

## Mission

The mission of the Head and Neck Cancer Program at the University of Colorado Cancer Center is to provide the highest quality multidisciplinary care to patients, while conducting innovative research and educational programs to improve outcomes.

The Head and Neck Cancer program includes:

- Physicians and other health providers from five different disciplines (medical oncology, radiation oncology, surgical oncology, speech rehabilitation and nutrition), all specializing in Head and Neck cancers.
- Multidisciplinary tumor boards, where patients and other cases are discussed by multiple specialists in one place.
- Cutting-edge research trials for patients with all stages of head and neck cancer.
- Tumor banking, basic research and translational research initiatives.
- Educational programs.



# Head and Neck Cancer Program

## In the Spotlight

### Research Funding

Several key members of the HNC Program have been recently awarded with research funding from the National Institutes of Health. Two teams have recently been awarded each with one of the highly competitive Challenge Grants derived from the American

Recovery and Reinvestment Act. One team led by Xiao-Jing Wang Ph.D. and including Antonio Jimeno M.D., Ph.D., John Song M.D., and Stephen Malkowski M.D., Ph.D. Received one to study Head and Neck Cancer stem cells. A second team led by Bryan Haugen M.D., and including also

Rebecca Scheweppe Ph.D. and Aik-Choon Tan Ph.D. Have received one award to generate and study new models of Thyroid cancer. In addition, Antonio Jimeno M.D., Ph.D. Received a R21 grant to generate a model of Head and Neck cancer derived directly from patients.

## Head and Neck Cancer Program Clinics

### Medical Oncology

Chemotherapy, both standard and investigational, for HNC cancers.

Faculty: Antonio Jimeno, MD, PhD; Madeleine Kane, MD, PhD.  
Referrals: 720-848-0300 (Christine Miller and Michelle (Shell) Adams - 720-848-0300)  
Clinical Trial Contact: Brittany Hines - 720-848-0634 or [brittany.hines@ucdenver.edu](mailto:brittany.hines@ucdenver.edu); or see individual trials for contact information.

### Radiation Oncology

Radiation therapy, both standard (including intensity modulated radiation therapy) and investigational, for HNC cancers.

Faculty: David Raben, MD; Changhu Chen, MD.  
Referrals: 720-848-0150 or fax to 720-848-0112  
Clinical Trial Contact: Tracy King - 720-848-0663 or [tracy.king@ucdenver.edu](mailto:tracy.king@ucdenver.edu)

### ENT Surgical Oncology

Operative approaches, both curative and palliative, in Head and Neck cancers.

Faculty: John Song MD  
Referrals:  
Clinical Trial Contact: Brittany Hines - 720-848-0634 or [brittany.hines@ucdenver.edu](mailto:brittany.hines@ucdenver.edu)

# Head and Neck Cancer Clinical Trials

General Eligibility Criteria: Biopsy-proven cancer. No chemotherapy or therapeutic radiotherapy 2-4 weeks prior to starting on study. Performance Status < 2 with life expectancy of > 12 weeks and adequate organ function. Some studies require PS < 1. No active brain metastasis (must have completed local therapy and be off steroids, anticonvulsants). 18 years or older, unless otherwise specified.

## • SQUAMOUS HEAD AND NECK CANCER

05-1125

Title: A Phase I Dose Escalation of Erlotinib Concurrently with Radiation Therapy in the Re-Irradiation Setting for Head and Neck Cancer

Rationale: Determine maximum tolerated doses of erlotinib given concurrently w/ radiation therapy to the head & neck patients in the re-irradiation setting.

Purpose: To determine if erlotinib and radiation therapy in combination improve progression free survival in patients with head and neck cancer

Eligibility: Eligibility criteria include but are not limited to 18 years or older with a tumor in the head and neck area that has returned after having radiation therapy

Treatment: In this study patients start taking erlotinib 7 days before radiation therapy. Patients continue to take erlotinib for a total duration of two years, unless disease progresses or unacceptable side effects occur.

