
BIOGRAPHICAL SKETCH

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NAME: Gregory N Gan

eRA COMMONS USER NAME: GAN.GREGORY

POSITION TITLE: Assistant Professor; Director of Basic Research for Section of Radiation Oncology

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Tufts University, Medford, MA	B.S.	05/1998	Biology
University of Pittsburgh SOM, Pittsburgh, PA	M.D.	05/2009	Medicine
University of Pittsburgh Graduate School, Pittsburgh, PA	Ph.D.	05/2009	Pharmacology
University of Pittsburgh Shadyside Hospital, Pittsburgh, PA	Intern	06/2010	Internal Medicine
University of Colorado, Aurora, CO	Residency	06/2014	Radiation Oncology
University of Colorado, Aurora, CO	Research	06/2014	Research Fellowship

A. Personal Statement

I am a Radiation Oncologist and physician-scientist with a research interest in tumor microenvironment, epithelial-to-mesenchymal transition (EMT) and radiation biology. I am pursuing translational research with the goal of developing novel treatment strategies for head and neck and thoracic cancers. We are testing the hypothesis that radiotherapy can up-regulate EMT which can lead to tumor repopulation, distant metastasis and overall treatment resistance. I am ideally suited to address this question because of my fellowship training and expertise in establishing head and neck cancer patient-derived tumor xenografts mouse models, developing a model for mouse head and neck irradiation, and evaluating tumor stem cell biology and its respective microenvironment. I am also interested in how radiotherapy (particularly high dose per fraction also known as stereotactic body radiotherapy) and EMT may affect local and distant control rates in both HPV positive and negative head and neck cancers and thoracic malignancies. I became interested in this area because local control and overall survival remain very poor for patients with HPV negative head and neck cancers. Insights gained from a better understanding of why these tumors fail locally and distantly can potentially improve outcomes.

1. **Gan GN**, Eagles J, Keysar SB, Wang G, Glogowska MJ, Altunbas C, Anderson RT, Le PN, Morton JJ, Frederick B, Raben D, Wang XJ, Jimeno A. Hedgehog signaling drives radioresistance and stroma-driven tumor repopulation in head and neck squamous cancers. *Cancer Res* 2014 Dec 1;74(23)
2. **Gan GN**, Altunbas C, Morton JJ, Eagles J, Backus J, Dzingle W, Raben D, Jimeno A. Radiation Dose Uncertainty and Correction for a Mouse Orthotopic and Xenograft Irradiation Model. *Int J Radiat Biol.* 2016 Jan; 92(1):50-6
3. Keysar SB, Le PN, Anderson R, Morton J, Paylor JJ, Astling D, Vogler B, Thornburn J, Fernandez P, Takimoto S, Sehrt D, **Gan GN**, Bowles D, Said S, Campbell V, Kutock J, Ross R, McGovern K, Thornburn A, Song J, Tan AC, Wang XJ, Jimeno A. The hedgehog pathway influences epidermal growth factor receptor (EGFR) signaling dependence and acquisition of resistance to anti-EGFR therapy in head and neck squamous cell cancer. *Cancer Res* 2013 Jun 1;73(11):3381-92
4. Anderson RT, Keysar S, Bowles D, Glogowska MJ, Astling DP, Morton JJ, Le P, Umpierrez A, Eagles Soukup J, **Gan G**, Vogler B, Sehrt D, Takimoto S, Wilhelm F, Frederick B, Varella-Garcia M, Tan AC, Jimeno A. The dual pathway inhibitor rigosertib is effective in direct-patient tumor xenografts of head and neck squamous cell carcinomas. *Mol Cancer Ther.* 2013 Oct; 12(10): 1994-2005

