

BIOGRAPHICAL SKETCH

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NAME: Adam Charles Yopp

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

POSITION TITLE: Associate Professor of Surgery, Division of Surgical Oncology

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 |
|---|---------------------------|----------------------------|-----------------------|
| University of Wisconsin-Madison | B.S. | 06/1993 | Molecular Biology |
| St. George's University School of Medicine | M.D. | 06/2000 | Medicine |
| Mount Sinai School of Medicine, New York, NY | Postdoctoral | 07/2005 | Transplant Immunology |
| Maimonides Medical Center, Brooklyn, NY | Postdoctoral | 07/2007 | Surgery |
| Memorial Sloan Kettering Cancer Center | Postdoctoral | 07/2009 | Surgical Oncology |
| University of Texas Southwestern Medical School | M.S. | 12/2019 | Clinical Sciences |

A. Personal Statement

I am a hepatopancreaticobiliary surgical oncologist and the co-director of the UT Southwestern Liver Cancer Program with a primary clinical and research focus on the reduction of the racial/ethnic and socioeconomic disparities in patients newly diagnosed with hepatocellular cancer (HCC). I have a proven track record as an investigator with over 100 peer reviewed publications and countless podium presentations at national meetings. I have recently transitioned to the role of an independent investigator as evidenced by the receipt of DOD- and NIH-funded grants as a principal investigator and the mentoring of 4 surgical residents in their studies of cancer health care disparities. Specially the research project proposed through NIH Loan Repayment Program Award will encompass my NIMHD funded grant, 1R01MD0112565-01, aimed at identifying patient-, provider-, and system-level factors associated with racial/ethnic and socioeconomic disparities in HCC tumor stage, guideline concordant treatment, and overall survival. This study will provide an understanding of *why* HCC prognosis disparities exist and *at what level* interventions should be implemented to reduce disparities improving overall survival. The NIH Loan Repayment Program Award will make a significant impact on my career trajectory including the continuing evolution as an independent researcher by allowing me to continue to pursue the training activities and maintaining my focus on my career goals without the distraction of my substantial medical school loan burden. The current application builds logically on my prior work, particularly the publications listed below:

- Singal AG, **Yopp AC**. Hepatocellular carcinoma: How can we move from racial/ethnic disparities to a model of health equity. *Cancer* 2016 122(6): 2454-6.
- Mokdad AA, Zhu H, Marrero JA, Mansour JC, Singal AG, **Yopp AC**. Hospital volume and survival after hepatocellular carcinoma diagnosis. *Am J Gastroenterol* 2016 111(7): 967-75.
- Rich NE, Hester C, Odewole M, Murphy CC, Parikh ND, Marrero JA, Singal AG, **Yopp AC**. Racial and ethnic differences in presentation and outcomes of hepatocellular carcinoma. *Clin Gastroenterol Hepatol* 2018; doi: 10.1016/j.cgh.2018.05.039.
- Mokdad AA, Murphy CC, Pruitt SL, Mansour JC, Marrero JA, Singal AG, **Yopp AC**. Effect of hospital safety net designation on treatment use and survival in hepatocellular carcinoma. *Cancer* 2018 124(4):743-751.

B. Positions and Honors**Clinical Training**

2007-2009 Fellow, Surgical Oncology

Memorial Sloan Kettering Cancer Center, NY

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| 2001-2007 | Resident, General Surgery | Maimonides Medical Center, NY |
| 2000-2001 | Intern, General Surgery | Maimonides Medical Center, NY |

Laboratory Training

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| 2002-2005 | Postdoctoral fellow in transplant immunology with Jonathan S. Bromberg, MD, PhD, Professor of Surgery and Gene Therapy, Mount Sinai Medical Center, New York, NY. T cell migration and transplant tolerance secondary to immunomodulator therapy. | |
|-----------|---|--|

Professional Appointments

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|-----------|----------------------------------|--|
| 2017- | Chief, Section of HPB Surgery | University of Texas Southwestern, Dallas, TX |
| 2017- | Associate Professor of Surgery | University of Texas Southwestern, Dallas, TX |
| 2016- | Director, UTSW Biorepository | University of Texas Southwestern, Dallas, TX |
| 2009- | Co-Director, Liver Tumor Program | University of Texas Southwestern, Dallas, TX |
| 2009- | Associate Staff | UT Southwestern Medical Center-Clements |
| 2009- | Faculty | Parkland Memorial Hospital, Dallas, TX |
| 2009-2017 | Assistant Professor of Surgery | University of Texas Southwestern, Dallas, TX |

