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Ge, Y.

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Modeling of the Cardiac Sympathetic Nervous System and the Contribution of Epicardium-derived Cells

1. A significant role of the epicardium in adequate cardiac structure and function has been shown in both the developing and regenerating heart. (*Pharmacological Research*, volume 127, Pages 129-140, 2018)
2. Epicardium-derived cells promote cardiac sympathetic innervation *in vitro*. (*this thesis*)
3. “The predominance of common types of cardiometabolic disorders such as heart failure, atrial fibrillation and ischemic heart disease is sex specific; our identification of these and the underlying mechanisms is only just emerging.” (*Nature Medicine*, volume 25, pages1657–1666, 2019)
4. Male epicardium-derived cells (EPDCs) display a higher stimulatory effect on cardiac sympathetic nerve outgrowth as compared to female EPDCs. (*this thesis*)
5. “Deleterious neural remodeling at the level of the stellate ganglion in response to myocardial injury and the subsequent increase in sympathetic nerve activity may be critical elements in the arrhythmogenicity of sympathetic nerves.” (*J Am Coll Cardiol*. 2012 Mar 6; 59(10): 962–964)
6. Although stellate ganglia have obtained great attention in cardiac research, the superior cervical ganglia, that interact closely with the carotid body and nodose ganglion, have a significant role in cardiac autonomic function and should not be ignored. (*this thesis*)
7. After myocardial infarction, neuronal remodeling in superior cervical ganglia occurs, accompanied by an increase in expression of neurotrophic factors in the adjacent carotid body. (*this thesis*)
8. “The scale and capabilities of single-cell RNA-sequencing methods have expanded rapidly in recent years, enabling major discoveries and large-scale cell mapping efforts.” (*Nature Biotechnology*. volume38, pages737–746, 2020)
9. Single-nucleus RNA sequencing data provides insight into the heterogenous composition and gene expression of cardiac sympathetic ganglia in a healthy

state, which provides a resource for further disease-oriented studies. (*this thesis*)

10. We can always learn from others if we intent to.

11. We work in the dark - we do what we can - we give what we have. Our doubt is our passion, and our passion is our task. The rest is the madness of art. (Henry James 1843 –1916) Scientific research is just like working on a black box, effort and passion guide us closer to the truth.

12. 合抱之木，生于毫末；九层之台，起于累土；千里之行，始于足下。
（老子《道德经》） Every big project must start from the very first thought and attempt.

Yang Ge, Leiden, 15 December 2021