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Evaluation of the therapeutic potential of a CDK9-inhibiting compound in human hypertrophic cardiomyopathy using hESC-derived cardiomyocytes

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Hypertrophic Cardiomyopathy (HCM) is a prevalent form of cardiovascular disease (CVD) characterized by enlargement of the myocardium of the heart as a result of increased cardio-myocyte cell volume. This elevation in cellular volume caused by hypertrophic stimuli, results in thickening of the ventricular walls, which can proceed to impairment of cardiac contractility and functionality, and ultimately lead to sudden cardiac arrest. Presently, the disease is reported to cause 36% of CVD-related deaths in competitive athletes and a curative pharmacological treatment is yet to be established. Recent research has identified involvement of the cyclin-dependent kinase 9 (CDK9)-related pathway as a fundamental factor in the induction of HCM. Through the hormonal induction of HCM within novel 'mini-heart' organ models consisting of human embryonic stem-cell (hESC)-derived cardiomyocytes, the effectiveness of the novel anti-cancer drug, CYC202, at preventing the onset of human HCM was evaluated. Our data has demonstrated that CYC202, a CDK9-inhibiting compound, targets the effects of Ang II and ET-1 stimulated hypertrophic growth in hESC-cardiomyocytes. The compound was successful in preventing the onset of hypertrophic growth through inactivation of CDK9. The 'mini-heart' cell-based assay holds great promise in bringing new and effective cardiovascular treatments to the market through providing an improved testing platform for pre-clinical drug screening, which is scalable, reproducible and from an inexhaustible source. Further research into the pharmacokinetics of CYC202 is required before potentially progressing to phase-I clinical trials and the development of a medical therapeutic for HCM in patients at high risk of developing the disease.

Biography

Kirsty Lewis completed her Bachelor's degree from Abertay University Dundee, where she gained first-class honors in Applied Biomedical Science. During her degree, she published a paper in a scientific journal, and is currently working as a Research Assistant within Professor Nikolai Zhelev's research group at Abertay University. Her main interests surround the use of stem cells in drug discovery and development in the field of cardiology.

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