

Figure 1

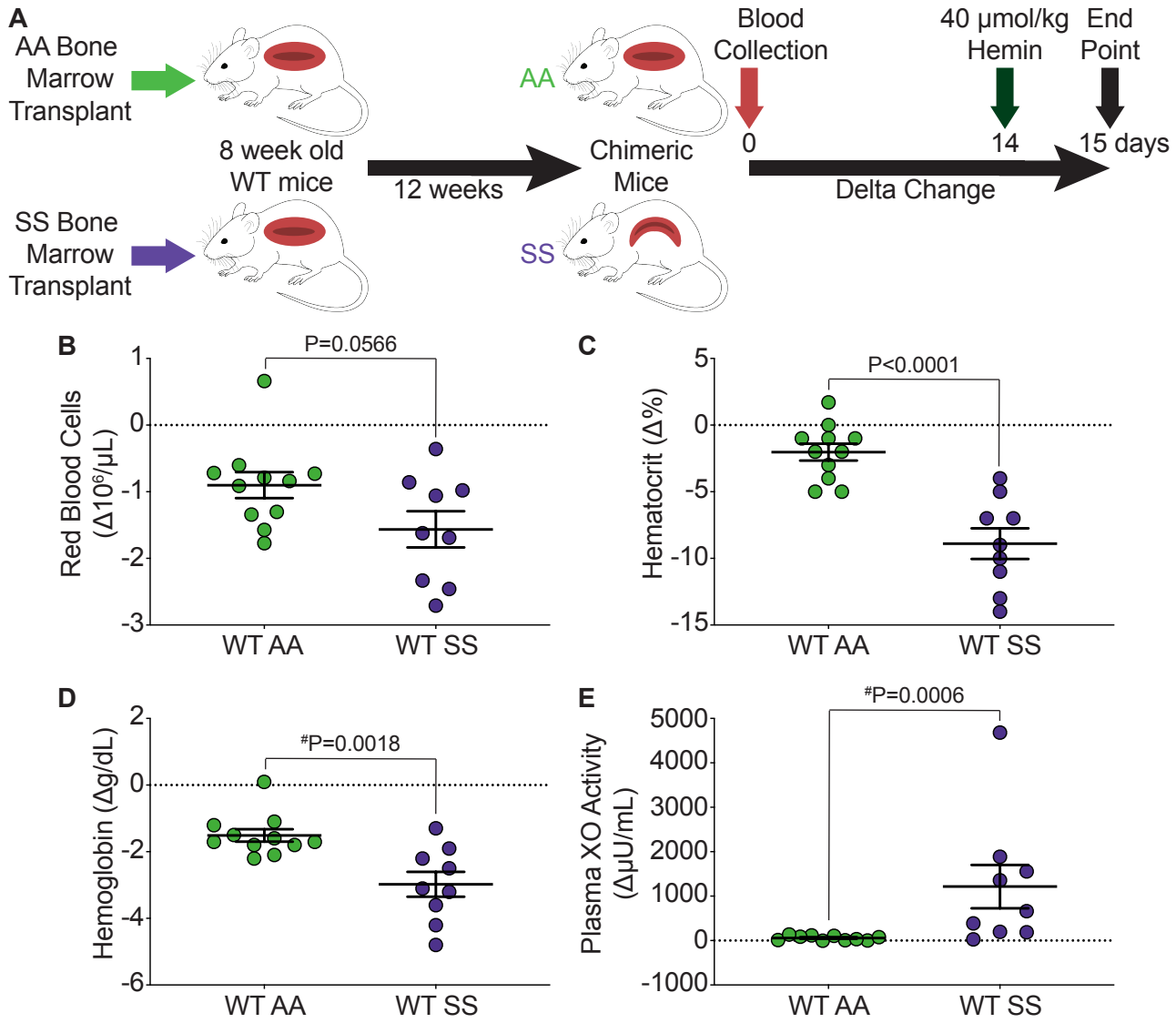


Figure 2

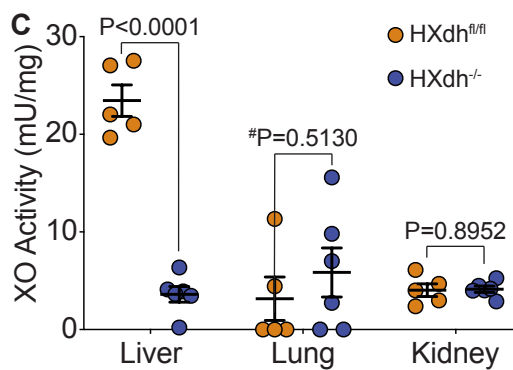