5. Morton JJ, Bird G, Keysar SB, Astling DP, Lyons TR, Anderson RT, Glogowska MJ, Estes P, Eagles JR, Le PN, **Gan G**, McGettigan B, Fernandez P, Padilla-Just N, Varella-Garcia M, Song JI, Bowles DW, Schedin P, Tan AC, Roop DR, Wang XJ, Refaeli Y, Jimeno A. XactMice: humanizing mouse bone marrow enables microenvironment reconstitution in a patient-derived xenograft model of head and neck cancer. *Oncogene*. 2015 Apr 20
6. **Gan GN**, Weickhardt AJ, Scheier B, Doebele RC, Gaspar LE, Kavanagh BD, Camidge DR. Stereotactic Radiotherapy Can Safely and Durably Control Sites of Extra-CNS Oligoprogressive Disease in ALK-Positive Lung Cancer Patients on Crizotinib. *Int J Radiat Oncol Biol Phys*. 2014 Mar 15;88(4):892-8

B. Positions and Honors

Positions and Employment

2014-Present	Assistant Professor, University of New Mexico Health Sciences Center, UNM Cancer Center, Section of Radiation Oncology
2013-2014	Chief Resident, Anschutz Cancer Center, Department of Radiation Oncology, University of Colorado Denver, Aurora, CO
2012-2014	Research Fellow, Anschutz Cancer Center, Department of Radiation Oncology, University of Colorado Denver, Aurora, CO
2010-2013	Resident, Anschutz Cancer Center, Department of Radiation Oncology, University of Colorado Denver, Aurora, CO
2009-2010	Intern, Shadyside- Presbyterian Hospital, Department of Medicine, University of Pittsburgh, Pittsburgh, PA

Other Experience and Professional Membership

2014-Present	Affiliate Member, American Society of Therapeutic Radiation Oncologists
2014-Present	Full Member, Radiological Society of North America
2014-Present	Full Member, American Association of Cancer Researchers
2009-early 2014	Member-in-Training, American Society of Therapeutic Radiation Oncologists
2007-Present	Member, American Medical Association

Awards and Honors

2014	Fellows Travel Grant Award Recipient, 2014 Multidisciplinary Head and Neck Cancer Symposium, Scottsdale, AZ
2013	ASTRO Resident/Fellow in Radiation Oncology Research Seed Grant Award Recipient
2013	Fellows Travel Grant Award Recipient, 13th Annual Targeted Therapies of Lung Cancer, Meeting, Santa Monica, CA
2012	Cancer League of Colorado Grant Award Recipient
2012	1st Place Radiation Physics Resident Award, ASTRO 53rd Annual Meeting, Miami, FL
2010	Intern of the Year 2009-2010, Shadyside Hospital Medicine Program, Pittsburgh, PA
2008	Inductee of the Arnold P. Gold Humanism Honor Society, Charles G. Watson Chapter, Pittsburgh, PA
2006	Eastman-Kodak Radiology Residents/Fellows Symposium Award Recipient, 3 rd Place, 104 th Annual NMA Conference, Dallas, TX

C. Contribution to Science

1. HPV negative head and neck cancer remains a scourge with poor local control and overall survival rates. A phenomenon known as accelerated tumor repopulation is thought to play role in local tumor failures. In recent years, scientists have identified a potential mechanism explaining why tumors may be failing locally and distantly and this process is known as epithelial-to-mesenchymal transition (EMT). The focus of my research (and the publications below) has been to elucidate how radiotherapy (and EGFR inhibition) activates the GLI1/Hedgehog pathway, up-regulates the EMT pathway and how EMT activation can lead to treatment resistance and tumor repopulation. The findings from this work demonstrate that activation of GLI1 and EMT play a role in tumor repopulation *in vivo* and may potentially explain why HPV negative

tumors have such a high local and distant failure rate. Our end goal will be to initiate a clinical study utilizing a Hedgehog pathway inhibitor combined with radiotherapy to try and improve tumor control rates. I served as the primary investigator or co-investigator in all of these studies.

