BIOGRAPHICAL SKETCH

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NAME: Hendifar, Andrew Eugene

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

POSITION TITLE: Assistant Professor of Medicine. Medical Director, Pancreas Oncology

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Maryland	B.S., B.A.	05/1998	Biochemistry and Philosophy
Tulane University	M.D., M.P.H.	05/2003	Medicine and Public Health
University of Southern California	Residency and Fellowship	05/2010	Internal Medicine and Hematology/Oncology

A. Personal Statement

Since joining the Gastrointestinal Disease Program at Cedars-Sinai, my career has been focused on improving the medical treatment of pancreatic cancer. I am convinced that a better understanding of the underlying biology of these tumors will lead to better therapies. We have investigated several novel targeted therapies in pancreatic cancers and I am currently helping to develop stromal therapies and other agents that target onco-inflammation. My immediate goals are to improve the survival of pancreatic cancer patients by investigating the biology of pancreatic cancer cachexia, optimizing supportive care measures and developing novel therapeutic strategies.

B. Positions and Honors

1998	University of Maryland Honors Citation
1999	Aron's MD/MPH Scholars Award: A Scholarship Awarded for Master of Public Health
2003	American Federation for Medical Research Student Recognition Award
2005	First Prize; American College of Physicians Regional Associate Abstract Competition
2006	Brautbauer Teaching Award
2006 – 2007	Chief Resident, Department of Medicine, University of Southern California
2007 – 2010	Chief Fellow, Hematology and Oncology, University of Southern California
2010	Top Doctors
2010 – 2012	Primary Investigator, Sarcoma Oncology Center
2012 – present	Assistant Professor of Medicine, David Geffen School of Medicine, Cedars-Sinai Medical Center
2012 – present	Member, Multi-Disciplinary Pancreatic Cancer Team
2013 – present	Super Doctors
2013 – present	Member, Pancreatic Cancer Research Team
2014 – 2017	Member, Pharmacy and Therapeutics Committee
2014 – present	Member, Cancer Committee
2014 – present	Member, Gastrointestinal Cancer Committee, SWOG
2014 – present	Member, PAR-14-242 Microflora & GI Cancer Committee
2014 – present	Lead, Gastrointestinal Oncology Algorithm Development
2016 – present	Lead, Gastrointestinal Disease Research Group
2016 – present	Medical Director, Pancreatic Cancer, Cedars-Sinai Medical Center
2016 – present	Member, End of Life Committee
2016 – present	Member, Diabetes Mellitus Chronic Pancreatitis Pancreatic Ductal Adenocarcinoma (DM CP PDAC) Working Group, Consortium for the Study of Chronic Pancreatitis, Diabetes, and Pancreatic Cancer (CPDPC)
2016 – present	Supportive Care Medicine Chair, Precision Promise Consortium, Pancreatic Cancer Action Network

2016 – present Primary Investigator, Precision Promise[SM] Clinical Trial Consortium Site, Samuel Oschin Comprehensive Cancer Center, Cedars-Sinai Medical Center
2018 – present Steering Committee Member, Precision Promise[SM] Clinical Trial Consortium
2018 – present Member, Neuroendocrine Tumors Task Force (NET TF) of the NCI Gastrointestinal Steering Committee
2019 Scientific Advisory Committee (SAC) for MK7339-002: A Phase 2 Study of Olaparib Monotherapy in Participants with Previously Treated, Homologous Recombination Repair Mutation (HRRm) or Homologous Recombination Deficiency (HRD) Positive Advanced Cancer
2019 Member, Center for Integrated Research on Cancer and Lifestyle (CIRCL)

C. Contribution to Science

1. Treatment and Underlying Mechanisms of Pancreatic Cancer Cachexia

My current focus is exploring the mechanisms and therapies for pancreatic cancer cachexia. I have initiated the first prospective clinical trial of jejunal tube feedings with an elemental diet in this patient population, PANCAX-1. My intent is to characterize this weight loss and its response to optimal nutrition. We hope to answer the fundamental question of whether optimal treatments should include approaches that increase caloric intake. I also hope to define meaningful clinical end-points to provide the basis for successful research in this field. PANCAX-2, a novel approach to combine anti-cachectic agents with cytotoxic chemotherapy for patients with advanced pancreatic cancer, has been recently funded and will be initiated soon. PANCAX-3 is a protocol designed to establish the efficacy of pancreatic enzyme replacement therapy in advanced pancreatic cancer.

