

EP300/H3K27AC/IDO1 SIGNALING AXIS REGULATES THE CROSSTALK BETWEEN TOLDCS AND T_{REG} CELLS TO PROMOTE LIVER REGENERATION IN ACETAMINOPHEN-INDUCED LIVER FAILURE

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Poster

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Study identifies EP300-mediated regulation of tolerogenic dendritic cells via H3K27ac/IDO1 signaling as a mechanism preserving hepatic immune homeostasis and promoting repair in acetaminophen-induced liver failure.

KEY POINTS

- Type 1 conventional dendritic cells (cDC1) were significantly reduced in both clinical AILF cohorts and mouse AILF models, with depletion magnitude showing dose- and duration-dependent associations with APAP exposure.
- cDC1 depletion impaired regulatory T cell priming capacity, disrupted hepatic immune homeostasis, and exacerbated AILF, while intravenous tolerogenic dendritic cell injection orchestrated hepatic Treg cell infiltration, attenuated inflammation, potentiated liver regeneration, and reversed AILF pathology.
- EP300-mediated histone 3 lysine 27 acetylation in the IDO1 promoter region enforced stable tolerogenic states of cDC1, which then initiated tryptophan catabolism to generate kynurenine metabolites triggering Treg cell differentiation and functional maturation.
- The therapeutic effect of tolerogenic dendritic cells was abolished after Treg cell depletion in Foxp3-DTR mice, and CD11c-cre-IDO1-f/f mice with APAP exposure had less Treg cell recruitment and worse phenotype.
- This research is relevant to investigators exploring immune-mediated mechanisms and potential therapeutic targets in acetaminophen-induced liver failure.

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