08-1385

Title: A Randomized Phase II Trial of Chemoradiotherapy Versus Chemoradiotherapy and Vandetanib for High-Risk Postoperative Advanced Squamous Cell Carcinoma of the

Head and Neck

Summary: Eligible patients will be stratified by relevant factors such as stage and HPV and randomized to receive standard chemoradiation with 3-weekly cisplatin and daily radiotherapy, or the same regimen with vandetanib 100 mg daily  
Eligibility: Patients with resected stage III or IV squamous cancer of the head and neck

06-0547

Title: Open label multicenter Phase I study to assess the maximum tolerated dose of ZD6474 (Zactima) given concomitantly with radiation therapy or concomitantly with weekly cisplatin chemotherapy and radiation therapy in patients with previously untreated unresected stage II-IV head and neck squamous cell carcinoma.

Rationale: To determine the maximum tolerated doses of ZD6474 in combination with radiation therapy and also in combination with radiation therapy plus cisplatin

Purpose: To determine the safety profile, tolerability, and maximum tolerated dose of ZD6474 in combination with radiation therapy and cisplatin in patients with untreated unresected stage II-IV squamous cell carcinoma of the head and neck

Eligibility: Eligibility criteria include but are not limited to 18 years or older with head and neck squamous cell carcinoma that cannot be treated with surgery

Treatment: Treatment lasts approximately 8 to 9 weeks.

07-0633

Title: RTOG 0514 Establishment of Head and Neck Cancer Tissue / Specimen Bank.

Rationale: To bank and maintain the resource material required for

research studies in human head and neck cancers.

Purpose: To establish a repository to serve as a resource for current and future scientific studies.

Eligibility: Eligibility criteria include but are not limited to 18 years or older with head and neck cancer or tissue that is suspected of being cancerous.

Treatment: N/A

08-0552

Title: Head and Neck Squamous Cell Cancer Tissue Collection for Animal Xenograft Studies

The purpose of this study is to collect tissue from patients undergoing standard of care surgical resection of a HNSCC. HNSCC tissue samples will be obtained from consenting patients at the University of Colorado Hospital and only tumor and normal tissue not required for histopathological analysis will be collected. Given the paucity of cell lines for some of the more rare locations in HNSCC, the need for xenografts is especially acute.

09-0179

Title: Retrospective Head and Neck Cancer Tissue Collection

The overall goal of this study is to construct an annotated retrospective tumor bank with sufficient cases of head and neck cancer (HNC) to permit global and subset analyses. We expect this number to be 500 cases. We will (1) construct tissue micro-arrays (TMA) to allow for efficient immunohistochemistry (IHC) studies following Pathology core guidelines, and we will (2) extract DNA from conventional slides for oncogenic gene mutation analyses. The first project we will accomplish will be to test for the presence and impact on progression-free and

overall survival, as well as in response to treatment for the cancer stem cells (CSC) markers CD44, CD24, and ALDH. A second project will be to determine the frequency of oncogenic mutations in the genes Smad, TGFII, PTEN and Kras.

### Upcoming:

09-0155

A Phase II, Open-label, 1:1 Randomized, Controlled Trial Exploring the Efficacy of EMD 1201081 in Combination with Cetuximab in Second-Line Cetuximab-Naïve Subjects with Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck

The purpose of this study is to determine the efficacy of adding the immune mediator toll-like receptor agonist EMD 1201081 to the standard treatment of cetuximab is safe and tolerable. The study will compare cetuximab alone with cetuximab plus EMD 1201081, and patients that have progression in the cetuximab arm are allowed to cross over and receive the investigational agent. EMD 1201081 is an investigational agent that promotes an immune response against cancer cells, which may make cetuximab more effective.

### • THYROID CANCER

07-0727

Retinoid Therapy for Poorly Differentiated Thyroid Cancer: A Pilot Clinical Trial and Correlation to Retinoid and PPAR $\gamma$  Receptor Expression

Rationale: Many thyroid cancer patients have a differentiated form and do very well with standard therapy (surgery, radioiodine, and thyroid hormone suppression).

Approximately 5-10% of patients have an aggressive form of thyroid cancer that does not respond to conventional therapy, chemotherapy older with head and neck cancer or tissue that is suspected of being cancerous.