- a. **Gan GN**, Eagles J, Keysar SB, Wang G, Glogowska MJ, Altunbas C, Anderson RT, Le PN, Morton JJ, Frederick B, Raben D, Wang XJ, Jimeno A. Hedgehog signaling drives radioresistance and stroma-driven tumor repopulation in head and neck squamous cancers. *Cancer Res* 2014 Dec 1;74(23)
 - b. **Gan GN**, Altunbas C, Morton JJ, Eagles J, Backus J, Dzingler W, Raben D, Jimeno A. Radiation Dose Uncertainty and Correction for a Mouse Orthotopic and Xenograft Irradiation Model. *Int J Radiat Biol.* 2016 Jan; 92(1):50-6
 - c. Anderson RT, Keysar S, Bowles D, Glogowska MJ, Astling DP, Morton JJ, Le P, Umpierrez A, Eagles Soukup J, **Gan G**, Vogler B, Sehr D, Takimoto S, Wilhelm F, Frederick B, Varella-Garcia M, Tan AC, Jimeno A. The dual pathway inhibitor rigosertib is effective in direct-patient tumor xenografts of head and neck squamous cell carcinomas. *Mol Cancer Ther.* 2013 Oct; 12(10): 1994-2005
 - d. Keysar SB, Le PN, Anderson R, Morton J, Paylor JJ, Astling D, Vogler B, Thornburn J, Fernandez P, Takimoto S, Sehr D, **Gan GN**, Bowles D, Said S, Campbell V, Kutock J, Ross R, McGovern K, Thornburn A, Song J, Tan AC, Wang XJ, Jimeno A. The hedgehog pathway influences epidermal growth factor receptor (EGFR) signaling dependence and acquisition of resistance to anti-EGFR therapy in head and neck squamous cell cancer. *Cancer Res* 2013 Jun 1;73(11):3381-92
 - e. Morton JJ, Bird G, Keysar SB, Astling DP, Lyons TR, Anderson RT, Glogowska MJ, Estes P, Eagles JR, Le PN, **Gan G**, McGettigan B, Fernandez P, Padilla-Just N, Varella-Garcia M, Song JI, Bowles DW, Schedin P, Tan AC, Roop DR, Wang XJ, Refaeli Y, Jimeno A. XactMice: humanizing mouse bone marrow enables microenvironment reconstitution in a patient-derived xenograft model of head and neck cancer. *Oncogene.* 2015 [epub ahead of print]
2. Lung cancer has experienced a revolution with the identification of specific driver mutations in lung adenocarcinoma. Treatment with specific tyrosine kinase inhibitors (ie. erlotinib, crizotinib) has resulted in near or total complete responses in metastatic patients. However, progression-free survival rates for patients with EGFR or ALK gene re-arranged cancers range from 10-14 months. The traditional paradigm has been to change systemic therapy at the time of recurrence. My colleagues and I have begun to challenge this notion. Instead of changing systemic therapy in patients with oligoprogressive disease, we have used local ablative therapy to eliminate resistant clonogens. Clinical trials are currently underway to address this question in a prospective fashion and I am collaborating on their design. I served as the primary investigator or co-investigator in all of these studies.
- a. Bansal P, Osman D, **Gan GN**, Simon GR, Bumber Y. Recent Advances in Targetable Therapeutics in Metastatic Non-squamous NSCLC. *Frontiers in Oncology.* 2016 May 4;6:112
 - b. **Gan GN**, Weickhardt AJ, Scheier B, Doebele RC, Gaspar LE, Kavanagh BD, Camidge DR. Stereotactic Radiotherapy Can Safely and Durably Control Sites of Extra-CNS Oligoprogressive Disease in ALK-Positive Lung Cancer Patients on Crizotinib. *Int J Radiat Oncol Biol Phys.* 2014 Mar 15;88(4):892-8
 - b. Weickhardt AJ, Scheier B, Burke, JM, **Gan G**, Lu X, Bunn P, Aisner, DL, Gaspar LE, Kavanagh BD, Doebele RC, Camidge DR. "Local Ablative Therapy of Oligoprogressive Disease Prolongs Disease Control by Tyrosine Kinase Inhibitors in Oncogene-Addicted Non-Small-Cell Lung Cancer." *Journal of Thoracic Oncology.* 2012 Dec; 7 (12):1807 - 1814
3. Additional selected manuscripts focusing on head and neck cancer, stereotactic body radiotherapy, and treatment-associated toxicity are listed below. These works demonstrate a continued focus on head and neck cancer as well as a growing acumen and interest in stereotactic body radiotherapy. Future work will be to further explore the radiobiology of stereotactic body radiotherapy in head and neck cancer and thoracic malignancies. I served as co-investigator and mentor in all of these studies.
- a. Amini A, McDermott JD, **Gan G**, Bhatia S, Sumner W, Fisher CM, Jimeno A, Bowles DW, Raben D, Karam SD. Stereotactic body radiotherapy as primary therapy for head and neck cancer in the elderly or patients with poor performance. *Front Oncol.* 2014 Oct 8;4:274