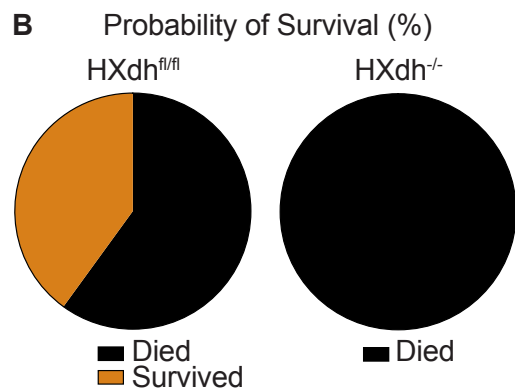
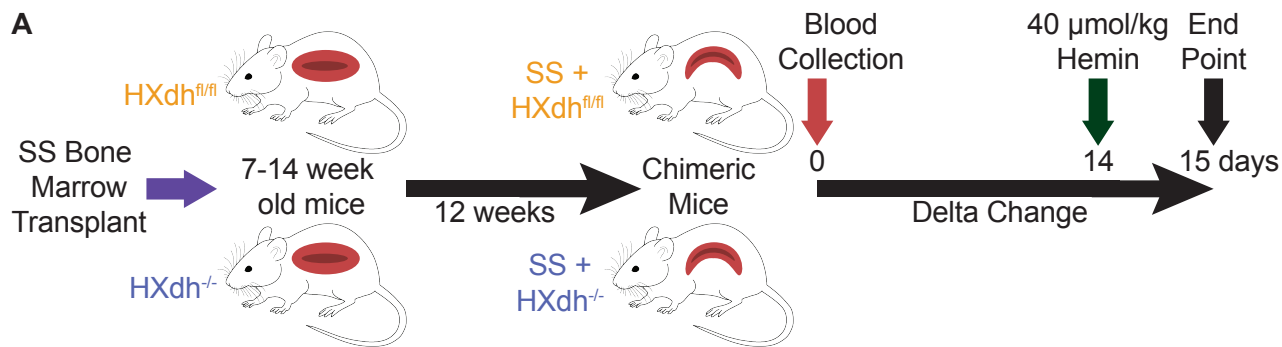