Treatment: N/A

05-0164

A Phase II Study of Bortezomib in Metastatic Papillary Thyroid Carcinoma or Follicular Thyroid Carcinoma

Rationale: VELCADE (Bortezomib) is a small molecule proteasome inhibitor currently approved by the FDA for the treatment of multiple myeloma patients who have had at least 2 prior therapies and demonstrated disease progression on the previous therapy. Recent findings have emphasized cell cycle dysregulation as one of the key steps in thyroid carcinogenesis. A proteasome inhibitor in malignant thyroid cells such as Bortezomib may reverse cell cycle dysregulation and could be a rational target for therapy. Contact: Dr. Bryan Haugen (bryan.haugen@ucdenver.edu).

08-0745

An International, Randomized, Double-Blinded, Phase III Efficacy Study of XL 184 versus Placebo in Subjects with Unresectable, Locally Advanced, or Metastatic Medullary Thyroid Cancer

Rationale: Currently available therapies for metastatic medullary thyroid cancer are not curative, and no large-scale or Phase 3 studies have been conducted. XL 184 is a new chemical entity that inhibits multiple receptor tyrosine kinases (RTKs) with growth-promoting and angiogenic properties. The primary targets of XL 184 are RET, MET, VEGFR2/KDR, and KIT. Contact: Dr. Madeleine Kane (madeleine.kane@ucdenver.edu).

07-1061

Phase I/II Study of CS-7017, An Oral PPAR $\gamma$  Agonist, In Combination with Paclitaxel in Subjects with Advanced Anaplastic Thyroid Cancer

Rationale: CS-7017 is a high affinity agonist that stimulates the PPAR – response element and inhibits cell proliferation and colony formation in the DRO anaplastic thyroid cancer cell line. This study combines CS-7017 with paclitaxel which has been shown to have antineoplastic activity in anaplastic thyroid cancer cells in vitro and in vivo. Contact: Dr. Joshua Klopper (joshua.klopper@ucdenver.edu).

07-0506

A Multicenter, Open-Label, Randomized, Phase II/III Study to Evaluate the Safety and Efficacy of Combretastatin A-4 Phosphate in Combination with Paclitaxel and Carboplatin in Comparison with Paclitaxel and Carboplatin Against Anaplastic Thyroid Cancer

Rationale: Anaplastic Thyroid Cancer (ATC) is a high-grade neoplasm, characterized by an aggressive clinical course with brief survival. Combretastatin A-4-Phosphate (CA4P) is a novel anti-cancer agent that displays potent and selective toxicity towards tumor vasculature. This study assesses the combination of standard therapies Paclitaxel and Carboplatin with and without the addition of CA4P against ATC. Contact: Dr. Bryan Haugen (bryan.haugen@ucdenver.edu).

## • PHASE 1

The HNC Cancer program at the University of Colorado Cancer Center strongly supports the developmental therapeutics program.

09-0065

Title: A Phase I, Multiple-Dose Escalation Study of the Safety and Tolerability of REGN421 in Patients with Advanced Solid Malignancies

Summary: Clinical trial of investigational drug REGN421 (a notch inhibitor) given intravenously. Eligible patients will receive both study drugs as there is no placebo. Eligibility: Patients with recurrent or metastatic cancer

08-0116

Title: A Phase I Trial of Oral PX-866 (a PI-3K Inhibitor) in Patients with Advanced Solid Tumors.

Summary: Clinical trial of investigational drug PX-866 (a PI3K inhibitor) given by mouth. Eligible patients will receive both study drugs as there is no placebo.

Eligibility: Patients with recurrent or metastatic cancer

08-1209

Title: A Phase 1b Study to Assess the Safety and Pharmacokinetics of ARRY 334543 with Docetaxel in Patients with Advanced Solid Tumors

Summary: Clinical trial of investigational drug ARRY-334543 given by mouth in combination with docetaxel given through an intravenous (IV) infusion. Eligible patients will receive both study drugs as there is no placebo.

