
NIH BIOSKETCH

Name: Tomer Cooks

Current Position Title: Principle investigator, Lab of Cancer Exosomes, Department of Microbiology, Immunology and Genetics, Ben-Gurion University of the Negev

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Education/Training

Institution, City, Country	Degree	Completion Date MM/YYYY	Field of Study
Tel Aviv University, Tel-Aviv, Israel	B.Sc.	10/2003	Life Sciences
Tel Aviv University, Tel-Aviv, Israel	Ph.D	10/2009	Cancer research

A. Personal Statement

I am the head of a research group in the department of Microbiology, Immunology and Genetics, the Faculty of Health Sciences, Ben-Gurion University of the Negev. I currently lead a group of twelve scientists that include a research associate, four PhD students and several MSc students.

The lab focuses on various aspects of the tumor microenvironment, particularly cell-to-cell communication via extracellular vesicles. Amongst many hallmarks of cancer, an 'in-depth' focus is dedicated to mutations in the tumor suppressor TP53 gene and the plethora of interactions this molecular event shares with its surrounding. These include tumor cells communicating with the immune compartment of the tumor as well as specific microbiome members promoting host-pathogen responses. In addition, the Cooks lab constantly strives to match basic novel molecular mechanisms with innovative translational approaches for the benefit of cancer patients. Therefore, we believe that combining the knowledge and toolset of the lab with the pioneering Diffusing Alpha-emitters Radiation Therapy (DaRT), will enable us to provide insights about molecular traits with fundamental relevance to clinical decision-making. Promoting precision medicine approaches will advance a better quality of the DaRT treatment for many cancer patients worldwide.

B. Positions, Scientific Appointments, and Honors

- Invited speaker for the AACR annual meeting, New Orleans, LA, 2016.
- Keystone Symposia Scholarship. Keystone Symposia: Exosomes/Microvesicles: Novel Mechanisms of Cell-Cell Communication, Keystone, CO, 2016.
- Best oral presentation at the annual meeting of the international society of extracellular vesicles. Toronto, Canada 2017.
- NCI Director Innovation Award– NCI, Bethesda, 2017.
- Invited speaker for the Extracellular Vesicles in Health and Disease meeting, Tel-Aviv, 2018
- Invited speaker for the Stress & Inflammation in Tumor Progression & Metastasis conference, Rehovot, Israel 2019
- Invited speaker for the Mutant p53 workshop, Lyon, France 2019
- Organizer of the EVI2019, Israeli society of extracellular vesicles annual meeting, Beer-Sheva, Israel, 2019

- Invited speaker at FISEB2020, the conference of Israeli federations of experimental biology, Eilat, Israel, 2020
- Organizer and invited speaker in the 18th International p53 workshop, Rehovot, Israel, 2020 (postponed to 2022 due to COVID-19)
- 8th International Meet on Cancer & Radiology. Radiosensitization of Solid Metastatic Tumors Harboring Mutant p53 to Alpha-Particle Based Radiotherapy. 2021, Prague, converted to a virtual event.
- International Society of Extracellular Vesicles annual meeting, ISEV2021 virtual meeting. The mutant p53 protein is shuttled through extracellular vesicles. Based in Lyon, France, 2021
- ISCR Virtual Annual Meeting, Cancer Research 2021- nOvel Insights and Discoveries. Unique radiotherapy combination modalities based on preclinical cancer models. Israel, virtual event, 2021.

C. Contributions to Science

- Among the founding research and development team that invented diffusing alpha-emitters radiation therapy (DaRT), a unique brachytherapy approach currently in clinical trials for various solid metastatic cancers.
- Developed numerous combination modalities with DaRT, aiming to treat specific cancer types, such as glioblastoma (DaRT+Avastin).
- Revealed the molecular connection between mutant p53 gain-of-function proteins with NF- κ B in chronic inflammation conditions.
- The first to show that extracellular vesicles shed from tumor cells harboring mutant p53 can functionally control the tumor microenvironment.
- Among the first groups to show that mutant p53 proteins are packaged and shuttled via extracellular vesicles taken up by tumor microenvironment cells.
- Among the team who unraveled the lung cancer microbiome and found correlation with specific bacteria, smoking and TP53 mutations.

