Cardiovascular dysfunction following cancer treatment greatly impacts the quality of life of cancer survivors. Dr Tetsuro Wakatsuki and his colleagues from InvivoSciences Inc. aim to develop therapeutic solutions to this problem, by exploring the cardiotoxic effects of novel anticancer drugs using pioneering technology, such as 3D-engineered micro heart tissue.

Testing the cardiotoxic effect of cancer therapies with micro-hearts

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Every 30 seconds in the United States a person is diagnosed with cancer. However, despite this depressing statistic, more people than ever are surviving the disease. Today, two out of every three patients are expected to live at least five years following their diagnosis, which corresponds to approximately 14.5 million cancer survivors in the US alone. For example, in the 1980s, the chance of surviving from breast cancer was 50:50, but now nearly 80% of patients survive. This is due to extensive research which has improved early detection, therapy and medication development.

However, length of survival is variable and depends on several factors, including tumour severity, the patient’s general fitness and the impact of treatment-related chronic diseases: chronic diseases, such as cardiomyopathy which affects the heart muscle, that arise as a result of treatment.

CANCER TREATMENT-RELATED CARDIAC DYSFUNCTION

Intensive cancer treatments can unfortunately have an adverse cardiovascular impact. For example, chemotherapy greatly weakens the heart muscle, and radiation results in cardiotoxic effects such as heart inflammation, atherosclerosis and rhythm disorders. Anticancer medication such as tyrosine kinase inhibitors (which suppress cancer cell growth), can also induce cardiomyocyte apoptosis, hypertension and congestive heart failure. Angiogenesis inhibitors (which suppress blood vessel formation, thus isolating cancerous cells and inhibiting their spread) can also cause hypertension, increasing the risk of blood clots and heart failure.

In fact, cancer-treatment-related cardiotoxicity is the third leading cause of therapy-associated mortality in cancer patients. Clearly, this severely impacts quality of life both physically and mentally – after all, it must be devastating for the cancer survivor to discover that they have another life-debilitating disease.

CARDIO-ONCOLOGY

Growing concern regarding cancer/cardioxicity comorbidity has led to the development of a novel clinical discipline – cardio-oncology. The aim of this emerging field is to investigate the physiological mechanisms that cause cardiovascular disorders in patients undergoing cancer treatment, to improve detection and prevention of these heart defects and

Cardio-oncologists face many challenges. There is a shortage of hospital funding; a lack of training opportunities; limited awareness; and inadequate research relating to the relationship between cancer, therapies and the heart.
Cardiovascular Stem cells

develop effective treatments. It is also essential that a balance is established between cancer elimination and cardiovascular protection.

However, cardio-oncologists face many challenges, mainly due to the novelty of the field. For example, there is a shortage of hospital funding to develop cardio-oncology units; a lack of opportunities for education and training; limited awareness regarding cardio-oncology; and inadequate research relating to the relationship between cancer, therapies and the heart. Most importantly, there is no simple diagnostic tool to monitor the impact of cancer treatment on cardiovascular damage caused by cancer treatment.

INVIVOSCIENCES
InvivoSciences (IVS), established in 2001, aims to tackle these problems. The ground-breaking research of Dr Wakatsuki and his colleagues explores potential solutions to cardiovascular issues, using innovative cardiac safety assessments. The team at IVS use their award-winning technology – laboratory-made human micro heart tissue called NuHeart™ – to test the effects of potential new anticancer drugs on cardiac safety. According to the U.S. Food and Drug Administration (FDA), effective drugs which have minimum impact on heart health should be used as a first-line treatment to newly diagnosed cancer patients.

Induced pluripotent stem cells (iPSCs) are the foundation of all the technological services that IVS offers. Patient-specific adult cells in blood, or even urine, samples can be reprogrammed into a pluripotent state. This means that the cell has the potential to differentiate into many different cell types in the body, including cardiomyocytes in the heart.

In collaboration with the FDA National Center for Toxicological Research (NCTR) in Jefferson, Arkansas, where he currently works as the Co-Founder and Chief Scientific Officer, Dr Wakatsuki studied for his PhD in BioPhysics and MS in Mechanical Engineering both at Washington University. He later went on to work as Assistant Professor at the Physiology, Biotechnoloogy and Bioengineering Center at the Medical College of Wisconsin before starting full-time at InvivoSciences, whose research provides solutions to cardio-oncology projects.

RESEARCH OBJECTIVES
Dr Wakatsuki’s research focuses on 3D engineered micro heart tissues and their applications to issues seen during and after cancer treatments. He is the co-founder of InvivoSciences – a company whose research provides solutions to cardiac issues.

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COLLABORATORS
FDA National Center for Toxicological Research (NCTR) in Jefferson, Arkansas

BIO
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Why do different cancer treatments result in cardiovascular dysfunction?

There are two different reasons; one is that target and non-target drugs can have cardio-safety risk. The other is that other toxic drugs cannot compromise cardiac safety, the team at InvivoSciences are taking science one step further to detecting cardiovascular dysfunction earlier by identifying novel anticancer drugs that could compromise cardiac safety, the team at InvivoSciences are taking science one step further to detecting cardiovascular dysfunction earlier by identifying novel anticancer drugs that could compromise cardiac safety, the team at InvivoSciences are taking science one step further to detecting cardiovascular dysfunction earlier by identifying novel anticancer drugs that could compromise cardiac safety, the team at InvivoSciences are taking science one step further to detecting cardiovascular dysfunction earlier by identifying novel anticancer drugs that could compromise cardiac safety.