Figure 3

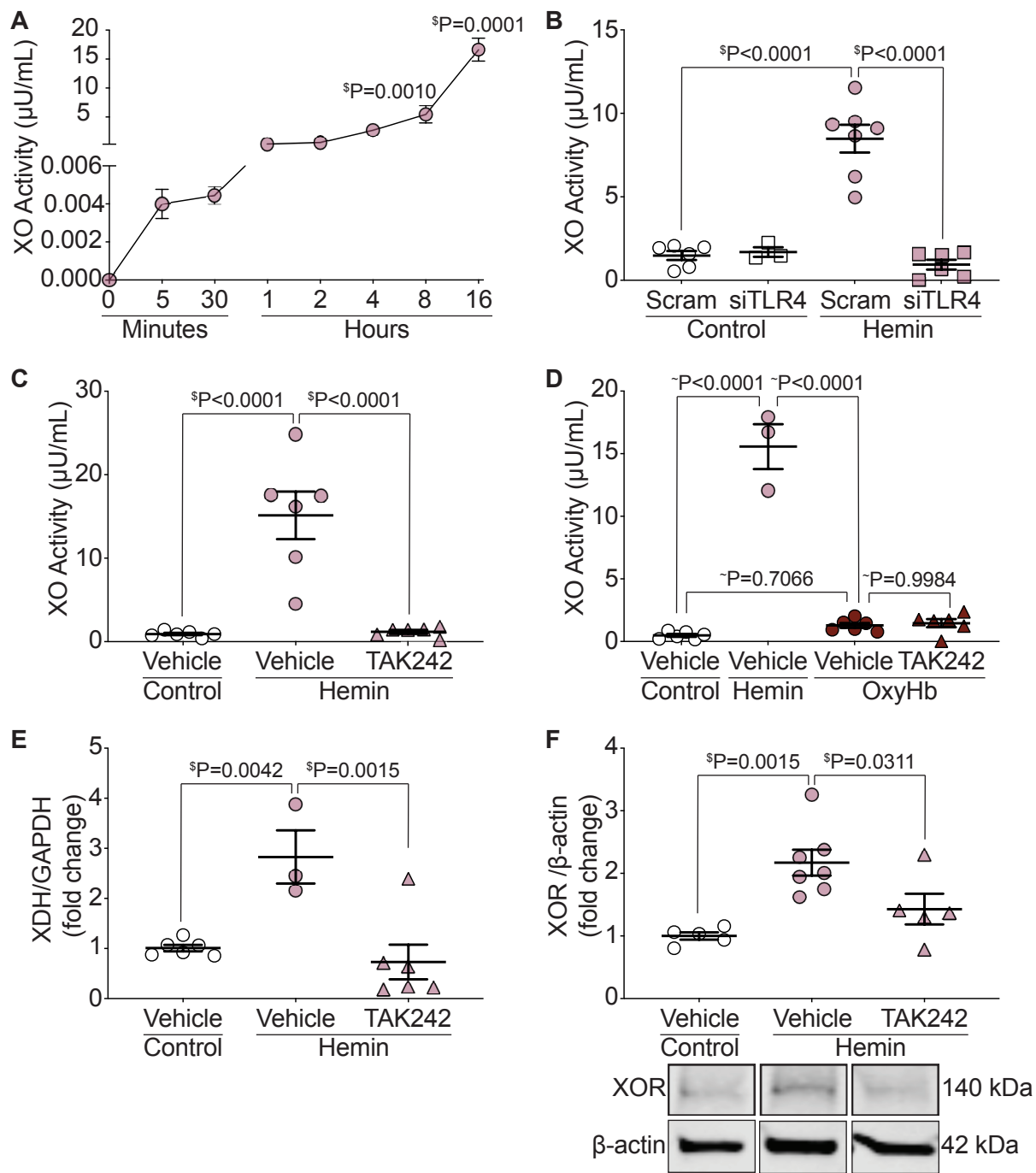
