Ping Zhou et al., J Obes Weight Loss Ther 2018, Volume 8
DOI: 10.4172/2165-7904-C6-072

Notoginsenoside R1 attenuates diabetic retinopathy *via* TFEB-dependent enhancement of mitophagy flux

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A growing evidence have proved that dysfunction of mitophagy in retinal micro-vascular endothelial cells is associated with Diabetic Retinopathy (DR). Notoginsenoside R1 (NGR1) is isolated from *P. notoginseng* and has many pharmacological effects such as anti-inflammatory, anti-oxidative and anti-apoptotic properties. However, its protective effects on DR and the underlying mechanism are still unknown. In the present study, we found that NGR1 could significantly attenuate DR in db/db mice, characterized by the reduced micro-aneurysm in the retina and increased amplitudes of B-wave. NGR1 pretreatment also significantly inhibited apoptosis in RF/6A cell model of hyperglycemia, which were detected by TUNEL and Annexin V/PI staining. NGR1 markedly reduced the production of VEGF, remarkably augmented the level of PEDF and significantly suppressed oxidative stress and inflammation in RF/6A cells exposed to HG and the retinas of db/db mice. Moreover, the increased PINK1 and Parkin expression, the elevated LC3-II/LC3-I ratio, and the lessened p62/SQTSM1 expression were observed in NGR1-treated RF/6A cells exposed to HG and the retinas of NGR1-treated db/db mice. Furthermore, NGR1 pretreatment promoted TFEB nuclear translocation, which resulted in up-regulation of LAMP-1 in RF/6A cells and the retinas of db/db mice. NGR1 pretreatment also increased co-localization of LAMP-1 and Tomm20 in RF/6A cells. Importantly, the knockdown of TFEB could abolish these protective effects of NGR1. In summary, these results demonstrated that NGR1 protected against DR *via* TFEB-dependent enhancement of mitophagy flux.

Biography

Ping Zhou is currently pursuing her PhD from the Institute of Medicinal Plant Development, Peking Union Medical College, Beijing, China. She has majored in Pharmacology of Traditional Chinese Medicine and her main focus is on the study of pathogenesis of diabetes and its complications and the protective effect of *Panax notoginseng*.

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