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Geraniin extracted from the nephelium lappaceum (rambutan) rind inhibits dengue virus type-2

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The fast spread of dengue pandemic especially in tropical countries is worrisome. The number of occurrences and amount of individuals being infected with dengue fever is growing every year. Despite its fast spread, there is yet no effective vaccine or antiviral drugs available. Nephelium lappaceum, or rambutan, is a type of fruit which can be found in abundance in Malaysia and other regions of tropical Southeast Asia. Consumption of rambutan results in the production of waste from its seed and rind. Currently, many reports have shown the various biological activities such as antioxidant, antimicrobial and anti-inflammatory of geraniin extracted from natural sources. Geraniin has also been shown to be the major compound found in the extract of rambutan rind. In this study, the antiviral activity of geraniin extracted from the rambutan rind against dengue virus type-2 (DENV-2) was investigated. Using plaque reduction assay, it was shown that geraniin possessed inhibitory potential towards DENV-2 with the mechanism of inhibiting its attachment to cells. The stage of DENV-2 replication cycle where geraniin impose its inhibitory action was also determined through the time-of-addition assay. Through this assay, it was shown that geraniin exhibits its inhibitory potential on DENV-2 at the early stage of DENV-2 life cycle, which primarily involves the envelope (E) protein. Docking study showed that geraniin interacts with this major protein. In conclusion, geraniin from the rind of Nephelium lappaceum possesses antiviral activity against DENV-2 through the mechanism of inhibiting viral attachment, most probably by binding to the E protein, hence disrupting the infection process.

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Preclinical drug discovery with patient-specific engineered heart tissues

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American healthcare system spends >$200 billion in cardiovascular treatment. Inter-individual variability in efficacy and toxicity response is rather large for cardiovascular treatments. InvivoSciences has developed an in vitro disease model that recapitulates individual patient's cardiomyopathy in engineered heart tissues (EHTs) using the patient-derived cells. Automated cell culture and novel cardiomyocyte-differentiation protocol improved the productivity and reproducibility for generating patient-specific disease models for drug and diagnostics development.

The application of our technology to establish a patient-specific disease model for a rare disease, Muscular Dystrophy (MD), will be discussed. While the exon skipping treatment could finally overcome skeletal muscle wasting of Duchenne muscular dystrophy (DMD), it depends on skeletal muscle's high regenerative capacity. Therefore, the limited regenerative capacity of cardiac muscle encounters challenges for treating DMD heart failure, which was recognized only recently. Mass-produced micro-scale EHTs from patient-derived cardiomyocytes using induced pluripotent stem cell technology recapitulate a patient-specific DMD heart failure phenotype in vitro and screen compounds for drug discovery. A detection of slowly developing DMD cardiac phenotypes in EHTs was required to comprehensively analyze their excitation-contraction-energy coupling (ECEC) by measuring their action potential, calcium transient, cardiac contractility, and mitochondrial metabolism by a high-throughput assay device under various stress conditions. Combining multi-scale (i.e., molecule to whole body) computational models of human physiology with the ECEC analysis of EHTs will predict clinical outcomes (e.g., cardiotoxicity and efficacy) of a potential treatment at the preclinical stage. The project will support discovery of disease mechanisms to identify potential targets for therapy

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