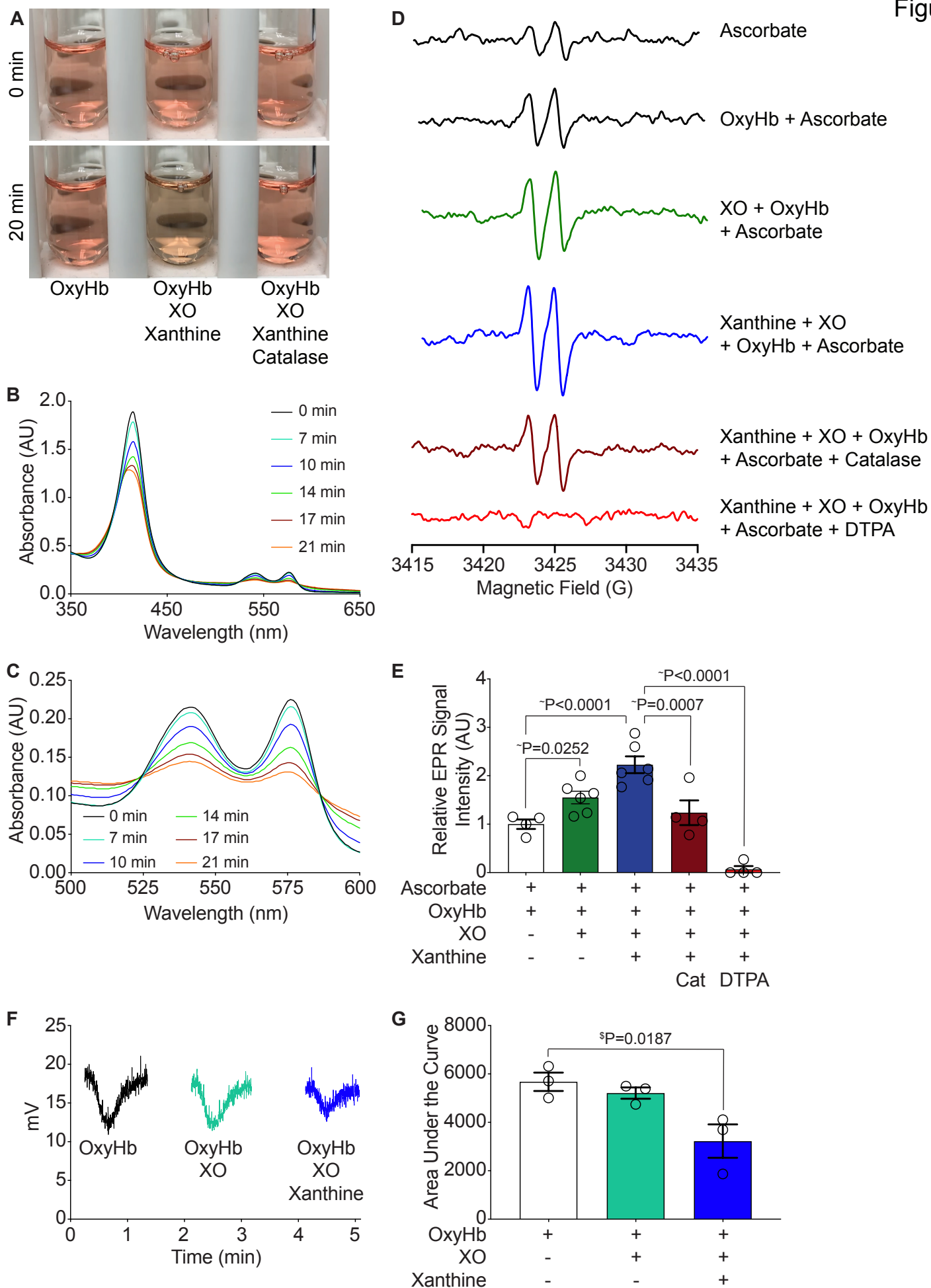
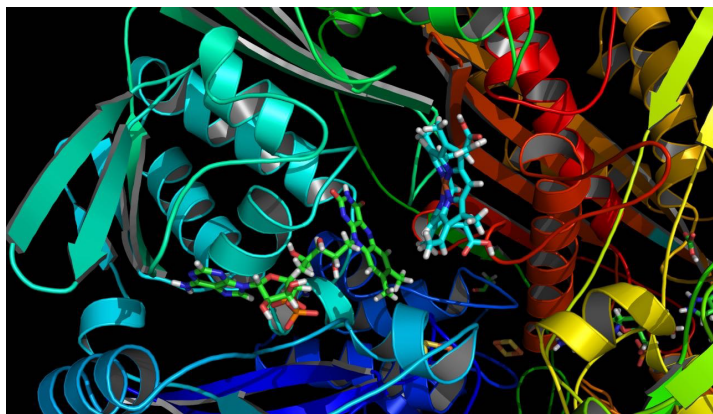


