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Hypoglycemia induces in vivo autophagy in mouse retinal ganglion cells

Abstract:

We studied the role of acute hypoglycemia in the mouse retina and we previously showed, that hypoglycemia induced ER stress and retinal cell death in mice. In addition, we showed that low glucose conditions are associated with autophagy defects in 661W photoreceptor cells and retinal explants, which led us to study autophagy in vivo. We used GFP-LC3+/- and C57BL/6 mice to assess and decipher the mechanism of hypoglycemia-induced autophagy in vivo. Retinal explants cultured at low glucose condition showed LC3-II accumulation (GFP fluorescence dots) characteristic of autophagy activation; a similar pattern was observed with autophagy modulators (Chloroquine, Rapamycin). Intra-ocular injection of Rapamycin, as well as 5-hour hypoglycemia, gave similar results, namely a high level of fluorescence specifically to the ganglion cell layer (GCL). We co-localized GFP fluorescence with two markers of GCL. We then isolated retinal ganglion cells (RGCs) and showed an increase of p62 protein expression and GFP dots when they were cultured at 1mM or 25mM in the presence of Rapamycin, while no sign of autophagy was detected at 5mM or 25mM glucose. We then assess autophagosome/lysosome fusion on C57BL/6 isolated RGCs infected with RFP-GFP-LC3 lentivirus and cultured at different conditions. We observed a defect in the fusion process only at 1mM and 25mM in the presence of Chloroquine, but a normal fusion at 5 and 25mM glucose. We showed that hypoglycemia induces autophagy in mouse RGCs. The modulation of this pathway, as well as apoptotic pathways, might be important to avoid complications in diabetes, especially diabetic retinopathy.

Biography

After a PhD thesis performed in the laboratory of Prof. Bernard Thorens at Lausanne University, Switzerland, Dr Roduit spent five years in Montreal for a prolific post-doc in the laboratory of Prof. Marc Prentki, "centre de recherche CHUM". After his return to Switzerland and spending five years as co-responsible of the laboratory of Dr Bonny (CHUV), he moved to the Institute for Research in Ophthalmology in Sion, Switzerland, where he rapidly created his proper research group focus on Diabetic Retinopathy (DR) and age-related macular degeneration (AMD). He joined the Jules-Gonin Eye Hospital, in 2015 where he pursue his research.