Other Experience and Professional Memberships

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|-------|---|
| 2007- | Member, Society of Surgical Oncology (SSO) |
| 2007- | Member, Americas Hepato-Pancreato-Biliary Association (AHBPA) |
| 2007- | Member, American Society of Clinical Oncology (ASCO) |
| 2007- | Member, International Liver Cancer Association (ILCA) |
| 2010- | Fellow, American College of Surgeons |
| 2013- | Editorial Board Member, Annals of Surgical Oncology |
| 2017- | Chairman, AHBPA Clinical Trials Committee |
| 2017- | Chairman, ILCA Education Committee |

Honors and Awards

| | |
|-----------|--|
| 2012-2018 | “Best Doctors in Dallas”, D Magazine |
| 2014 | Fischer Traveling Fellowship Award, Society of Surgery of the Alimentary Tract |
| 2011 | Faculty Teaching Award, UT Southwestern Medical Center, Dallas, TX |
| 2010 | AACR/ASCO Methods in Clinical Cancer Research, Vail, CO |
| 2007 | Chief Resident Teaching Award, Maimonides Medical Center, NY |
| 2005 | American College of Surgeons Research Fellowship Award |
| 2001 | Resident of Year Award, Maimonides Medical Center, NY |
| 2000 | Intern of the Year Award, Maimonides Medical Center, NY |

C. Contribution to Science

1. System- and patient-level factors and HCC prognosis. HCC has a high degree of heterogeneity with both tumor characteristics and underlying liver function determining appropriate treatment and thus overall outcomes. This heterogeneity leads to multiple different providers caring for newly diagnosed HCC patients. We have shown that outcomes can be improved through the implementation of system-level interventions including the initiation of a multidisciplinary HCC clinic and a voice messaging system where radiologic findings consistent with HCC are directly reported to the HCC providers. Patient-level factors including HCC tumor characteristics demonstrating an infiltrative radiographic pattern and vascular invasion portend worse HCC specific survival.

- a. Mokdad AA, Browning T, Mansour JC, Zhu H, Singal AG, **Yopp AC**. Implementation of a voice messaging system is associated with improved time-to-treatment and overall survival in patients with hepatocellular carcinoma. J Natl Compr Can Netw 2016 14(1): 38-46.
- b. **Yopp AC**, Mansour JC, Beg MS, Arenas J, Trimmer C, Reddick M, Pedrosa I, Khatri G, Yahoo T, Meyer JJ, Shaw J, Marrero JA, Singal AG. Establishment of a multidisciplinary hepatocellular clinic is associated with improved clinical outcome. Ann Surg Oncol 2014 21(4);1287-1295.
- c. **Yopp AC**, Mokdad AA, Zhu H, Mansour JC, Balch GC, Choti MA, Singal AG. Infiltrative hepatocellular carcinoma: national history and comparison with multifocal, nodular hepatocellular carcinoma. Ann Surg Oncol 2015 22(3): 1075-1082.

d. Mokdad AA, Singal AG, Marrero JA, Zhu H, **Yopp AC**. Vascular invasion and metastasis is predictive of outcome in Barcelona Clinic Liver Cancer stage C hepatocellular carcinoma. *J Natl Compr Canc Netw* 2017 15(2):197-204.

2. Surveillance and HCC. Currently less than 25% of patients with cirrhosis are currently undergoing surveillance ultrasonography and blood tests aimed at detecting HCC at an early stage where curative therapies are a possibility. The work by our group has determined both patient- and physician-derived factors associated with failure to obtain surveillance tests. We have demonstrated that lower rates of HCC surveillance are associated with racial and socioeconomic disparities. In addition, primary care physicians have misconceptions regarding tests to detect HCC.

- a. Singal AG, Marrero JA, **Yopp A**. Screening process failures for hepatocellular carcinoma. *JNCCN* 2014 12(3): 375-82.
- b. Dalton-Fitzgerald E, Tiro J, Kandunoori P, Halm EA, Singal AG, **Yopp A**. Practice patterns and attitudes of primary care providers and barriers to surveillance of hepatocellular carcinoma in patients with cirrhosis. *Clin Gastroenterol Hepatol* 2015 13(4): 791-8.
- c. Singal AG, Li X, Kandunoori P, Adams-Huet B, Nehra MS, **Yopp A**. Racial, social, and clinical determinants of hepatocellular surveillance. *Am J Med* 2015 128(1): 1-7.
- d. Singal AG, Waljee AK, Patel N, Chen EY, Tiro JA, Marrero JA, **Yopp AC**. Therapeutic delays lead to worse survival among patients with hepatocellular carcinoma. *J Natl Compr Canc Netw*. 2013 11(9):1101-8.

