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T Helper Subset Cell Activation and Activated T Cell Autonomous Death (ACAD) Dedicated by Peptidylarginine Deiminase 2 through an ER Stress and Autophagy Mechanism

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Peptidylarginine deiminase type 2 (PADI2) is a post-translational modification enzyme that catalyzes arginine residues into the citrulline residues. Previous studies have shown that PADI2 promotes protein citrullinations in lymphocytes and it might play an important role in cell-mediated inflammation. We have found that overexpression of PADI2 promotes apoptosis in activated T cells previously. Whether does PADI2 participate in the pathway of activated T cell autonomous death (ACAD) is still curious. In this delicate PADI2-mediated ACAD study, we found that overexpression of PADI2 displayed higher levels of citrullinated protein which would induce the ER stresses significantly. The high levels of citrullinated protein results in unfolding protein response (UPR) of ER stresses and increases the huge protein degradation loading. Autophagy might embrace the engulfment and degradation capacity of the citrullinated and unfolding proteins. Herein, PADI2 could enhance autophagy in Jurkat T cells and lead to a degradation of p62 and the accumulation of LC3-II, BCEN1, ATG5 and ATG12. Autophagy and apoptosis are two critical mechanisms both which participate against cellular stresses and decide T cell activation, survival and immuno-homeostasis. PADI2-overexpressed Jurkat T cells caused the activation of Th17 cells due to the increase mRNA expression of cytokines, such as IL-17, IL-21, IL-22 and TNFα. Cytokines declined autophagy, provoked caspase cascade expression, and led to ACAD by IL-6 shRNA inspection. Simultaneously, autophagic BCEN1 could reduce Bcl-xL expression, increase caspase cascade and cause to cell insults. Knockdown of BCEN1 possibly will rescue Jurkat T cell activation, increase cytokine release and induce ACAD. We suggested that PADI2 participated in the activated T cell-induced autonomous death through triggering ER stress pathway coupling with regulating autophagic processing, and stimulating Th17 activation and the expression of cytokines by PADI2-citrullinating mechanism.

Biography

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