a. Tan CR, Yaffee PM, Jamil LH, Lo SK, Nissen N, Pandol SJ, Tuli R, **Hendifar AE**. Pancreatic cancer cachexia: a review of mechanisms and therapeutics. *Front Physiol*. 2014;Mar 3;5:88. doi: 10.3389/fphys.2014.00088. eCollection 2014. Review.
b. **Hendifar AE**, Tan CR, Yaffee P, Osipov A, Tuli R, Jeon C. Evaluating outcomes of pancreatic cancer patients with cachexia. *Clin Oncol*. 2014;32. (suppl; abstr e15208)
c. **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.
d. **Hendifar AE**, Chang JI, Huang BZ, Tuli R, Wu BU. Cachexia, and not obesity, prior to pancreatic cancer diagnosis worsens survival and is negated by chemotherapy. *J Gastrointest Oncol*. http://jgo.amegroups.com/article/view/17616.

2. Exploring Targeted Approaches to Advanced Pancreatic Cancer

Despite advances in systemic therapy, the five-year survival of advanced pancreatic cancer patients is less than 1%. The International Cancer Genome Consortium and other investigators have further characterized the genetic alterations associated with pancreatic cancer development. As a result of this new understanding, several novel therapeutic approaches are being investigated. In collaboration with the Know Your Tumor Program through the Pancreatic Cancer Action Network, we have identified several promising approaches. For example, BRCA mutations, both germ line and somatic, accounts for 5-10% of all pancreatic cancer cases. I have participated in several clinical trials using parp inhibitors as therapies in relapsed patients as well as a maintenance therapy. We have also supported all Southwest Oncology Group efforts in the treatment of pancreatic cancer and have positions in the Gastrointestinal Disease Research Group.

a. Iriana S, Ahmed S, Gong J, Annamalai AA, Tuli R, **Hendifar AE**. Targeting mTOR in pancreatic ductal adenocarcinoma. *Front Oncol*. 2016;Apr 25;6:99. doi: 10.3389/fonc.2016.00099.
b. Chung V, McDonough S, Philip PA, Cardin D, Wang-Gillam A, Hui L, Tejani MA, Seery TE, Dy IA, Al Baghdadi T, **Hendifar AE**, Doyle LA, Lowy AM, Guthrie KA, Blanke CD, Hochster HS. Effect of selumetinib and MK-2206 vs oxaliplatin and fluorouracil in patients with metastatic pancreatic cancer after prior therapy: SWOG S1115 Study Randomized Clinical Trial. *JAMA Oncol*. 2016 Dec 15.
c. Pishvaian MJ, Bender RJ, Matrisian LM, Rahib L, **Hendifar A**, Hoos WA, Mikhail S, Chung V, Picozzi V, Heartwell C, Mason K, Varieur K, Aberra M, Madhavan S, Petricoin E 3rd, Brody JR. A pilot study evaluating concordance between blood-based and patient-matched tumor molecular testing within pancreatic cancer patients participating in the Know Your Tumor (KYT*). Oncotarget*. 2016 Nov 8.

d. Singhi AD, Ali SM, Lacy J, **Hendifar A**, Nguyen K, Koo J, Chung JH, Greenbowe J, Ross JS, Nikiforova MN, Zeh HJ, Sarkaria IS, Dasyam A, Bahary N. Identification of targetable ALK rearrangements in pancreatic ductal adenocarcinoma. *J Natl Compr Canc Netw*. 2017 May;15(5):555-562. PubMed PMID: 28476735.

3. Targeting the Pancreatic Cancer Microenvironment

Pancreatic ductal adenocarcinoma desmoplasia is a notorious barrier to effective therapy. Promising approaches include pegylated hyaluronidase and burton kinase inhibitors, both of which are being evaluated in phase 3 studies at our center. We are also evaluating tumor biopsies of 300-advanced pancreatic and lung cancer patients who have received chemotherapy. We hope to establish the prognostic and predictive significance of hyaluronan in pancreatic cancer. We are also developing the only stromal biomarker, currently in phase 3 investigations for this disease.

