

BIOGRAPHICAL SKETCH

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NAME: Osipov, Arsen, M.D.

eRA COMMONS USER NAME (credential, e.g., agency login): AOSIPOV1

POSITION TITLE: Assistant Professor, Gastrointestinal Medical Oncologist

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

| INSTITUTION AND LOCATION | DEGREE (if applicable) | Completion Date MM/YYYY | FIELD OF STUDY |
|--|---------------------------|----------------------------|--------------------------------------|
| University of California, San Diego, La Jolla, CA | B.S | 06/2008 | Biochemistry and Cell Biology |
| University of California, San Diego, La Jolla, CA | B.A | 06/2008 | History |
| Virginia Commonwealth University School of Medicine, Richmond, VA | M.D | 06/2013 | Medicine |
| Cedars Sinai Medical Center & WLA Veterans Hospital, Los Angeles, CA | Resident | 06/2016 | Internal Medicine Residency Training |
| Cedars Sinai Medical Center & WLA Veterans Hospital, Los Angeles, CA | Chief Resident | 06/2017 | Internal Medicine |
| Johns Hopkins University School of Medicine, Baltimore, MD | Fellow | 06/2019 | Medical Oncology Fellowship Training |
| Johns Hopkins University School of Medicine, Baltimore, MD | Chief Fellow | 06/2020 | Medical Oncology |

A. Personal Statement

I am currently an assistant professor, gastrointestinal medical oncologist and pancreas cancer translational investigator at Cedars-Sinai. I am also currently an adjunct assistant professor at Johns Hopkins University (JHU) and health sciences assistant clinical professor at UCLA. My focus is on elucidating the innerworkings of the tumor microenvironment (TME), stroma and immune milieu of pancreatic cancer with the hope of unlocking novel therapeutic strategies and making a significant impact on patient outcomes. I am specifically investigating novel targets and a master regulator of the TME, focal adhesion kinase (FAK), in the context of understanding the role of immunotherapy and mechanisms of immune resistance and response mediated by the stroma and TME. I have developed an expertise and further advanced the novel multiplex IHC technique, with the development of a FAK and stroma focused biomarker panel for comprehensive immune and stromal analysis. This method is novel in that it allows for sequential staining of up to 24 biomarkers on a single tissue slide, and utilizes a digital platform for full tissue quantitative and topographic marker/cell phenotype analysis. I have also conducted and overseen extensive preclinical work assessing the stromal and TME implications of FAK inhibition in murine PDAC models. I have developed a novel investigator initiated translational clinical trial which uses a sequential combinatorial therapeutic strategy targeting the TME via FAK inhibition in order

overcome resistance to immunotherapy and enhance anti-tumor immune response with the goal of leading to improved clinical outcomes in patients with PDAC. My overarching goal is to develop an independent pancreas cancer research program, utilizing innovative translational approaches with the hope of making a meaningful impact for patients with pancreatic cancer.

B. Positions and Honors

Positions and Employment

2004-2008 Research Assistant, Cellular and Molecular Medicine, UCSD, La Jolla, CA
2008-2009 Biotechnology Engineer, Baxter Bioscience, Los Angeles, CA
2010 International Healthcare Worker/Medical Aid, Nogorno-Karabakh, Armenia
2010 Research Assistant, Department of Neurosurgery, Cedars-Sinai Medical Center, Los Angeles, CA
2013-2017 Research Associate, Co-Investigator, GI Oncology Group, Samuel Oschin Cancer Center, Cedars- Sinai Medical Center, Los Angeles, CA
2016-2017 Chief Medical Resident, Department of Medicine, Cedars-Sinai Medical Center & WLA Veterans Affairs Hospital, Los Angeles, CA
2017-2019 Clinical and Research Fellow, Johns Hopkins University, Baltimore, MD
2019-2020 Chief Clinical and Research Fellow, Johns Hopkins University, Baltimore, MD
2020- Assistant Professor, GI Medical Oncologist, Cedars-Sinai Medical Center, Los Angeles, CA
2020- Adjunct Assistant Professor, Department of Oncology, Johns Hopkins University, Baltimore, MD
2021 Health Sciences Assistant Professor Step II, David Geffen School of Medicine, UCLA, Los Angeles, CA.