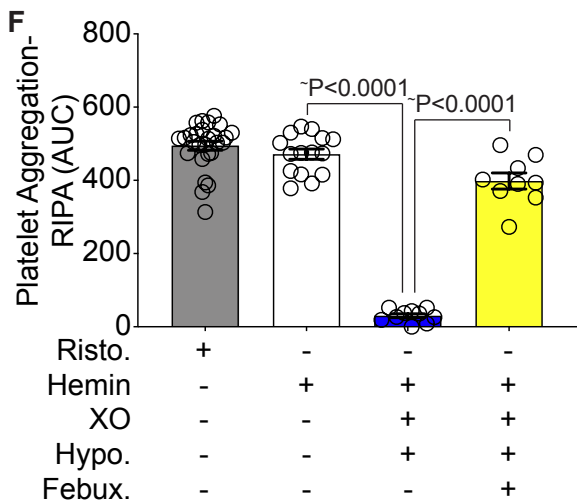
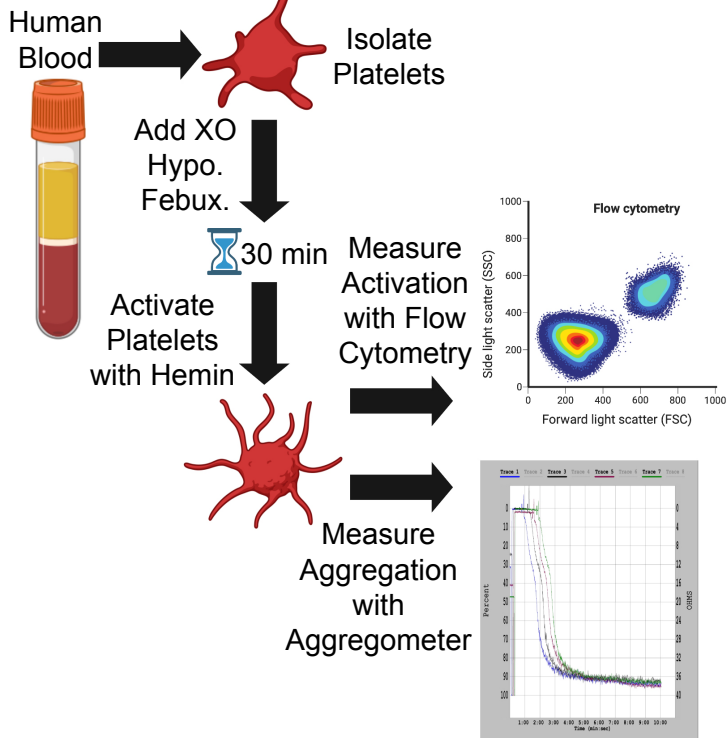
Figure 4



