30 Jun 2016 **Immediate release**

News Release

SMART advances cancer therapy – Tumour Treating Fields – with a novel microfluidic device

- Tumour Treating Fields (TTFields) are low intensity, alternating electric fields that disrupt cell division through physical interactions with key molecules during mitosis. This non-invasive treatment targets solid tumours and has been FDA-approved for Glioblastoma (brain cancer).

- SMART innovation - 3D microfluidic device with embedded electrodes - enables the application of an electric field therapy to single or aggregated cancer cells in a 3D microenvironment. This not only expedites and lowers the cost of the entire research process, but also renders customised therapy a reality as patient's own cancer cell can be injected into the microfluidic device and tested.

(L to R): PDMS microfluidic device with embedded electrodes; Lung cancer aggregates in the 3D hydrogel within device, in co-culture with non-cancerous cells; Injecting lung cancer cells into device

(Bottom pix): Images of stimulated (left) & dispersed non-stimulated cancer aggregates

1. Singapore – Cancer is prevalent in Singapore, with 37 people being diagnosed daily, according to the Singapore Cancer Society. The three known tools to fight cancer are: Surgery, radiation and chemotherapy. A novel treatment, known as Tumour Treating Fields (TTFields), is gaining traction and is FDA-approved for Glioblastoma, a type of brain cancer. Pre-clinical trials are gathering pace for breast, cervical and colorectal cancers, amongst others.

2. Having worked on microfluidic devices (integrated, portable devices that provides a 3D microenvironment for cells, allowing laboratory tests to be done swiftly) since 2012, research scientists at the Singapore-MIT Alliance for Research and Technology (SMART) [新加坡-麻省理工学院科研中心] have engineered a novel 3D microfluidic culture platform for TTFields application.

3. This unique microfluidic device (2.5cm x 2.5cm), embedded with electrodes and made from PDMS (Polydimethylsiloxane), renders the application of an alternating electric field to cancer cells in a 3D environment more physiologically relevant than in standard 2D cell culture. The research showed that the metastatic prowess of cancer cells and cancer cell aggregates (akin to tumour mass) were reduced after electric field treatment. In fact, the proliferation rate of the treated cancer cell aggregates was 35% lower than the one of the untreated cells. And non-

cancer cells, like the endothelial cells (cells lining the blood vessels, closest to the cancer cells), were not significantly affected.

4. This groundbreaking research '[Engineering a 3D microfluidic culture platform for tumor-treating field application]' was published in *Nature Scientific Reports* on 24 May 2016 and validates that the system can be used to rapidly screen the effect of TTFields on cancer and non-cancer cells alike, within an in vivo-like microenvironment with the potential to optimise treatment protocols and evaluate synergies between TTFields therapy and chemotherapy.

5. Novocure (NASDAQ: NVCR), a commercial-stage oncology company developing a novel solid tumour cancer therapy – TTFields - received FDA approval of Optune in 2015 for newly diagnosed glioblastoma in combination with temozolomide; and in 2011 for recurrent glioblastoma as a monotherapy. With SMART innovation, research of TTFields for other solid tumor cancers could be expedited and performed at a lower cost as only a small volume of reagents (such as cells, media, hydrogels and drugs) are needed.

6. Each microfluidic device cost less than S$1 (material cost only) and the experiments in the microfluidic device lasted three days. The alternatives –experiments in a mouse model– would require more time, effort and resources.

7. On the possibility of customising individualised treatment for patients, lead author and research scientist at SMART BioSystems and Micromechanics (BioSyM) Interdisciplinary Research Group (IRG), Dr Andrea Pavesi [安德日亚], said: "By leveraging this device, doctors can actually test the intensity of electric fields needed for each different patient before dispensing the right settings for each TTFields patient. This increases the efficacy of each patient's treatment."

8. Co-lead author and research scientist at SMART BioSyM, Dr Giulia Adriani (吉乌利亚), adds: "The fact that this device is able to host cancer cell aggregates, mimicking a 3D malignant tumour mass, as opposed to other standard *in vitro* approaches using single cancer cells on a 2D petri dish, means that we are able to have a more accurate picture of how the cancer mass will react to an electric field treatment. This will allow clinicians to find the right parameters and duration of TTFields application, rendering the therapy more effective."

9. Prof Roger Kamm, SMART Principal Investigator (PI) for BioSyM, said: "Innovating a device to help expedite research in this novel cancer therapy is a way forward to help reduce the global cancer burden. Our approach provides new insights not only to the understanding of the treatment effects on cancer cells but also on healthy tissues, allowing the possible side effects of each treatment to be estimated."

10. Having worked on this research since 2015, the BioSyM team hopes to collaborate with other institutions and corporations to advance this research. This research was funded by the National Research Foundation Singapore under its Campus for Research Excellence and Technological Enterprise (CREATE) programme and was conducted with the contributions from the Singapore Immunology Network (SIgN, A*STAR).

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About Singapore-MIT Alliance for Research and Technology (SMART)
[新加坡-麻省理工学院科研中心]
Singapore-MIT Alliance for Research and Technology (SMART) is a major research enterprise established by the Massachusetts Institute of Technology (MIT) in partnership with the National Research Foundation of Singapore (NRF) since 2007. It is the first entity in the Campus for Research Excellence and Technological Enterprise (CREATE) developed by NRF.

SMART serves as an intellectual hub for research interactions between MIT and Singapore. Cutting-edge research projects in areas of interest to both Singapore and MIT are undertaken at SMART. SMART comprises an Innovation Centre and five Interdisciplinary Research Groups (IRGs): BioSystems and Micromechanics (BioSyM), Center for Environmental Sensing and Modeling (CENSAM), Infectious Diseases (ID), Future Urban Mobility (FM) and Low Energy Electronic Systems (LEES).

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