Other Experience and Professional Memberships

2009- Member, American Medical Association
2013- Member, American College of Physicians
2015- Member, American Society of Clinical Oncology (ASCO)
2016-2017 Leader, Journal Club, Department of Medicine, CSMC
2016-2017 Advisor, Governor's Advisory Council of the American College of Physicians Southern California Region 1
2018- Member, American Association of Cancer Research (AACR)
2018- Member, Society for Immunotherapy of Cancer (SITC)
2018 Selected Participant, AACR, Methods in Clinical Cancer Research Workshop, Vail, Colorado
2019- Member, American Pancreatic Association (APA)
2019-2020 Member, Fellowship Executive Committee, Johns Hopkins University
2019- Pancreas Club
2020- Core Faculty, Hematology Oncology Fellowship Program Cedars-Sinai
2021 Leader of Pancreas Multidisciplinary Program and Precision Medicine Program

Honors

2005-2008 UCSD Provost's Academic Honors 2005-2008
2009 Baxter Bioscience Distinguished Award for Fractionation 2009 Shutdown Protocol Project
2009-2013 VCU Dean's Merit Scholarship
2014 Resident of the Year, Saban Community Clinic
2015 Leo Rigler Award for Academic Achievement "Resident of the year" CSMC
2015 Finalist for Rubenstein Award in excellence for resident research CSMC
2016 Leo Rigler Award for Academic Achievement "Resident of the year" CSMC
2016 PHASE ONE Young Investigator Award for Cancer Translation
2018 ASCO Conquer Cancer Foundation, Young Investigator Award
2019-2020 Selected for Endowed Position as the Linda Rubin Fellow in Pancreas Oncology
2021 ASCO Conquer Cancer Foundation, Career Development Award
2021 Clinical Scholars Grant, Cedars-Sinai Medical Center

C. Contributions to Science

1. **Biology of Nutritional Status and Cachexia in Pancreatic Cancer**

My primary research focus has been on pancreatic cancer. Through collaborative efforts, our team at Cedars-Sinai have contributed by showing the prognostic value of nutritional status in pancreatic cancer. Our team focused on the significance of cachexia, how it was treated, and whether diagnosis or medical treatment impacted clinical outcomes in pancreatic cancer. We also investigated the role of nutritional perioperative factors, such as BMI and albumin in resected pancreatic cancer patients.

- a. Hendifar A, **Osipov A**, Khanuja J, Nissen N, Naziri J, Yang W, Li Q, Tuli R. Influence of Body Mass Index and Albumin on Perioperative Morbidity and Clinical Outcomes in Resected Pancreatic Adenocarcinoma. *PLoS One*. 2016 Mar 25;11(3):e0152172. PMID: PMC4807776.

2. **Role of Adjuvant Chemoradiotherapy in Pancreatic Cancer**

Our team also made significant contributions in understanding the role of adjuvant chemoradiotherapy in the treatment of pancreatic ductal adenocarcinoma. I designed the clinical and genomic database for pancreas cancer at Cedars-Sinai Oncology. Through multidisciplinary efforts our team at Cedars-Sinai investigated the prognostic implications of comprehensive lymph node evaluation as well as surgical margin clearance in patients with resected pancreatic adenocarcinoma; in order to assess the potential impact on clinical outcomes and their role in better defining the subset of resected patients who would benefit most from adjuvant chemoradiotherapy. I designed a follow-up archival study and developed a standardized methodology to reassess resection margins. The findings of these studies have the potential to influence the treatment decisions particularly involving adjuvant radiation therapy.

- a. **Osipov A**, Naziri J, Hendifar A, Dhall D, Rutgers JK, Chopra S, Li Q, Tighiouart M, Annamalai A, Nissen NN, Tuli R. Impact of margin status and lymphadenectomy on clinical outcomes in resected pancreatic adenocarcinoma: implications for adjuvant radiotherapy. *J Gastrointest Oncol*. 2016 Apr;7(2):239-47. PMID: PMC4783734
- b. **Osipov A**, Nissen N, Rutgers J, Dhall D, Naziri J, Chopra S, Li Q, Hendifar AE, Tuli R. Redefining the Positive Margin in Pancreatic Cancer: Impact on Patterns of Failure, Long-Term Survival and Adjuvant Therapy. *Ann Surg Oncol*. 2017 Nov;24(12):3674-3682. doi: 10.1245/s10434-017-6076-z. Epub 2017 Sep 5.