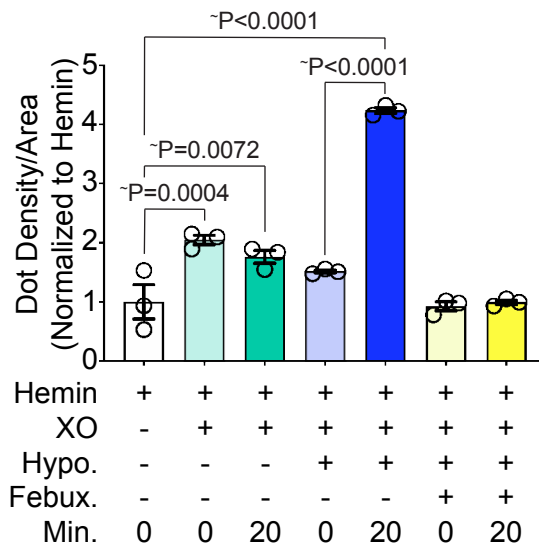
A



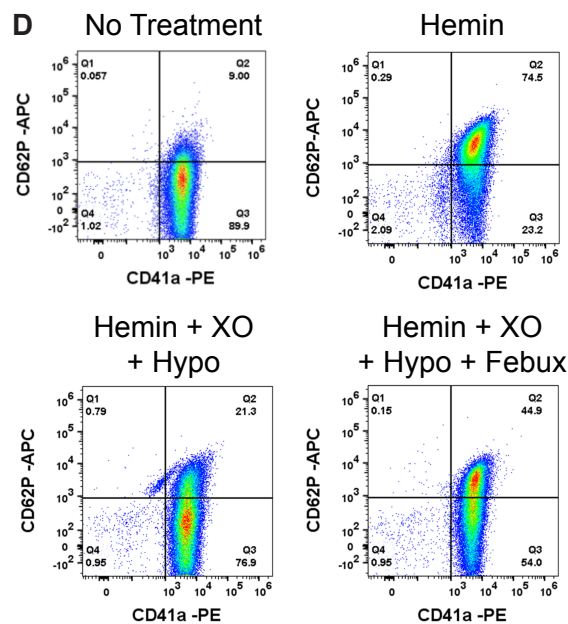
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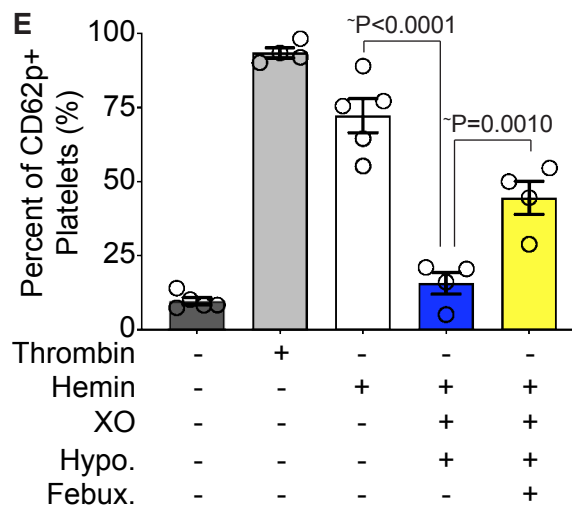
B



D



E



Supplemental Table I. Blood cell indices for Townes AA bone marrow transplanted mice at baseline and 24 hours post-hemin challenge.

	Baseline		Post-Hemin Challenge		Delta Change		Significance WT AA vs WT SS Delta Change
	WT AA (n=11)	WT SS (n=9)	WT AA (n=11)	WT SS (n=9)	WT AA (n=11)	WT SS (n=9)	
WBC, 10 ³ /μL	16.36 ± 0.96	17.44 ± 1.43	15.72 ± 1.62	17.11 ± 2.84	-0.65 ± 1.08	-0.29 ± 2.49	+P=0.8978
RBC, 10 ⁶ /μL	10.78 ± 0.19	5.65 ± 0.16	9.88 ± 0.15	4.08 ± 0.21	-0.90 ± 0.19	-1.56 ± 0.27	P=0.0566
HCT, %	35.45 ± 0.76	28.11 ± 0.70	33.64 ± 0.65	19.22 ± 0.85	-2.03 ± 0.63	-8.89 ± 1.15	P<0.0001
MCV, fl	32.79 ± 0.22	49.58 ± 0.39	33.84 ± 0.34	47.20 ± 0.54	1.05 ± 0.20	-2.38 ± 0.50	+P<0.0001
RDW, %	26.82 ± 0.50	34.89 ± 0.79	26.93 ± 0.34	37.83 ± 0.58	0.11 ± 0.29	2.94 ± 0.87	+P=0.0117
HGB, g/dL	11.91 ± 0.16	9.39 ± 0.30	10.40 ± 0.15	6.41 ± 0.31	-1.51 ± 0.19	-2.98 ± 0.37	#P=0.0018
MCH, pg	11.04 ± 0.13	16.66 ± 0.19	10.52 ± 0.08	15.79 ± 0.22	-0.52 ± 0.07	-0.87 ± 0.20	+P=0.1235
PLT, 10 ³ /μL	674.73 ± 18.16	376.56 ± 21.43	597.00 ± 31.65	351.22 ± 31.18	-77.73 ± 35.65	-25.33 ± 36.03	P=0.3194
MPV, fl	6.78 ± 0.06	6.41 ± 0.07	6.62 ± 0.10	6.70 ± 0.11	-0.16 ± 0.10	0.29 ± 0.09	P=0.0033
Retic, %	5.09 ± 0.23	50.09 ± 0.76	5.18 ± 0.25	45.99 ± 1.50	0.09 ± 0.18	-4.10 ± 1.32	+P=0.0128