Complete list of publications:

1. Shalom-Feuerstein R, Cooks T, Raz A, Kloog Y. Galectin-3 regulates a molecular switch from N-Ras to K-Ras usage in human breast carcinoma cells. *Cancer Res.* 2005; 65(16): 7292-300.
2. Arazi L, Cooks T, Schmidt M, Keisari Y, Kelson I. Treatment of solid tumours by interstitial release of recoiling short-lived alpha emitters. *Phys. Med. Biol.* 2007; 52 5025-5042.
3. Cooks T, Arazi L, Schmidt M, Marshak G, Kelson I, Keisari Y. Growth retardation and destruction of experimental Squamous cell carcinoma by interstitial radioactive wires releasing diffusing alpha-emitting atoms. *Int J Cancer.* 2008; 122(7):1657-64.
4. Cooks T, Arazi L, Efrati M, Schmidt M, Marshak, G, Kelson I, Keisari Y. Treatment with interstitial wires releasing diffusing alpha-emitting atoms in combination with chemotherapy improved local tumor control and survival in squamous cell carcinoma bearing mice. *Cancer* 2009;115(8):1791-1801.
5. Cooks T, Schmidt M, Bittan H, Lazarov E, Arazi L, Kelson I, Keisari Y. Local control of lung derived tumors by diffusing alpha-emitting atoms released from intratumoral wires loaded with Radium-224. *Int J Radiat Oncol Biol Phys.* 2009; 74(3):966-73.
6. Arazi L, Cooks T, Schmidt M, Keisari Y, Kelson I. The treatment of solid tumors by alpha emitters released from (224)Ra-loaded sources-internal dosimetry analysis. *Phys Med Biol.* 2010; 55(4):1203-18.
7. Lazarov E, Arazi L, Cooks T, Schmidt M, Keisari Y, Kelson I. Comparative in vitro microdosimetric study of murine and human-derived cancer cells exposed to alpha particles. *Rad Res.* 2012; 177(3):280-7.
8. Horev-Droroi G, Cooks T, Bittan H, Lazarov E, Schmidt M, Arazi L, Efrati M, Kelson I, Keisari Y. Local control of experimental malignant pancreatic tumors by treatment with a combination of chemotherapy and intratumoral 224Radium-loaded wires releasing alpha-emitting atoms. *Translat. Res.* 2012; 159(1):32-41.
9. Cooks T, Tal M, Raab S, Efrati M, Reitkopf S, Lazarov E, Etzyoni R, Schmidt M, Arazi L, Kelson I, Keisari Y. Intratumoral 224Ra-Loaded Wires Spread Alpha-Emitters Inside Solid Human Tumors in Athymic Mice Achieving Tumor Control. *Anticancer Res.* 2012; 32(12):5315-21.
10. Cooks T, Pateras IS, Tarcic O, Solomon H, Schetter AJ, Wilder S, Lozano GC, Pikarsky E, Forshew T, Rosenfeld N, Harpaz N, Itzkowitz S, Harris CC, Rotter V, Gorgoulis VG, Oren M. Mutant

p53 Prolongs NF- κ B Activation and Promotes Chronic Inflammation and Inflammation-Associated Colorectal Cancer. *Cancer Cell*. 2013; 23(5):634-46.

