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Autonomous role of Wiskott-Aldrich Syndrome platelet deficiency in inducing autoimmunity and inflammation

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Intrinsic defect of WASp-- PLTs sustains their peripheral elimination MANUSCRIPT Sinusoidal Periphery vessel WASp PLTs Phagocytes Uptake WKO: Was KO mice +++ all blood cells WASp phagocytosis α-granule CoWas: conditional WKO mice MKs and PLTs WASp-/all other blood cells WASp+ WASp-/-Higher expression of activation markers (CD62P) and PS in WASp. PLTs. **PLTs** WASp'-PLTs CD40 **B-cells** WASp-/-MKs CD40L Increased number of MKs Normal morphology and localization Normal thrombopoiesis in vitro α-granule 8008 Autoantigens IgG anti-WASp-/- PLTs Enhanced expression and release of CD40L from WASp. PLTs activate B cells. Wasp -- PLTs are the target of Anti-PLTs Abs in WKO and CoWas. These autoAbs are specific for the mutant PLTs which have increased proteasomic activity and exposure of autoantigens. Abbreviations Was: Wiskott-Aldrich Syndrome PSGL1:P-selectin glycoprotein ligand-1 PS: Phosphatidylserine WASp: Wiskott-Aldrich Syndrome protein CD62P: P-selectin IgG: Immunoglobulin MKs: Megakaryocytes N: Neutrophils B: B-cells PLTs: Platelets MФ: Macrophages

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