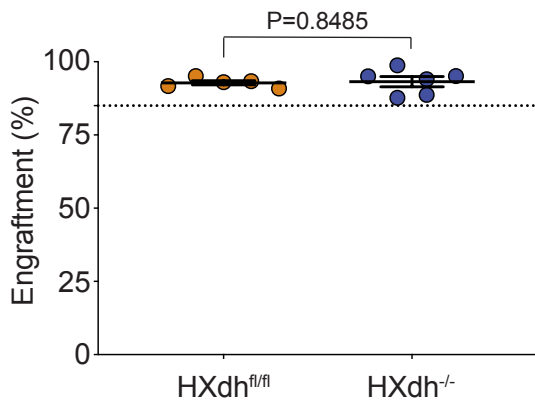
Definition of abbreviations: WBC = white blood cells; RBC = red blood cells; HCT = hematocrit; MCV = mean corpuscular volume; RDW = red blood cell distribution width; HGB = hemoglobin; MCH = mean corpuscular hemoglobin; PLT = platelets; MPV = mean platelet volume; retic = reticulocytes. Values are mean ± SEM using an unpaired Students t test unless noted otherwise (# Mann Whitney test, + unpaired Students t test with Welch's correction)

Supplemental Table II. Hemin injection significantly increased uric acid concentration and XO activity in plasma of SS sickle mice 24 hours post-hemin challenge of treatment.

	Baseline		Post-Hemin Challenge		Delta Change		Significance WT AA vs WT SS Delta Change
	WT AA (n=10)	WT SS (n=9)	WT AA (n=10)	WT SS (n=9)	WT AA (n=10)	WT SS (n=9)	
Plasma Uric Acid, μM	0.53 ± 0.15	1.91 ± 0.41	1.51 ± 0.40	22.18 ± 8.38	0.98 ± 0.28	20.27 ± 8.13	#P=0.0006
Plasma XO Activity, μUnits/mL	31.62 ± 9.03	114.65 ± 24.76	90.29 ± 24.14	1330.62 ± 502.84	58.67 ± 16.85	1215.97 ± 487.55	#P=0.0006

Definition of abbreviations: XO = xanthine oxidase. #Values are mean ± SEM using a Mann Whitney test.

Supplemental Figure 2



Supplemental Table III. Hepatocyte specific XO knockout decreased liver XO activity without impacting lung or kidney XO activity.

		Post-Hemin Challenge		Significance
		HXdh ^{f/f} (n=5)	HXdh ^{-/-} (n=6)	
Liver	Uric Acid, μM	99.76 \pm 7.37	14.24 \pm 3.20	P<0.0001
	XO Activity, mU/mg	23.46 \pm 1.61	3.62 \pm 0.81	P<0.0001
Lung	Uric Acid, μM	4.01 \pm 2.82	6.69 \pm 3.06	#P=0.3939
	XO Activity, mU/mg	3.16 \pm 2.22	5.86 \pm 2.52	#P=0.5130
Kidney	Uric Acid, μM	13.70 \pm 2.15	13.35 \pm 1.30	P=0.8898
	XO Activity, mU/mg	4.04 \pm 0.65	4.14 \pm 0.32	P=0.8952

Definition of abbreviations: XO = xanthine oxidase. Values are mean \pm SEM using an unpaired t test unless otherwise noted. #Values are mean \pm SEM using a Mann-Whitney test.