a. Hingorani SR, Zheng L, Bullock AJ, Seery TE, Harris WP, Sigal DS, Braiteh F, Ritch PS, Zalupski MM, Bahary N, Oberstein PE, Wang-Gillam A, Wu W, Chondros D, Jiang P, Khelifa S, Pu J, Aldrich C, **Hendifar AE**. HALO 202: Randomized phase II study of PEGPH20 plus nab-paclitaxel/gemcitabine versus nab-paclitaxel/gemcitabine in patients with untreated, metastatic pancreatic ductal adenocarcinoma. *J Clin Oncol*. 2017 Dec 12: JCO2017749564. doi: 10.1200/JCO.2017.74.9564. [Epub ahead of print]

4. Exploring Novel Approaches in Cancer Therapy

Exploiting genomic alterations and tumor characteristics are keys to successful targeted therapy. Over the last five years, I have helped develop several unique compounds and novel approaches that are effective in targeting the tumor tissue while avoiding harm to normal cells.

a. Leahy MG, Nguyen BB, Patel SR, Hohenberger P, Santoro A, Staddon AP, Penel N, Piperno-Neumann S, **Hendifar AE**, Lardelli P, Nieto A, Alfaro V, Chawla SP. Randomised phase III trial of trabectedin versus doxorubicin-based chemotherapy as first-line therapy in translocation-related sarcomas. *Eur J Cancer*. 2014;Apr;50(6):1137-47. doi: 10.1016/j.ejca.2014.01.012.
b. Chawla SP, Cranmer LD, Van Tine BA, Reed DR, Okuno SH, Butrynski JE, Adkins DR, **Hendifar AE**, Kroll S, Ganjoo KN. Phase II study of the safety and antitumor activity of the hypoxia-activated prodrug TH-302 in combination with doxorubicin in patients with advanced soft tissue sarcoma. *J Clin Oncol*. 2014;Oct 10;32(29):3299-306.
c. Chawla SP, Chua VS, **Hendifar AE**, Wieland DS, Quon DV, Soman N, Levitt DJ. A phase 1B/2 study of aldoxorubicin in patients with soft tissue sarcoma. *Cancer*. 2015;Feb 15;121(4):570-9.
d. Strosberg J, El-Haddad G, Wolin E, **Hendifar A**, Yao J, Chasen B, Mittra E, Kunz PL, Kulke MH, Jacene H, Bushnell D, O'Dorisio TM, Baum RP, Kulkarni HR, Caplin M, Lebtahi R, Hobday T, Delpassand E, Van Cutsem E, Benson A, Srirajaskanthan R, Pavel M, Mora J, Berlin J, Grande E, Reed N, Seregni E, Öberg K, Lopera Sierra M, Santoro P, Thevenet T, Erion JL, Ruszniewski P, Kwekkeboom D, Krenning E; NETTER-1 Trial Investigators. Phase 3 Trial of (177)Lu-Dotatate for Midgut Neuroendocrine Tumors. N Engl J Med. 2017 Jan 12;376(2):125-135. doi: 10.1056/NEJMoa1607427. PubMed PMID: 28076709.

D. Research Support

<u>Current Research Support</u>

Contract No.: AAA-III-01 Hendifar (PI) 02/12/2013 – 10/31/2019
Advanced Accelerator Applications
Title: A Multicenter, Stratified, Open Randomized, Comparator-controlled, Parallel Group Phase III Study Comparing Treatment with 177Lu-DOTA0-Tyr3-Octreotate to Octreotide LAR in Patients with Inoperable, Progressive, Somatostatin Receptor Positive, Midgut Carcinoid Tumours
Role: PI

Contract No.: 2012-PT023 Hendifar (PI) 02/05/2014 – 01/31/2019
XBiotech, USA, Inc.
Title: *A Pivotal Phase III, Monotherapy Study to Evaluate Survival Using MABp1 as a Monotherapy in Metastatic Colorectal Cancer Patients with Cachexia*
Role: PI

Contract No. IIT2014 Hendifar-PanCax Hendifar (PI) 04/27/2015 – 04/2019
Cedars Sinai Medical Center (UCLA CTSI)
Title: Enteral Feeding for Pancreatic Cancer Cachexia - A Longitudinal, Single Institution Study of Enteral Feeding in Advanced Pancreatic Cancer Patients (Treatment and Underlying Mechanisms of Pancreatic Cancer Cachexia)
Role: PI

Contract No.: 50-PDA, 150 LUNG Hendifar (PI) 05/21/2015 – 5/20/2019
Halozyme, Inc.
Title: Evaluation of Higher Hyaluronan (HA) in Human Tumor
Goal: To investigate the correlation of tumor associated HA and overall survival in clinically annotated baseline tumor tissue biopsies and an investigational IHC-like assay for HA in pancreatic, non-small cell lung cancer and small cell lung cancer.
Role: PI

