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Editorial

# Knowns and unknowns of coronary artery development and anomalies

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Sudden cardiac death is the number one killer in the world and affects about 230,000–350,000 Americans every year. Among those patients, coronary artery disease is the majority cause of death of elder patients. Coronary artery diseases involve atherosclerotic plaque in the main coronary arteries, which block the coronary blood flow and lead to ischemic heart injury and thereafter heart failure. A lot of effort has been devoted toward the revascularization in the ischemic heart and cardiac regeneration after myocardial infarction, but the clinical effect is modest. A better understanding of the coronary development and regulation of coronary growth will lead to new approaches to treat ischemic heart diseases.

In the younger patients of sudden cardiac death, coronary artery anomalies are the second most common cause [1,2]. Congenital or acquired coronary anomalies are rare, with the incidence from 0.7% in autopsy cases to 1.2% in angiographically evaluated cases. Around 20% of coronary anomalies lead to life-threaten symptoms [3]. Preclinical coronary anomalies in infants and children are unexpected. It is essential to diagnose this silent myocardial ischemia in time, but it is challenging because younger patients do not have the typical symptoms of adult coronary artery diseases [4].

Despite the importance and potential relevance of clinical implications, coronary artery development and anomalies have been understudied. In this issue, a review article titled "Embryology of coronary arteries and anatomy/pathophysiology of coronary anomalies. A comprehensive update [5]" from Drs. Tomanek and Angelini, two world-renown experts in the field, covers this timely topic of coronary artery development and anomalies. The review provides a concise and comprehensive overview on the development and diseases of the coronary vascular system and underlying mechanism of normal and abnormal formation of the coronary arterial system. Update of newer methods of coronary development in animals and humans is well integrated with clinical relevance of coronary anomalies, such as the newly recognized entity "left ventricular noncompaction" and fixed *versus* phasic stenosis or intermittent spasm.

With the new technology of transgenic mice (for lineage tracing) and fluorescent imaging systems, a lot of progress has been made toward understand coronary development, including the cellular origin of coronary artery and the progenitor cells that build it. Progenitors for coronary vessels have been identified within the endocardium, epicardium, and sinus venosus. Also, the cellular and molecular programs that regulate coronary artery development also have been elucidated [6]. But other challenges remain: 1) How do different progenitor cells or transcription factors orchestrate during coronary vascular development? It is challenging to get a 3D fluorescent view of coronary vasculatures *via* lineage tracing with the limitations of imaging of the whole adult mouse heart: the technical issues of clearing the muscular heart and high fluorescent background of cardiac tissue [7]; 2) How does the coronary blood flow affect the remodeling and maturation of coronary artery postnatally? How can we study it *in vivo*? Interestingly, more progress has been made on studying the cerebral vessels *in vivo*. With two-photon laser scanning microscopy and cranial windows, both blood flow and the activity of individual cells below the surface of the brain of rodent can be imaging *in vivo* [8]. Unlike cerebral blood flow, coronary blood flow is hard to image *in vivo* because of higher heart beating rate; 3) How does genetic, epigenetic and metabolic change regulate the coronary artery growth and arteriogenesis or collateral growth? Coronary collateral growth is a nature bypass in the ischemic heart. Well-developed collaterals can restore blood flow in the ischemic myocardium, reduce ischemic injury and preserve cardiac function during occlusion of coronary arteries [9].

To overcome these barriers, research from multiple disciplines of development, stem cell biology, genetics, physiology, and advanced imaging techniques are needed in the future. The development and anomalies of coronary artery are an important field for cardiovascular repair and regeneration. More insight into this process will lead to novel therapeutic strategies for coronary diseases and sudden cardiac death.

## Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

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