeting: Stress Pathways and Cancer Xiamen university, China: "Regulation of chromatin and nuclear organization by Ub/UbL system".

2015 Epigenetic and development, The Switzerland institute of developmental biology, TAU, Tel-Aviv:
"Regulation of chromatin and nuclear organization determines enterocyte identity".

2016 Eighth International Conference SUMO, Ubiquitin, UBL Proteins: Implications for Human Diseases, Shanghai, China: Regulation of enterocyte identity by UB/UbL network.

2016 FEBS Intracellular proteolysis and its biological implication, Lisbon Portugal: "Regulation of the differentiated cell identity by ubiquitin and ubiquitin like pathways"

2017 Bat-Sheva Rothschild Seminar; The nuclear lamina and nuclear organization. Maa'le Hachamisha, Israel, "Regulation of cell identity by Hey and nuclear lamins".

2017 SignGene Symposium in Neuruppin, Germany, September 2017 Ubiquitin: One Traveler, Two Roads: "Ubiquitin and cell identity".
2019 Future Biotech, St. Petersburg, Russia; "Aging and supervisor of cell identity".
2019 Zome-X international meeting on COP9 Signalosome, Acre; "Ubiquitin and degradation resistant tumors".

PLENARY INVITED TALKS IN MEETINGS AND CONFERENCES - NATIONAL

2006 Annual meeting of the Israeli Society of Developmental and Cell Biology: Eilat "Integration of Transcriptional Networks During Development".
2007 *Drosophila- C. Elegance* joint Meeting Tel-Aviv University: "Role of dMyc in early development".
2008 Israeli Fly-Worm meeting, Jerusalem: "Role SUMO-Targeted ubiquitin ligases in *Drosophila* development".
2009 TISBD -Annual meeting of the Israeli society of developmental and cell biology: Weizmann Institute, Rehovot: "Transcriptional co-factors and the Notch Pathway".
2011 Ilanit-FISEB-Eilat: "SUMO-Targeted ubiquitin ligases as molecular selectors".
2013 Bi-Annual meeting of the Israeli Society of Developmental and Cell Biology Tiberia; A genetic network that maintains the differentiated state.
2014 Ilanit-FISEB-Eilat: "Maintaining the differentiated state, lessons from flies".
2014 ICSR-6th annual meeting of the Israeli Society for Cancer Research: Role of RNF4 in cancer.

INTERNATIONAL INVITED LECTURES AND SEMINARS:

2006 Institute für Molekularbiologie und Tumorforschung, Philipps-Universität, Marburg Germany. "Myc-From small flies to global views"
2010 Institute für Molekularbiologie und Tumorforschung Philipps-Universität Marburg Germany. "Role of Selectors, in transcription and beyond"
2010 Department of Biochemistry and Physiology II, Würtzburg, Germany. "Role of Selectors, in transcription and beyond".
2010 Signaling Pathways, Cancer Division MDC, Berlin. "Role of STUbL in transcription during development."
2010 UPR 9022 University of Strasbourg, France. "To be or Notch to be, regulation of the Notch pathway by STUbL proteins"
2010 Department of developmental biology, Washington University School of Medicine St. Louis. USA "Inhibiting the repressive arm by STUbL proteins".
2010 Department of Biochemistry Seminar Series, John Hopkins University Baltimore MD, USA. STUbLs as molecular selectors
2010 National Cancer Institute NCI-Fredrick, MD, USA. "SUMO-targeted ubiquitin ligases as molecular selectors".
2011 Molecular Biology Institute, UCLA Los-Angeles; "Molecular selectors in development".
2013 National Cancer Institute NCI-Fredrick, MD, USA "Activation of oncogenic pathways by SUMO-targeted ubiquitin ligase".
2013 Department of Biochemistry, John Hopkins University Baltimore MD "STUbL and gene expression selectivity during immune response".
2014 Stowers Research Institute, Kansas City MO, USA; A genetic network that maintains the differentiated identity of enterocytes and gut homeostasis.
2014 Sanford Burnham Research Institute, La-Julla, CA; Gut homeostasis lessons from flies.
2014 Fred Hutchinson Cancer Research Center. Seattle WA. A genetic network that maintains the differentiated identity of enterocytes, and gut homeostasis.
2014 Jackson laboratories Bar-Harbor, Maine: A genetic network that maintains the differentiated identity of enterocytes and gut homeostasis.

