AB035. Lactate receptor GPR81 modulates epigenetic modification in the subretina

Xiaojuan Yang[1], Raphael Rouget[2], Tang Zhu[2], Christiane Quiniou[2,3], Shasha Lv[4], Suna Jung[4], Francois Duhamel[2,3], Houda Tahiri[5], Samy Omri[5], Baraa Noueihed[1], Xin Hou[3], José Carlos Rivera[5], Mathieu Nadeau-Vallée[2], Pierre Lachapelle[4], Sylvain Chemtob[1,2,3,5,6,7]

[1]Department of Pharmacology, McGill University, Montréal, QC, Canada; [2]Department of Pharmacology, [3]Research Center CHU Sainte-Justine, Université de Montréal, Montréal, QC, Canada; [4]Department of Ophthalmology and Neurology-Neurosurgery, Montréal Children's Hospital-Research Institute, McGill University, Montréal, QC, Canada; [5]Research Center Hôpital Maisonneuve-Rosemont, [6]Department of Ophthalmology, [7]Department of Pediatrics, Université de Montréal, Montréal, QC, Canada

Background: Retinal pigment epithelium (RPE) is vital for the homeostasis of the subretina including photoreceptors and choroid. Interestingly, our previous results suggested that the recently discovered lactate receptor GPR81 is abundantly expressed in RPE. To date, only one previous study has shown that activating GPR81 could enhance DNA repair by activating HDAC1. Consequently, we investigated whether GPR81 exhibits epigenetic modification in the subretina by using GPR81–/– mice.
Methods: GPR81–/– mice and wide type littermates were generated on a background of C57BL/6J mice. The thicknesses of their choroid were evaluated by immunohistochemistry. Meanwhile, Q-PCR, western blot and choroid sprout assay were performed. *In vitro*, primary retinal pigment epithelium (pRPE) cells were isolated from mice, and cultured for treatments.
Results: The thickness of choroid was reduced in GPR81–/– mice compared to GPR81+/+ mice, suggesting that GPR81 is important for the integrity of choroid. In the choroid sprout assay, lactate treated RPE/choroid complex showed a significant increase in angiogenesis compared to controls while lactate treated KO RPE/choroid complex showed no difference compared to their controls. For Q-PCR, most of the genes screened elevated their expression in GPR81–/– mice compared to WT mice, suggesting epigenetic modification may exist, which were confirmed by histone acetylation and HDACs activity assay.
Conclusions: Taking together, the lactate receptor GPR81 in RPE is very important for maintaining homeostasis of the subretina. This novel discovery sheds new light on the relationship between metabolism and epigenetic modification.
Keywords: Subretina; GPR81; epigenetic modification

doi: 10.21037/aes.2018.AB035
Cite this abstract as: Yang X, Rouget R, Zhu T, Quiniou C, Lv S, Jung S, Duhamel F, Tahiri H, Omri S, Noueihed B, Hou X, Rivera JC, Nadeau-Vallée M, Lachapelle P, Chemtob S. Lactate receptor GPR81 modulates epigenetic modification in the subretina. Ann Eye Sci 2018;3:AB035.