3. Biomarkers and upper gastrointestinal malignancies. I have a longstanding interest in the development of blood and radiologic based biomarkers as both prognostic and predictive biomarkers. As part of my clinical fellowship as a mentored investigator at Memorial Sloan Kettering Cancer Center I investigated predictive biomarkers of treatment response in patients with intrahepatic cholangiocarcinoma as part of phase II clinical trial. I demonstrated that tissue hypoxia biomarkers, HIF-1a and CAIX, correlated with DCE-MRI findings of treatment response and correlated to overall survival. In addition, we demonstrated that tumor expression of CXCR4 was correlated with survival measures in patients with colorectal liver metastases.

- a. **Yopp AC**, Schwartz LH, Kemeny N, Gultekin DH, Gonen M, Bamboat Z, Shia J, Haviland D, D'Angelica MI, Fong Y, Dematteo RP, Allen PJ, Jarnagin WR. Antiangiogenic therapy for primary liver cancer: correlation of changes in dynamic contrast-enhanced magnetic resonance imaging with tissue hypoxia markers and clinical response. *Ann Surg Oncol* 2011. 18:2192-9.
- b. Kemeny NE, Schwartz L, Gonen M, **Yopp AC**, Gultekin D, D'Angelica MI, Fong Y, Haviland D, Gerwitz AN, Allen PJ, Jarnagin WR. Treating primary liver cancer with hepatic arterial infusion of floxuridine and dexamethasone: does the addition of systemic bevacizumab improve results? *Oncology* 2011. 80:153-9.
- c. **Yopp AC**, Shia J, Butte JM, Allen PJ, Fong Y, Jarnagin WR, DeMatteo RP, D'Angelica MI. CXCR4 expression predicts patient outcome and recurrence patterns after hepatic resection for colorectal metastases. *Ann Surg Onc* 2012. 3:339-346.

4. Sphingosine 1-phosphate (S1P) and T cell migration. As a post-doctoral fellow in the lab of Jonathan Bromberg at Mount Sinai School of Medicine, I explored the mechanistic interplay between S1P and T cell migration in murine transplant models. Specifically we demonstrated that S1P activation enhances T cell migration to chemokine-chemokine receptors, CCR2, CCR5, CCR7, and CXCR4, through activation of the multidrug transporters, Abcb1 and Abcc1, and through 5-lipoxygenase activity. In addition, we demonstrated that S1P and chemokine receptor signaling are integrated within a T cell serving as the underlying premise for how naïve T cells enter and egress from peripheral lymphoid organs.

- a. **Yopp AC**, Fu S, Honig SM, Randolph GJ, and Bromberg JS. FTY720 enhanced T cell homing is dependent on CCR2, CCR5, CCR7, and CXCR4: evidence for distinct chemokine compartments. *J Immunol* . 2004. 173(2): 855-865.
- b. Honig SM, Fu S, Mao X, **Yopp AC**, Gunn MD, Randolph GJ, and Bromberg JS.

The goal of this study was to identify biomarkers associated with prognosis in HCC patients treated with bavituximab and sorafenib in a phase I/II clinical trial.

Role: PI

American Cancer Society
Early Development Award

Yopp (PI)

8/1/14-7/31/15

Genetic profiles of hepatocellular carcinoma by stage of tumor presentation

The goal of this study was to identify preliminary gene signatures in HCC patient derived tumors stratified by BCLC stage.

Role: PI

UTSW Medical Center, Department of Surgery
Discovery grant

Yopp (PI)

7/1/16-6/30/17

Patient-and system-based factors associated with racial/ethnic disparities in hepatocellular carcinoma

The goal of this study was to identify patient- and system-level factors associated with disparate survival in racial/ethnic minority patients with HCC.

Role: PI

Peregrine Pharmaceuticals

Yopp (PI)

7/1/10-12/30/17

Investigator initiated clinical trial

A phase I/II study of bavituximab and sorafenib in patients with advanced hepatocellular carcinoma.

The goal of this trial was to study the efficacy of a novel phosphatidylserine inhibitor combined with a multikinase inhibitor in patients with BCLC C HCC.

Role: PI

Novartis Pharmaceuticals

Yopp (PI)

2/1/15-1/31/18

Investigator initiated clinical trial

A phase II study of LEE011 and transarterial chemoembolization in patients with advanced HCC

The goal of this trial was to study the efficacy of combining locoregional TACE therapy with a novel CDK 4/6 inhibitor in patients with BCLC B HCC.

Role: PI