INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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Thesis Title: Insight into stem cell niche defense mechanism in TB reactivation and head and neck cancer recurrence

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SHORT ABSTRACT

Adult stem cells, residing within protective niches, can be threatened by invading pathogens and cancer cells. To counter these threats, stem cells have evolved defense mechanisms, including "trained immunity" and the adoption of a transient, p53-deficient "altruistic stem cell" (ASC) phenotype that prioritizes community survival over self-preservation. However, we propose that this ASC-based niche defense can be exploited by pathogens and cancer cells, leading to disease reactivation. Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (*Mtb*), and cancer both exhibit dormancy and reactivation patterns, posing significant therapeutic challenges. Our research demonstrates that CD45-/CD271+ mesenchymal stem cells (MSCs) mount a defense against both *Mtb* and head and neck squamous cell carcinoma (HNSCC)-derived cancer stem cells (CSCs). We observed that crosstalk between MSCs and *Mtb* or HNSCC-derived CSCs triggers the reprogramming of MSCs into ASCs. This, in turn, facilitates *Mtb* reactivation and promotes the pro-tumorigenic activity of CSCs, respectively. Furthermore, utilizing a rural telemedicine network, we found evidence linking ASC niche defense to TB and HNSCC recurrence in clinical subjects. These findings suggest that the ASC-based stem cell niche defense mechanism can be hijacked, contributing to disease relapse. This highlights a novel therapeutic target for preventing reactivation in both infectious diseases and cancer.