UC San Diego
MOORES CANCER CENTER

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Uncovering monocyte origin during radiotherapy and its implications for head and neck cancer

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Scientific Abstract:

Radiotherapy (RT) is used in over 50% of head and neck squamous cell carcinoma (HNSCC) patients, emphasizing the need of dissecting its mechanisms of therapeutic action. Besides its known role at killing tumor cells, RT modulates immune mechanisms that can fuel or inhibit cancer. Here, *we will investigate an immune mechanism poorly understood during RT of HNSCC: RT's capacity to promote the recruitment of developmentally different monocyte subtypes into tumors.*

Until recently, two main technical limitations impaired the analysis of monocyte subtypes and their recruitment following RT. First, we lacked techniques to dissect at a high-resolution all the possible fates and functions of tumor-infiltrating monocytes. Second, we lacked approaches to model clinically relevant modes of RT in small animals. In the last years, we have overcome these limitations and dissected the fates of monocytes post-RT in several tumor types, with the exception of HNSCC. Our work shows that the function of monocyte-derived cell is linked to the infiltration of different monocyte subtypes post-RT. Based on these findings, we hypothesize that monocyte-derived cell function is not only dependent on environmental-dictated plasticity, but it is rather encoded developmentally.

Here, we will apply our expertise to study monocyte subtype recruitment in HNSCC post-RT. We propose to reconstruct the trajectory of monocytes as they differentiate into pro- or anti-tumor cells in mice and human patients. We anticipate that findings from this proposal will enhance our current understanding of monocyte biology and function, and positively impact the rational design of combinatory cancer treatments for HNSCC
patients.

Lay Abstract:

Radiotherapy, or RT, is a common treatment for patients with head and neck cancer. While RT is known for killing cancer cells, it also influences the immune system, which can either fight the cancer or help it grow. This study will explore how RT affects a type of immune cell called monocytes in patients with head and neck squamous cell carcinoma (HNSCC).

In the past, researchers found it hard to study monocytes during cancer treatment because they lacked the right tools. Recently, advancements have been made, but there has not been much focus on HNSCC yet. Our initial results with other tumor types suggest that the way monocytes work after RT depends on the types of monocytes that enter the tumor. We think that the behavior of monocytes is influenced not only by their surroundings, but also by their original development. Researchers in this project plan to track how monocytes change into cells that help fight cancer or support its growth after RT, using both experimental animals and samples obtained from human patients.

By better understanding how monocytes respond to RT in HNSCC, this research could lead to improved treatment strategies that combine RT with newer therapies for better cancer care.