Eligibility: Patients with recurrent or metastatic cancer

08-1083

Title: A Phase 1 Dose-escalation Study of OSI-906 and Erlotinib (Tarceva) in Patients with Advanced Solid Tumors

Summary: Clinical trial of investigational drug OSI-906 given in combination with erlotinib by mouth. Eligibility: Patients with recurrent or metastatic cancer

Primary contact for Phase 1 studies Antonio Jimeno MD, PhD and Sharon Hecker as Clinical Research Coordinator

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## Faculty and Research Groups

### Medical Oncology

#### Antonio Jimeno, MD, PhD

(Assistant Professor,



Director of the Developmental Therapeutics/ Pharmacodynamic Laboratory) obtained his MD from the

University of Valladolid Spain, trained in Madrid and Johns Hopkins University in Medical Oncology and Drug Development. His clinical interest is squamous cell cancer of the head and neck and Phase 1 trials, and his research interest is cancer stem cells and novel therapeutic approaches in head and neck cancer. Office: 303-724-2478  
antonio.jimeno@ucdenver.edu

#### Madeleine Kane, MD, PhD



(Professor; Director, Clinical Investigations Core) got her MD from the University of Miami and her PhD (Biochemistry) from the

University of Maryland. She joined the UCCC faculty in 1985 and specializes in Thyroid and Head and Neck Cancers. Dr. Kane serves as the Director of the Clinical Investigations Core at UCCC.

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### Radiation Oncology

#### Changhu Chen, MD



(Associate Professor) is a radiation oncologist specialized in head and neck cancer radiation therapy. His clinical focus is

utilizing Intensity-Modulated Radiation Therapy (IMRT) technique to maximize the chance of cure and minimize side effects in patients

with a head and neck cancer. His research interest is on combining chemoradiation with biologic targeting agents for patients with a newly diagnosed head and neck cancer, and re-irradiation for patients who recurred after prior radiation therapy.

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#### David Raben, MD



(Professor) received his medical degree from The Bowman Gray School of Medicine, Wake Forest University, Winston Salem,

North Carolina, and completed his residency in Radiation Oncology at Johns Hopkins University, Baltimore, Maryland. Dr. Raben is internationally known and has established himself in the area of translational research combining radiation with biologic agents that alter the cancer cell growth cycle to enhance the effectiveness of radiation therapy for head and neck cancer. He serves on various local, national and international committees including the head and neck Steering Committee of the Radiation Therapy Oncology Group.

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### Surgical Oncology

#### John Song, MD



(Associate Professor) Department of Otolaryngology at the University of Colorado Denver School of Medicine and the Director of head

and neck oncologic surgery at the University of Colorado Hospital. He also serves as chief of otolaryngology at the Denver VA Hospital. Dr. Song is a board-certified otolaryngologist

and he specializes in head and neck, skull base, thyroid and parathyroid surgery, swallowing disorders, and rehabilitation after head and neck cancer. He received his medical degree from New York University School of Medicine, completed his residency at University of California Los Angeles Medical Center, and completed a fellowship in head and neck surgery and skull base surgery at the University of Pittsburgh Medical Center. His research interests include targeted therapies in head and neck cancer.

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### Endocrinology

#### Joshua Klopper, MD



(Assistant Professor of Medicine) joined the faculty of the Division of Endocrinology, Metabolism and Diabetes in July 2006. Dr.

Klopper was born and raised in Atlanta, GA. His educational background includes a B.S. in Psychology in 1995 from Indiana University in Bloomington, IN. He received his medical degree from the Emory University School of Medicine in Atlanta, GA in 1999. He relocated to Colorado in 1999 where he completed his internship and residency in internal medicine at the University of Colorado Denver in 2002. Dr. Klopper then did a postdoctoral research fellowship in the Endocrinology Division from 2002-2003 prior to starting his endocrinology fellowship at UCD which he completed in June 2006. Dr. Klopper's research interests are in the treatment of poorly differentiated thyroid cancer by the investigation of molecular targets in the nuclear hormone receptor superfamily. Specifically he is investigating the

activation of retinoid, PPAR $\gamma$  and Vitamin D receptors to inhibit cell growth and potentially induce redifferentiation in aggressive thyroid cancers.  
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### **Bryan R. Haugen, MD**