3. **DNA Repair and Mutational Burden in Pancreatic Cancer and Other Malignancies**

Our team has also contributed by revealing the role and implications of genetic mutations within pancreatic ductal adenocarcinoma and how mutations in DNA repair pathway genes may lead to increased sensitivity to combination chemoradiotherapy with PARP inhibition. We have also contributed by elucidating the relationship of biomarkers of nonsynonymous mutations such as TMB and with the clinical response and toxicity of all checkpoint inhibitors across PDAC, as well as all major tumor types.

- a. Tuli R, Shiao SL, Nissen N, Tighiouart, M Kim S, **Osipov A**, Bryant M, Ristow L, Placencio-Hickok VR, Hoffman D, Rokhsar S, Scher K, Klempner SJ, Noe P, Davis MJ, Wachsman A, Lo S, Jamil L, Sandler H, Piantadosi S, Hendifar A. A phase 1 study of veliparib, a PARP-1/2 inhibitor, with gemcitabine and radiotherapy in locally advanced pancreatic cancer. *EBioMedicine*. 2019;40:375–381. doi:10.1016/j.ebiom.2018.12.060. PMID: PMC6412162
- b. **Osipov A**, Lim SJ, Popovic A, Azad NS, Laheru DA, Zheng L, Jaffee EM, Wang H, Yarchoan M. Tumor Mutational Burden, Toxicity, and Response of Immune Checkpoint Inhibitors Targeting PD(L)1, CTLA-4, and Combination: A Meta-regression Analysis. *Clin Cancer Res*. 2020 Sep 15;26(18):4842-4851. doi: 10.1158/1078-0432.CCR-20-0458. Epub 2020 Jun 25. PMID: 32586938; PMID: PMC7501151.

4. **Evaluating and Targeting the TME and Stroma in Pancreatic Cancer**

My current contribution is in investigating the role of the stroma and TME in immune escape and how modulation of the TME can potentially sensitize pancreatic cancer to immunotherapy. Our team has developed a clinical trial to investigate the combination of immune TME and stromal modulator, focal adhesion kinase inhibitor (FAKi) with immunotherapy for patients with high risk pancreatic cancer and will

investigate the clinical and biologic implications of such therapies. Our lab has further created and validated a FAK specific multiplex panel. I am also investigating the role of FAK inhibition as an immunomodulator and sensitizer for radiation therapy in PDAC, as well as other mechanisms of immunotherapy sensitization.

