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Singapore creates 3D models to fine-tune radiation dose for nasopharyngeal cancer

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Novel patient-derived 3D models IBN and SIAMH, reduces the chances of tumor recurrences by determining radiobiological parameters

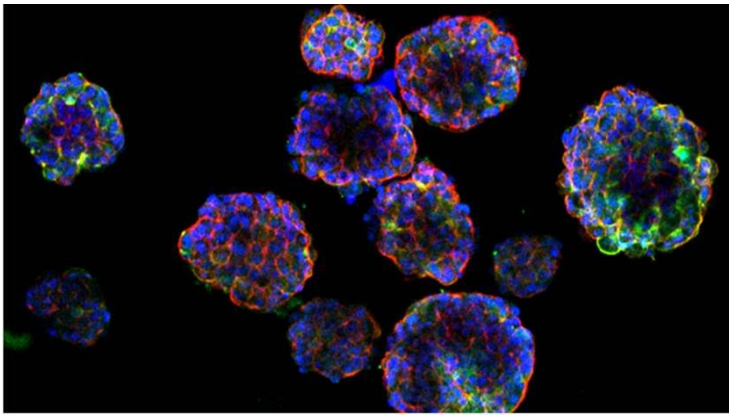


Image Caption: *Fluorescence staining of the epithelial markers of the NPC organoids*

Singapore, A*STAR's Institute of Bioengineering and Nanotechnology (IBN) has teamed up with Singapore Institute of Advanced Medicine Holdings Pte Ltd (SIAMH) to establish the first of its kind in-vitro patient-derived 3D organoid models of Nasopharyngeal Cancer (NPC).

It is the first direct experimental evidence to predict optimal Radiation Treatment (RT) boost dose required to cause sufficient damage to recurrent hypoxic (low oxygen level) NPC tumour cells, which can be further used to develop dose-painting algorithms in clinical practice.

Two patient-derived xenograft (PDX) lines were used to further establish in-vitro 3D models of hypoxic radioresistant NPC for the first time. This collaboration helps to fine-tune radiation treatment, lower the chances of recurrence of NPC and reduce the mortality rate.

The current treatment for NPC includes Radiation Treatment. There are recurrent cases that occur due to insufficient radiation. This poses a clinical challenge to the oncologists. Usually, radiotherapy is used as re-treatment on inoperable advanced recurrent cases. This results in patients having complications during treatment and the 5-year survival rate will be reduced further. The lack of disease-specific in-vitro models of NPC has further hindered the development of personalized therapeutic options.

IBN and SIAMH collaborated with the Singapore General Hospital and The Hong Kong University of Science and Technology to create the new in-vitro hypoxic 3D organoid models. These mimicked the hypoxic radioresistant sub-volumes of recurrent NPC, and were found to closely resemble NPC patient tumours.

By using novel patient-derived 3D models, IBN and SIAMH were able to determine experimentally on the radiobiological parameters which provides a better guide in radiation dosing, such that hypoxic radioresistant NPC cells could be eliminated,

thus reducing the chances of tumour recurrences.

The study has demonstrated that radiation dose escalation by about 1.4 folds to the hypoxic radioresistant areas in the tumour would further improve the outcome of the treatment. Delivering high dose radiation - in a smaller number of fractions (hypofractionated radiotherapy) may be the way to treat hypoxic radioresistant NPCs. This could reduce long-term side effects, mortality rates due to recurrence, and improve patients' quality of life.

The use of in-vitro 3D organoid models of patient-derived xenografts for the first time opens up unlimited opportunities for further research with proton beams when it is available towards the end of 2021.

SIAMH's Proton Therapy Centre is a member of the FlashForward^{TM} Consortium and it will be extremely exciting to study the effects of Flash Therapy on hypoxic radioresistant 3D models of NPC.