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## PARP1 activation impedes survival aspect of autophagy upon oxidative stress in RPE cells

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Degeneration of retinal pigment epithelial (RPE) cells is crucial in the progression of dry age-related macular degeneration (dry-AMD). Here, we investigated the status of autophagy and found that autophagic flux was downregulated in human cultured RPE cells (ARPE-19) upon H<sub>2</sub>O<sub>2</sub>. Furthermore, autophagic inhibition sensitized ARPE-19 cells to H<sub>2</sub>O<sub>2</sub>, implying that protective aspect of autophagy plays a significant role in RPE survival against oxidative stress. Our previous study reported that poly (ADP-ribose) polymerase 1 (PARP1)-dependent necrosis, parthanatos, plays predominant roles in the pathogenesis of dry-AMD (CDDis, 8(1):e2526, 2017). This led us to investigate whether parthanatos process is related to that of the autophagy in RPE cells under oxidative stress. To this end, we examined whether inhibition of PARP1 affects autophagy process in ARPE-19 cells. Treatment of PARP1 inhibitor, olaparib, restored autophagic flux and protected ARPE-19 cells upon H<sub>2</sub>O<sub>2</sub>. Hence, PARP1 activation accomplishes necrosis of RPE cells via suppression of survival aspect of autophagy upon H<sub>2</sub>O<sub>2</sub>. Collectively, our data demonstrate the presence of parthanatos-autophagy crosstalk in the pathogenesis of dry AMD. [This research was supported by the Bio & Medical Technology Development Program of the National Research Foundation (NRF) funded by the Korean government (MSIP) (NRF-2017M3A9C8021844).].

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