1U01DK108314 Hendifar (Consultant) 09/01/2015 – 08/31/2020
National Institute of Health
Title: Pathophysiology, Epidemiology, and Prevention of Pancreatogenic Diabetes
Role: Other Significant Contributor: Consultant

Contract No.: EA2142 Hendifar (PI) 11/06/2015 – 01/01/2024
Alliance (Cooperative Group Study)
Title: Randomized Phase II Study of Cisplatin and Etoposide versus Temozolomide and Capecitabine in Patients with Advanced G3 Non-Small Cell Gastroenteropancreatic Neuroendocrine Carcinomas
Role: PI

Contract No.: PCYC-1137 Hendifar (PI) 04/20/2016 – 04/19/2019
Pharmacyclics
Title: A Randomized, Double-blind, Placebo-controlled, Phase 2/3 Study of Ibrutinib in Combo with Nab-paclitaxel and Gemcitabine vs. Placebo in Combo with Nab-paclitaxel and Gemcitabine, in the First Line Treatment of Metastatic Pancreatic Adenocarcinoma
Role: PI

Contract No.: MK-3475-158-00 Hendifar (PI) 06/16/2016 – 06/15/2019
Merck
Title: *A Clinical Trial of Pembrolizumab (MK-3475) Evaluating Predictive Biomarkers in Subjects with Advanced Solid Tumors (KEYNOTE 158)*
Role: PI

Contract No.: HALO-109-301 Hendifar (PI) 10/13/2016 – 10/12/2019
Halozyme, Inc.
Title: A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multicenter of PEGylated Recombinant Human Hyaluronidase (PEGPH20) in Combination with nab-Paclitaxel Plus Gemcitabine Compared with Placebo Plus nab-Paclitaxel and Gemcitabine in Subjects with Hyaluronan-High Stage IV Previously Untreated Pancreatic Ductal Adenocarcinoma
Role: PI

Contract No.: EA2161 Hendifar (PI) 02/01/2017 – 08/01/2019
Alliance (Cooperative Group Study)
Title: A Phase II Study of MLN0128 (TAK-228) in Rapalog-Resistant Advanced Pancreatic Neuroendocrine Tumors (PNET)
Role: PI

Contract No.: IIT-2016-01-Tuli-DURVARAD Hendifar (co-PI) 02/20/2017 – 02/19/2020
AstraZeneca
Title: A Phase 1/II Study of Durvalumab and Stereotactive Ablative Body Radiotherapy in Borderline Resectable and Locally Advanced Pancreatic Adenocarcinoma
Role: co-PI

Protocol No. 00049091 Hendifar (PI) 03/2017 – present
Pancreatic Cancer Action Network
Title: PancPROMIS
Role: PI

Contract No.: SCRX001-006 Hendifar (PI) 05/23/2017 – 05/22/2020
Stemcentrx, Inc.
Title: An Open-Label Study of Rovalpituzumab Tesirine in Subjects with Delta-Like Protein 3-Expressing Advanced Solid Tumors
Role: PI

Contract No.: IIT2016-07-Hendifar-OnFX Hendifar (PI) 06/26/2017 – 06/25/2020
Ipsen Pharmaceuticals
Title: Phase I Study of Onivyde (MM-398) and 5-Fluorouracil/Folinic Acid in Combination with Xilonix™ for Advanced Pancreatic Cancer Patients with Cachexia (ONFX)
Role: PI

Contract No. NA Hendifar (PI) 01/01/2018 – 12/31/2018
Cedars-Sinai Precision Health
Title: A Modified "Universal" Testing Algorithm to Improve the Delivery of Genetic Care to Patients and Families with Hereditary "High-Risk" Cancer Conditions
Role: PI

Contract No.: XmAb18087-01 Hendifar (PI) 03/2018 – 03/2021
Xencor, Inc.
Title: A Phase 1 Multiple Dose Study to Evaluate the Safety and Tolerability of XmAb®18087 in Subjects with Advanced Neuroendocrine and Gastrointestinal Stromal Tumors.
Role: PI

DoD CA170974 Hendifar (Consultant) 08/01/2018 – 07/31/2021
Department of Defense
Title: *Sensitization of Therapeutic-Resistant Pancreatic Cancer by Cancer Cell-Specific Drug Delivery*
Role: Consultant