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COX-1 derived thromboxane A_2 plays an essential role in early B cell development via regulation of JAK/STAT5 signaling

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Cyclooxygenases (COXs) and their prostanoid products play important roles in a diverse range of physiological processes, including in the immune system. Here, evidence was provided that COX-1 is an essential regulator in early stages of B cell development. COX-1-deficient mice displayed systematic reduction in total B cells, which was attributed to the arrest of early B cell development from pro-B to pre-B stage. Further it was demonstrated that this defect was mediated through down-regulation of the Janus kinase/signal transducer and activator of transcription 5 (JAK/STAT5) signaling and its target genes, including Pax5, in COX-1-/- mice. Mechanistic studies revealed that COX-1 derived thromboxane A_2 (TxA_2) could regulate JAK3/STAT5 signaling through cAMP-PKA pathway, via binding with its receptor-TP. Administration of TP agonist could be able to rescue the defective B cell development and JAK/STAT5 signaling activity in COX-1-deficient mice. Moreover, administration of low-dose aspirin caused a significant reduction in total B cells in peripheral blood of healthy human volunteers, coincidentally with reduced TxA_2 production and downregulation of JAK/STAT5 signaling. Taken together, our results demonstrate that COX-1 derived TxA_2 plays a critical role in the stage transition of early B cell development through regulation of JAK/STAT5 signaling, and indicate potential immune-suppressive effect of low-dose aspirin in humans.

Biography

Jie Zhou received PhD degree (2004) in Xiangya School of Medicine, Central South Univerisity, China. She did her Postdoctoral training in University of Pittsburgh and H. Lee Moffitt Cancer Center in USA till 2009. She is Professor in Zhongshan School of Medicine, Sun Yat-sen University since 2010. Her research focuses on the mechanisms regulating immune cell differentiation (including B cell and myeloid cells), as well as their significance in immune related disorders. She has published 20 papers in peer-reviewed journals.

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