- b. Robin TP, **Gan G**, Tam M, Westerly D, Riaz N, Karam S, Lee N, Raben D. A Multicenter Review of Contralateral Submandibular Gland Sparing in Locally Advanced Oropharyngeal Cancers: Is It Safe? *Head Neck*. 2014 Dec 6 [Epub ahead of print]
- c. Jones BL, **Gan G**, Kavanagh B, Miften M. Effect of endorectal balloon positioning errors on target deformation and dosimetric quality during prostate SBRT. *Phys Med Biol* 2013 Nov 21;58(22):7995-8006.
- d. Jones BL, **Gan GN**, Diot D, Timmerman RD, Kavanagh B, Miften M. " Dosimetric and Deformation Effects of Image-Guided Interventions during Stereotactic Body Radiation Therapy of the Prostate using an Endorectal Balloon." *Med Phys* 2012 Jun; 39 (6): 3080 - 3088

D. Research Support

Ongoing Research Support

ACS-IRG_14-187-19 (PI: Gan) 09/01/15 - 10/31/16
American Cancer Society

The role of irradiated microenvironment on head and neck cancer tumor repopulation

The specific aim of this project is to develop an in vitro and in vivo cancer associated murine fibroblast model to study the effects of radiation and TGFb1 on this tumor microenvironment cell type and to begin identifying the cytokine(s) which may be associated with tumor repopulation.

Role: Principal Investigator

RSNA #RSCH1511 (PI: Gan) 07/01/15 - 06/30/17
Radiological Society of North America

Mechanism of hedgehog pathway-mediated head and neck cancer radio-resistance

The specific aim for this project is to: (1) Establish a head and neck cancer patient-derived tumor xenograft model and determine how the stromal compartment can affect tumor repopulation and (2) Determine the mechanism for radiation induced Hedgehog pathway activation in cancer associated mouse fibroblasts.

Role: Principal Investigator

Completed Research Support

Resident/Fellow in Radiation Oncology Research Seed Grant (PI: Gan) 07/01/13 - 06/30/14
ASTRO

The specific aims for this project were to: (1) Determine whether the DNA damage response pathway signals through mTOR/S6K1 and effects GLI1 translocation into the nucleus following radiotherapy in head and neck cancer and (2) Determine whether Hedgehog pathway inhibition on tumor stroma/microenvironment contributes to enhanced head and neck tumor control following radiotherapy *in vivo*.

Role: Principal Investigator

Paul Wehling Cancer Fund (PI: Gan, Jimeno) 07/01/13 - 06/30/14

The specific aims for this project were to: Determine whether hedgehog pathway /GLI1 is expressed in mice and whether its inhibition can enhance radiosensitivity

Role: Co-Investigator

Research Seed Grant (PI: Gan) 07/01/12 -06/30/14
Cancer League of Colorado

The specific aims for this project were to: (1) Determine whether radiotherapy could induce Hedgehog pathway/GLI1 expression in head neck cancer and (2) Determine whether inhibition of GLI1 with cyclopamine could enhance head and neck cancer radiosensitivity *in vitro* and *in vivo*.

Role: Principal Investigator