CIRCULATING ALTRUISTIC STEM CELLS AS A MARKER OF IMMUNOSUPPRESSION IN ORAL CANCER

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Abstracts

Background Head & neck cancer is the 4th cancer, and most of them are diagnosed late, and treated with cisplatin monotherapy. In these subsets of patients, immunotherapy has been tried, but without major success. We speculate that circulating altruisitic stem cells may serve as biomarker for immunotherapy. Previously, we showed that oral cancer CSCs reprogram MSCs to altruisitic phenotype, and an embryonic stem cell like phenotype having niche defending ability. Here, we propose to test the immunosuppressible ability of ASCs, and their detection in the circulation of head & neck cancer subjects undergoing platinum based chemotherapy.

Methods We obtained ASCs by culturing CD271+ BM-MSCs with the conditioned media of EPCAM+/ABCG2+ CSCs of SCC-25 cancer cell line or primary tumors as previously described. The immunosuppression test: immunosuppressive secretory factors, mixed lymphocyte reaction (MLR) assay, and a Boyden chamber based co-culture assay with NK cells. Next, we obtained circulating CD271+/CD45- cells of stage IV head and neck cancer subjects (n=20) (S). Kaplan-Meier survival analysis and log-rank test to find association between the presence of circulatory ASCs and overall survival (OS).

Results CSCs including primary tumor obtained CSCs reprogram CD271+ MSCs to ASC phenotype; these cells secrete high level of Nitric oxide, IDO, TGF-beta, IL-10 and PGE-2. In Boyden chamber assay, ASCs markedly decreased the number of CD4+/FoxP3+/CD25+ T cells by 4-5 fold (p<0.02; n=3), whereas increased the CD4+/FoxP3+/CD25- T-reg cells by 3-fold (p<0.05, n= 4). Moreover, ASCs, upon co-culture, increases the clonogenic capacity of non-CSCs (EPCAM+/ABCG2-ALDH- cells) by 5-fold (p<0.02; n=4), while significantly decreasing the secretion of NKG2DL of these cancer cells. Next, we isolated circulating CD271+/CD45- cells from the 12/20 subjects with oral cancer and confirmed their ASC phenotype (figure 1A-E). These cells were in vitro cultured (figure 1D), and the conditioned media obtained showed marked immunosuppressive activities including significant reduction of NKG2DL+ NK cells in the in vitro Boyden chamber assay. Importantly, these 12 out of 20 patients showed poor treatment response to platinum therapy. The OS at 6 months was 24.6% for circulating ASC-positive patients and 47.4% for circulating ASC-negative patients (log-rank test, p<0.001).

Conclusions The circulatory ASCs could be a promising biomarkers for immunotherapy.

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Ethics Approval The clinical study was approved by ‘Institutional Ethics Committee’ of KaviKrishna Laboratory, Guwahati, India and KaviKrishna Telemedicine Care, Sualkuchi, Assam, India. The stem cell study was conducted following the guidelines of NAC-SCRT and was approved by Institutional Committee for Stem Cell Research (ICSCR), KaviKrishna