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Self morphogenesis of pluripotent stem cells into cardioids

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Embryogenesis is an ordered yet knotty process that displays crucial stages of the development of primitive cells into complex compartmental tissues. Learning the subtleties of this process is essential to mimic nature in vitro. With the advent of stem cell technology, the urge to recreate and simulate embryonic conditions to make stem cells develop into healthy tissues and organs propelled researchers to solve the mysteries of embryology. Establishing organoid cultures in laboratories, such as brain organoids, optic cup organoids for the eye and gut organoids for intestines is a novel approach. However, developing heart organoids has posed many hurdles on account of the cardiac organisation being the first to develop during foetal development consequently with the most complexities. Recently, scientists revealed self-organising assemblies of human pluripotent stem cells (hPSCs) by temporally controlling key cardiogenic signalling pathways, such as WNT, ACTIVIN and BMP using a differential approach into what are being called cardioids. These recapitulated developmental conditions differentiated hPSCs into cardiac mesoderm and beating cardiomyocyte progenitors in 2D culture.

The miraculous self-assembly into hollow beating 3D structures was observed post addition of laminins prior to mesoderm induction. These cardioids expressed TNNT2 cardiomyocyte markers (CM) after several days of differentiation. As a result, rapid and reproducible self-assembled structures produced cavity-containing beating organoids positive for the CM markers. To replace existing animal models as in vitro blueprints of human diseases and associated cascades, organoids are a perfect candidate. Cardioids engineered with the newest genome editing tools such as CRISPR-cas9 provide a direct observation of the onset of congenital cyanotic and acyanotic heart defects including the growth of improper valves and weak endocardium. Congenital cardiac conditions can be confirmed with the help of cardioids. Alternatively, the drugs being discovered could be tested for efficacy and toxicity on 3D-human heart models established by growing cardioids successfully. A definitive future thus lies beyond current proceedings and must be pursued actively by researchers to achieve exceptional milestones.

Keywords: Organogenesis, Morphogenesis, Induced pluripotent stem cells, Cardiomyocyte progenitors, Self-assembly

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