2014 CNRS, UPR9220 University de Strasbourg: "A genetic network that maintains the differentiated state".
2014 MDC-Berlin; "A genetic network that maintains the differentiated identity".
2015 Feinberg Medical School, North Western University Chicago; "Genetic Networks that maintain the differentiated identity of adult gut enterocytes".
2015 Dpt. of Pulmonary & Critical Care Medicine, North Western University, Chicago, IL: Colon cancer: From identity networks to non-oncogenic addiction networks.
2015 Dpt. of Developmental Biology, Washington University School of Medicine, Saint-Louis; "Regulation of gut homeostasis by Ub/UbL gene-network".
2015 Princess Margaret Cancer Centre, UHN Toronto, Canada: "Oncogene activation by SUMO-Targeted ubiquitin ligases in immunity and cancer."
2015 The Berlin Institute for Medical Systems Biology (BIMSB); Berlin: Regulation of gut homeostasis by Ub/UbL gene-network.
2015 Dpt. of Molecular and Cellular biology (LUMC) Leiden University, Netherland, "Regulation of gut homeostasis by Ub/UbL gene-network".
2016 Dpt. of Molecular, Cellular, & Developmental Biology, U. of Michigan Ann-Arbor MI. "Roles for ubiquitin-like pathways in modulating gene regulatory networks and cell identity"
2016 Stowers Institute for Medical Research, Kansas City MO, USA "Regulation of the differentiated identity".
2017 University of Zagreb, School of Medicine, Zagreb, Croatia, "Identity and non-oncogenic addiction gene networks",
2018 College de France: Aging Cell identity and Ubiquitin, Paris, France.
2018 Bio-centrum, Würzburg university, "Aging Cell identity and Ubiquitin" Würzburg, Germany.
2018 Sanford Burnham Prebys Medical Discovery Institute, San-Diego CA, USA. "Aging Cell identity and Ubiquitin."
2018 USCD, Department of Cell Biology, San-Diego CA, USA; "Aging Cell identity and Ubiquitin".
2020 Medizinische Fakultät Mannheim der Universität Heidelberg, Germany: Hallmarks of Skin Cancer seminar series; Ubiquitin, "degradation resistant" tumors, and Melanoma.
2021 Dpt. of Biochemistry & Molecular Biology LSU, New-Orleans USA: "Degradation resistant tumors".
2021 Robert Eisenman's Zoom Meeting series, FHCRC, Seattle WA. " Ubiquitin-dependent protein stabilization and degradation-resistant cancer" (by zoom)
2023 School of Biological and Chemical Sciences, Division of Genetics, Developmental, and Evolutionary Biology, university of Kansas city MO, ubiquitin, cell identitiy and cancer

NATIONAL INVITED LECTURES AND SEMINARS (PARTIAL LIST):

2005 Developmental seminar, Tel-Aviv university: "Taking Myc out from the Mad box"
2006 Department of Genetics, Faculty of Life sciences, Hebrew University: "Myc from small flies to global views".
2007 Developmental Seminar, School of Medicine, Hebrew University: " Role of a Myc-Gro complex in neuronal development".
2008 Department of Genetics, Faculty of medicine Tel-Aviv university: "Role of SUMO-Targeted Ubiquitin ligase in development".
2009 Department of Genetics, Faculty of Life sciences, Hebrew University: "Role of SUMO-Targeted Ubiquitin ligase in development".
2010 Department of Cell Biology, Weizmann Institute: "Inhibiting the repressive arm of the Notch pathway by STUbL".
2010 Developmental Seminar, School of Medicine, Hebrew University: "Molecular Selectors."
2011 Sheba Medical Center Tel-Hashomer, "Molecular selectors in development and cancer."
2011 Department of biological chemistry, Weizmann Institute: "Role of SUMO-Targeted ubiquitin ligases in gene-expression selectivity".
2011 Molecular Forum, Department of Biology, University of Haifa: "Role of SUMO-Targeted ubiquitin ligases in gene-expression selectivity".
2013 Department of cell biology and immunology Tel-Aviv University: "Role of SUMO-Targeted ubiquitin ligases in gene-expression selectivity".

2013 Faculty of Medicine seminar series Tel-Aviv University: "Maintaining the differentiated state lessons from flies."
2015 Department of Biology- Oranim educational college/University of Haifa. Maintaining the differentiated identity.
2016 Dept. of Genetics, Sackler School of Medicine, Tel-Aviv University. "Regulation of differentiated identity by nuclear lamins and Ub/UbL genes."
2017 Lautenberg Center for Immunology and Cancer Biology, Hadassah Medical School, HUJI, Jerusalem. "Regulation of differentiated identity by nuclear lamins and Ub/UbL genes."
2021 Department of human biology, University of Haifa: Ubiquitin-dependent protein stabilization and "degradation resistant" tumors

15. PARTICIPATION IN ORGANIZING CONFERENCES

2009 Israeli Fly-Worm meeting, Technion, Haifa, Israel (with Prof. Adi Salzberg).
2010 International Rappaport Research Ubiquitin Day, Haifa, Israel.
2013 SignGene 1st. International seminar MDC-Berlin
2014 SignGene International Winter School; "The biology of differentiation and cancer" Technion, Haifa.
2014 ICSR-6th annual meeting of the Israeli Society for Cancer Research: member of organizing committee.
2017 Israeli ubiquitin day September 2017 Faculty of Medicine, Technion Haifa.
2018 Israeli ubiquitin day May 2018 Faculty of Medicine, Technion Haifa.