- a. **Osipov A**, Saung MT, Zheng L, Murphy AG, Small Molecule Immunomodulation: The Tumor Microenvironment and Overcoming Immune Escape. *Journal of Immunotherapy of Cancer*, 7(1):224. Aug 22, 2019. PMID: PMC6704558
- b. **Osipov A**, Murphy AG, Zheng L. From Immune Checkpoints to Vaccines: The Past, Present and Future of Cancer Immunotherapy, *Advances in Cancer Research: Immunotherapy of Cancer*. Elsevier Science Publishing. 2019.
- c. **Osipov A**, Wang J, Li S, Choi D, Henderson M, Pachter J, Lee J, Maneval D, Zheng L, Blair A. PEGylated recombinant human hyaluronidase, PEGPH20, significantly enhances the anti-tumor activity of the combination of focal adhesion kinase inhibitor and anti-PD-1 antibody by targeting CXCR4-expressing myeloid cells in a murine model of PDAC, AACR 2020, Abstract 1588
- d. Zheng L, Ding D, Edil BH, Judkins C, Durham JN, Thomas DL 2nd, Bever KM, Mo G, Solt SE, Hoare JA, Bhattacharya R, Zhu Q, **Osipov A**, Onner B, Purtell KA, Cai H, Parkinson R, Hacker-Prietz A, Herman JM, Le DT, Azad NS, De Jesus-Acosta AMC, Blair AB, Kim V, Soares KC, Manos L, Cameron JL, Makary MA, Weiss MJ, Schulick RD, He J, Wolfgang CL, Thompson ED, Anders RA, Sugar E, Jaffee EM, Laheru DA. Vaccine-Induced Intratumoral Lymphoid Aggregates Correlate with Survival Following Treatment with a Neoadjuvant and Adjuvant Vaccine in Patients with Resectable Pancreatic Adenocarcinoma. *Clin Cancer Res*. 2020 Dec 4. PMID: 33277370.
- e. Hayashi K, Nikolos F, Lee YC, Jain A, Tsouko E, Gao H, Kasabyan A, Leung HE, **Osipov A**, Jung SY, Kurtova AV, Chan KS. Tipping the immunostimulatory and inhibitory DAMP balance to harness immunogenic cell death. *Nat Commun*. 2020 Dec 7;11(1):6299. doi: 10.1038/s41467-020-19970-9; PMID: PMC7721802.
- f. **Osipov A**, Blair A, Liberto J, Wang J, Li K, Herbst B, Xu Y, Li S, Niu N, Rashid R, Ding D, Liu Y, Wang Z, Wolfgang C, Burkhart R, Laheru D, Zheng L. Inhibition of Focal Adhesion Kinase Enhances Antitumor Response of Radiation Therapy in Pancreatic Cancer Through CD8 T Cells. *Cancer Biol Med* 2021. doi: 10.20892/j.issn.2095-3941.2020.0273 PMID: PMC787717.

Complete List of Published Work in My Bibliography:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=osipov%2C+arsen>

D. Additional Information: Research Support and/or Scholastic Performance

Current Research Support

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| <p>ASCO Conquer Cancer Foundation, Career Development Award Title: Manipulating the Tumor Microenvironment by FAK Inhibition to Enhance the Anti-tumor Immune Response to Anti-PD-1 Therapy Sponsor: ASCO-Conquer Cancer Foundation Total direct costs \$200,000 Role: Awarded, Principal Investigator, Arsen Osipov, MD</p> | <p>Osipov (PI)</p> | <p>07/2029 - 06/2024</p> |
| <p>K08 CA259456-01 Targeting the Stroma for Pancreatic Cancer Treatment Sponsor: NIH/NCI Total direct costs 1,220,885 Role: Awarded, Principal Investigator, Arsen Osipov, MD</p> | <p>Osipov (PI)</p> | <p>04/2021 - 03/2026</p> |
| <p>Precision Platform for Pancreatic Cancer Response Prediction Sponsor: Cedars Sinai Clinical Scholars Total direct costs: \$30,000 Role: Awarded, Principal Investigator, Arsen Osipov, MD</p> | <p>Osipov (PI)</p> | <p>08/2021 - 08/2023</p> |

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|---|-------------|-------------------|
| UL1TR001881 | Osipov (PI) | 09/2020 - 07/2021 |
| CTSI Core Voucher Award, Cedars-Sinai/UCLA | | |
| Title: Exploring the Role of Focal Adhesion Kinase in Pancreatic Cancer | | |
| Role: Awarded, Principal Investigator | | |
| Direct Costs Awarded: \$10,000 | | |

Completed Research Support

| | | |
|---|-------------|-------------------|
| ASCO Conquer Cancer Foundation, Young Investigator Award | Osipov (PI) | 07/2019 - 06/2020 |
| Title: Dissecting the Tumor Microenvironment of Pancreatic Cancer: Mechanisms of Potentiation of Anti-PD1 Therapy by Targeting Focal Adhesion Kinase Through a Neoadjuvant Approach | | |
| Role: Principal Investigator | | |

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|--|-------------|-------------------|
| Linda Ruben Fellowship in Pancreatic Cancer Research | Osipov (PI) | 07/2019 - 06/2020 |
| Role: Awarded and Appointed | | |

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| NIH T32 | Armanios (PI) | 07/2018 -06/2019 |
| Molecular Targets for Cancer Detection and Treatment | | |
| Grant #: 5T32CA009071-38 | | |
| Role: Awarded and Appointed | | |