Cancer stem cells in malignant peripheral nerve sheath tumor: Biology and therapeutic ramifications

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Although monoclonal in origin, most tumors appear to contain heterogeneous populations of cancer cells. One possible explanation of this tumor heterogeneity is that human tumors are not merely monoclonal expansions of a single transformed cell, but rather caricatures of normal tissues, and their growth is sustained by cancer stem cells (CSCs). This conceptual shift has important implications, not only for understanding tumor biology but also for developing and evaluating effective anticancer therapies. These CSCs are thought to be more resistant to apoptosis, to survive therapy and to eventually give rise to second-line tumors, which are harder to eliminate by the first-line therapy.

In this proposal, *we are introducing our data in detection of CSCs in malignant peripheral nerve sheath tumors (MPNSTs) for the first time*, and explain our plans for studying the biology of these cells in order to develop a therapeutic strategy for targeting them. We have identified a sub-population of cells in primary human MPNST cells which are positive for CD133 (a well-known marker for CSCs) and other stem cell markers. We have also studied the characteristics of Ras signaling pathway in these cells showing enhanced activation of Ras, Ral, PI3K and ERK. Now, we plan to not only study the biological characteristics of these cells further but also intend to “custom design” a new protocol for targeting them on the basis of specific characteristics of Ras pathway in these cells. If MPNST CSCs could be targeted, it can result in an efficient regression of tumors and enhancement of therapeutic success in MPNST patients.