(Professor of Medicine and Pathology at the University of Colorado Denver) He is Chief of the division of Endocrinology, Metabolism & Diabetes and Director of the Thyroid Tumor Program which monitors and manages more than 2000 patients with thyroid

cancer. He currently holds the Marry Rossick Kern and Jerome H Kern Chair in Endocrine Neoplasms Research. Dr Haugen received is BA degree in Chemistry from Saint Olaf College and medical degree from the Mayo Medical School in 1987. Internship, medical residency and endocrine fellowship were completed at the University of Colorado Health Sciences Center. Dr Haugen is a Fellow in the American College of Physicians, and member of the American Thyroid Association, the Endocrine Society, the American Association of Clinical Endocrinologists and the American Society for Biochemistry

and Molecular Biology. His current clinical interests include thyroid neoplasms, advanced thyroid cancer, thyroid dysfunction and other endocrine tumors (parathyroid, adrenal, carcinoid). Dr Haugen's research interests include molecular studies of thyroid neoplasm diagnosis and pathophysiology as well as the study of molecular therapeutic targets. Specific areas of research include nuclear hormone receptors (RXR, TR, PPAR) and kinase signaling pathways as therapeutic targets in thyroid cancer, as well as proteomic approaches to molecular markers in thyroid neoplasms.  
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## **Clinical Trial Coordination Team**

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### **Medical Oncology**

Team leader:  
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### **Radiation Oncology**

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## Squamous Cancer Basic Researchers



Xiao-Jing Wang received her M.D. (1984) and Ph.D (1989) from Beijing Medical University. She came to the United States for

her postdoctoral training at the M.D. Anderson Cancer Center in 1990. In 1992, she joined Baylor College of Medicine as a Research Associate. At Baylor, she became Assistant Professor in 1995 and tenured Associate Professor in 2000 in the Departments of Molecular and Cellular Biology and Dermatology. In 2003, she was recruited to Oregon Health & Science University (OHSU) as a tenured Full Professor in Otolaryngology, and Director of Molecular Biology-Head and Neck Cancer Research Division. Dr. Wang came to the University of Colorado Denver in 2008. Dr. Wang's laboratory has constructed the first genetically engineered mouse model that develops head and neck squamous cell carcinoma (HNSCC) with full penetrance. These lesions mimic human HNSCC at genetic and pathological levels. These mouse models are an invaluable resource for evaluating the mechanisms and efficacy of the existing clinical trials for HNSCC prevention and treatments. Research in the Wang laboratory includes: 1) Identification of biomarkers for diagnosis and therapy for human head and neck cancer, 2) Development of animal models for head and neck cancer, 3) Molecular mechanisms of head and neck cancer including the properties

of cancer stem cells, transcriptional machinery and microRNA functions, and 4) Experimental therapeutics of head and neck cancer



Stephen Malkoski, M.D., Ph.D. completed his degrees at the University of New Mexico School of Medicine in 2000.

He did a residency and fellowship at Oregon Health and Sciences University and moved to University of Colorado Denver as an assistant professor in 2008. Although lung cancer is the leading cause of cancer death in both men and women, the 5 year survival from lung cancer remains less than 20%. Many lung cancers have reduced expression of transforming growth factor beta (TGF $\beta$ ) signaling molecules. The lab is interested in the mechanisms by which defective TGF $\beta$  signaling promote the growth of non-small cell lung cancer and approach these questions using a combination of human lung cancer samples, cultured human lung epithelial cells, and mouse lung cancer models.



Shi-Long Lu obtained his M.D. from China Medical University in 1987, and his Ph.D. from Tokyo Medical and Dental University

in 1999. He was an assistant professor at the Oregon Health and Sciences University, and moved to the University of Colorado Denver

in 2008 as an assistant professor. The mission of his laboratory is to understand the molecular basis of squamous cell carcinomas (SCCs) of the upper aerodigestive (UAD) tract, including head and neck, esophagus, and lung. UAD-SCCs are among the most common cancers in the United States, accounting for nearly one third of all malignancies, but little is known about the underlying mechanisms. Although comprised of heterogeneous tissue types, UAD-SCCs often have similar histopathology, genetic alterations, and environmental risk factors. The major areas of research in our laboratory include: 1) Role of PI3K/PTEN/AKT signaling in development and metastasis of UAD-SCCs. 2) Identification and functional analysis of metastasis genes in UAD-SCCs. 3) Molecular characterization of esophageal stem cells and their link to esophageal SCC. 4) Development of novel molecular markers to monitor head and neck cancer progression using fine needle aspirates. The ultimate goal of our laboratory is to bridge basic research into the clinical setting.

