

HERBERT IRVING COMPREHENSIVE CANCER CENTER
A NATIONAL CANCER INSTITUTE COMPREHENSIVE CANCER CENTER

Postdoctoral position in pancreatic cancer translational research:

Cancer Metabolism

We are seeking a leader for a high-impact project on Cancer Metabolism within the pancreatic cancer research program at Columbia University Irving Medical Center. The position will be mentored by Dr. Kenneth Olive, an Assistant Professor of Medicine who leads a multidisciplinary translational therapeutics research program in pancreatic cancer.

Scope of planned research project: This project will advance the seminal efforts of our former Ph.D. student Michael Badgley, whose initial findings on this topic are currently under review at Science. Briefly, Mike found that pancreatic tumors depend on the import of exogenous cystine (oxidized cysteine) in order to manage the high ROS flux induced by activating K-ras mutations and severe intratumoral hypoxia. Intracellular depletion of cysteine in pancreatic tumor cells rapidly induces ferroptosis, an oxidative form of non-apoptotic cell death. Cystine is imported from the outside the cell via the system x_c^- glutamate/cystine antiporter, a targetable protein that is upregulated in many cancers and associated with poor survival in human patients. Acute genetic deletion of system x_c^- in the context of established Kras/p53 mutant pancreatic tumors resulted in the induction of ferroptosis *in vivo* and significantly increased overall survival. To our knowledge, this is the first clear demonstration of *in vivo* ferroptosis, presenting a unique opportunity to characterize the nature of this phenomenon in mammalian tissues. The goals of the project will be to: 1) characterize the cellular and metabolic features of ferroptosis *in vivo*; 2) elucidate the metabolic roles of cysteine and its derivatives *in vivo* in genetically engineered mice with pancreatic tumors; and 3) to study how inhibition of cystine import leads to ferroptosis. In addition, the project will pursue therapeutic approaches to targeting cysteine metabolism, with the goal of translating into the clinic during the time period of the postdoctoral fellowship.

The Olive Laboratory: The Olive Lab is devoted to two overarching missions: first, a **research mission** to identify critical tumor-specific dependencies of pancreatic cancer and facilitate the development and translation of related therapeutic approaches; second, an **educational mission** to educate and mentor junior scientists in translational oncology research. We utilize multiple pancreatic cancer model systems including genetically engineered mouse models, patient-derived xenografts, primary human tissue samples, and tumor explant cultures. The Olive Lab is organized around our “Mouse Hospital”, a translational therapeutics infrastructure designed to leverage mouse models for translational applications. The Mouse Hospital incorporates multidisciplinary expertise in small animal imaging, surgery, pathology, pharmacology, *ex vivo* molecular biology, and information management. Individual projects in the lab span the range of biological sub-disciplines, with particular emphases on Systems Biology, Cancer Metabolism, Stroma/Immune interactions, DNA damage response, Small Animal Imaging, and Translational Therapeutics. Our lab also makes extensive use of the clinical research-oriented resources of the Columbia Pancreas Center, a high volume clinical multidisciplinary team focused on the care and treatment of pancreatic cancer patients, including access to a large-scale biorepository of frozen pancreatic tumor samples. The ultimate goal of our work is to translate key findings into clinical practice, with multiple clinical trials and protocols, both at Columbia University and beyond, already having emerged from our research.

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Preferred and required skills and expertise: The successful candidate for this position will have deep experience in the area of cancer metabolism during their graduate studies, including the use of stable isotope labeling and the interpretation on mass spectrometry data. The candidate will also exhibit superior skills in written and oral communication, personal leadership, and a commitment to team science in a diverse, multidisciplinary setting. While prior experience using *in vivo* model systems is not a requirement, at least basic familiarity with mouse handling is desirable; experience with *in vivo* metabolism studies and/or genetically engineered mouse models of cancer is ideal.

Contact information: For questions or inquiries about this position, please contact Isabel Goncalves: ig2384@cumc.columbia.edu. For applications, please provide a cover letter, a copy of your CV, and drafts of any manuscripts in preparation that you wish to be considered. In your CV, please include a statement indicating your role in writing each listed paper. Please also provide the names and contact information of up to 3 referees.