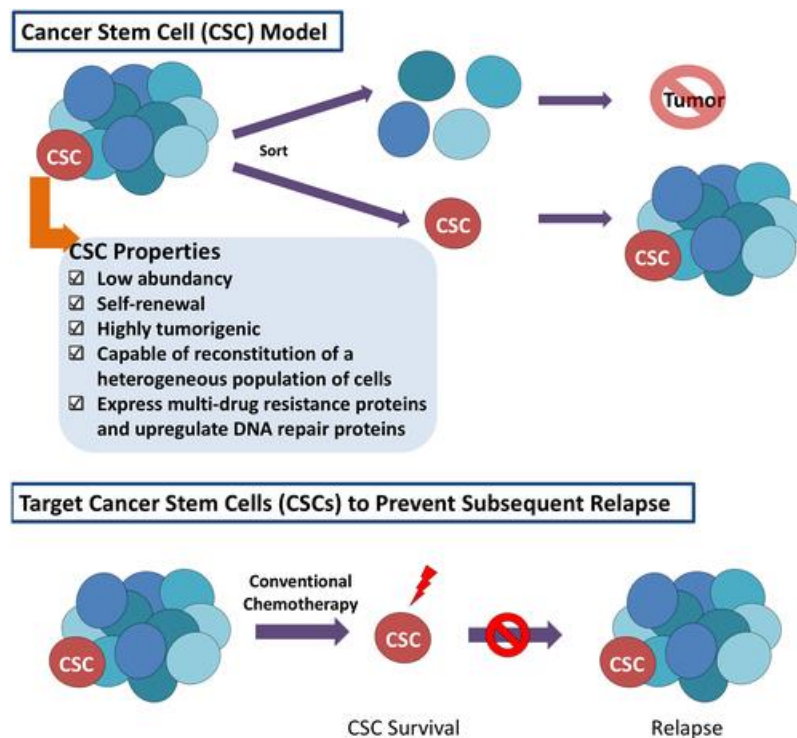


Targeting the drug resistance in oral cancer by inhibiting CSC maintaining cell signalling

To study the oral cancer (OC) - cancer stem cells (CSCs) population *in-vitro*, Scientists at DBT's National Institute of Biomedical Genomics (NIBMG), Kalyani, have developed the CSC enriching 3D-spheroid culture model. Team has found that conventional platinum based chemotherapeutic agent cisplatin treatment is not effectively inhibiting the OC-CSCs population. Rather, results have shown resistance against cisplatin is due to upregulation of Notch signalling. The recent evidence strongly addresses the involvement of Notch signaling in maintaining CSCs phenotypes and drug resistance properties in other cancers.



Normally, Notch signaling orchestrates the balance between self-renewal and differentiation to maintain the stem cell population in epithelium layer. Targeting the Notch signalling individually does not affect the viability and frequency of OC-CSCs in 3D-spheroid culture. These ques led us to combine treatment of OC-CSCs with cisplatin and Notch pathway inhibitors. The co-treatment significantly abrogates the cisplatin resistance and shows its killing effects in OC-CSCs. These findings promising are towards a cure for advance and cisplatin resistance OC.

From decades, the human OC remains a major health burden for the South-East Asian population, mainly in Indian subcontinent. According to Globocan-2018, oral cavity cancer accounts for 10.4% of all new cancer cases in India. OC development is a complex multistage process. Throughout the initiation and progression of tumor there is structural and functional alteration in DNA. As a final consequence each tumor is composed of different cell types with unique tumorigenic properties.

In spite of a significant improvement of therapeutic approaches, the overall survivability remains poor for OC. Usually surgery and conventional chemotherapy before or after surgery are the treatment options. But the heartbreaking story is that eventually after years, months or even after few weeks, the tumor recurs with more aggressive behaviours.

Cancer drug resistance remains one of the biggest hurdles for therapeutic intervention in tumor progression. This results in poor response for chemotherapeutic agents. There are multiple factors that contribute to drug resistance in cancer. The emerging evidence has demonstrated that OC is originated by a specific cell type which is called CSCs. A small fraction of the overall tumor cells is represented by CSCs. These cells share common properties of multipotency and self-renewal with physiological stem cells. The ever-evolving studies are suggesting that CSCs play key roles in tumor relapse and recurrence.

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