11. Reitkopf-Brodutch S1, Confino H, Schmidt M, Cooks T, Efrati M, Arazi L, Rath-Wolfson L, Marshak G, Kelson I, Keisari Y. Ablation of experimental colon cancer by intratumoral ²²⁴Radium-loaded wires is mediated by alpha particles released from atoms which spread in the tumor and can be augmented by chemotherapy. *Int J Radiat Biol* 2015; 91(2):179-86.
12. Tarcic O, Pateras IS, Cooks T, Shema E, Kanterman J, Ashkenazi H, Boocholez H, Hubert A, Rotkopf R, Baniyash M, Pikarsky E, Gorgoulis VG, Oren M. RNF20 Links Histone H2B Ubiquitylation with Inflammation and Inflammation-Associated Cancer. *Cell Rep*. 2016;14(6):1462-76.
13. Solomon H, Dinowitz N, Pateras IS, Cooks T, Shetzer Y, Molchadsky A, Charni M, Rabani S, Koifman G, Tarcic O, Porat Z, Kogan-Sakin I, Goldfinger N, Oren M, Harris CC, Gorgoulis VG, Rotter V. Mutant p53 gain of function underlies high expression levels of colorectal cancer stem cells markers. *Oncogene* 2018. doi: 10.1038/s41388-017-0060-8.
14. Cooks T, Pateras IS, Jenkins LM, Patel KM, Robles AI, Morris J, Forshew T, Appella E, Gorgoulis VG, Harris CC. Mutant p53 cancers reprogram tumor associated macrophages via exosomal miR-1246. *Nature Comm*. 2018;9(1):771. doi: 10.1038/s41467-018-03224-w.
15. Greathouse LK, White JR, Vargas AJ, Bliskovsky VV, Beck JA, Von Muhlinen N, Polley E, Bowman ED, Robles AI, Khan MA, Robles AI, Cooks T, Ryan BM, Dzutsev AH, Trinchieri G, Pineda MA, Bilke S, Meltzer PS, Hokenstad AN, Stickrod TM, Walther-Antonio MR, Earl JP, Mell JC, Krol JE, Balashov SV, Bhat AS, Ehrlich GD, Valm A, Deming C, Conlan S, Oh J, Segre JA, Harris CC. Microbiome-TP53 Gene Interaction in Human Lung Cancer. *Genome Biol*. 2018;19(1):123. doi: 10.1186/s13059-018-1501-6.
16. Bhatta B, Luz I, Krueger C, Teo FX, Lane DP, Sabapathy K, Cooks T. Cancer Cells Shuttle Extracellular Vesicles Containing Oncogenic Mutant p53 Proteins to the Tumor Microenvironment. *Cancers (Basel)*. 2021 Jun 15;13(12):2985.
17. Cooks T, Puzis R, Cohen O. Tissue resilience: lessons from social resilience: Social sciences research on community resilience could inspire biology to understand homeostasis. *EMBO Rep*. 2021 Aug 4;22(8): e52926.

Reviews/news and views

1. Oren M, Cooks T. NF κ B and p53: A life and death affair. *Cell Cycle*. 2010; 9(6).
2. Cooks T, Oren M, Harris CC. Caught in the cross fire: p53 in inflammation. *Carcinogenesis*. 35:1680-90, 2014.
3. Cooks T, Harris CC. p53 mutations and inflammation-associated cancer are linked through TNF signaling. *Mol Cell*. 2014;56(5):611-2.
4. Cooks T, Pateras IS, Gorgoulis VG. When mutant p53 fires up. *Cancer cell & Microen*. 1: e135, 2014.
5. Myrianthopoulos V, Evangelou K, Vasileiou PVS, Cooks T, Vassilakopoulos TP, Pangalis GA, Kouloukoussa M, Kittas C, Georgakilas AG, Gorgoulis VG. Senescence and senotherapeutics: a new field in cancer therapy. *Pharmacol Ther*. 2018 Aug 16. pii: S0163-7258(18)30144-X. doi: 10.1016/j.pharmthera.2018.08.006.
6. Luz I, Cooks T. Extracellular vesicles: what secrets do they hold inside? *Cell Death Dis*. 2019; 10(6):406. doi: 10.1038/s41419-019-1643-9.
7. Pateras IS, Cooks T. Determination of Polarization of Resident Macrophages and Their Effect on the Tumor Microenvironment. *Methods Mol Biol*. 2019; 1928:101-112. doi: 10.1007/978-1-4939-9027-6_7.
8. Azulay EE, Cooks T, Elkabets M. Potential oncogenic roles of mutant-p53-derived exosomes in the tumor-host interaction of head and neck cancers. *Cancer Immunol Immunother*. 2020 doi: 10.1007/s00262-019-02450-5.
9. Bhatta B, Cooks T. Reshaping the tumor microenvironment: extracellular vesicles as messengers of cancer cells. *Carcinogenesis*. 2020; 41(11):1461-1470.

D. Mentorship and Other Intellectual Contributions

- Direct mentorship for 4 Ph.D. students and 3 M.Sc. students.

- 2021: Guest editor in Frontiers Cell and Developmental Biology journal in a special issue: infectious diseases and cancer
- 2020: Guest editor in Frontiers Cell and Developmental Biology journal in a special issue: Reprogramming Stromal Cells in Chronic Inflammation and Cancer
- 2020: Handling editor for the journal Frontiers in Oncology
- 2020: Associate editor for the journal Frontiers in Immunology
- 2018-present: Scientific board member for the journal Carcinogenesis.
- Ad-hoc reviewer for the following journals: Carcinogenesis, Scientific reports, Frontiers in Immunology Nature Communications, Cancer cell, Cell Reports, Cancer research, Frontiers in cell and developmental Biology, Frontiers in Oncology, PNAS, FEBS letters, Cancer Microenvironment, British Journal of cancer, Journal of Controlled Release, Molecular Therapy-Nucleic Acids.