

Supplementary Materials for

Oxytocin antagonism prevents pregnancy-associated aortic dissection in a mouse model of Marfan syndrome

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Supplementary Materials

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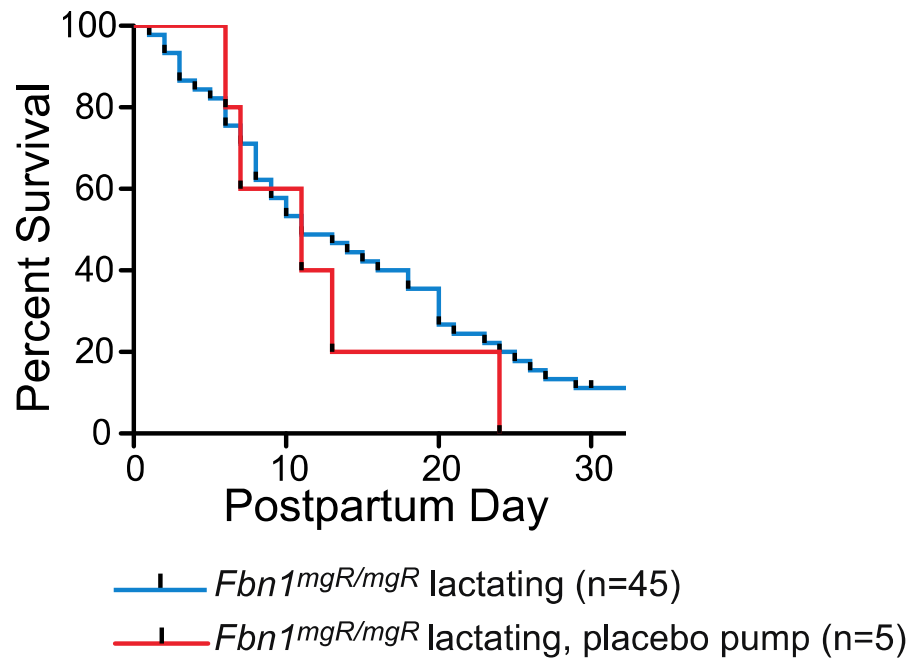


Fig. S1. Subcutaneous pump placement effect on survival. Kaplan-Meier curve demonstrating survival with (n=5) or without (n=45) implantation of subcutaneous mini osmotic pump in lactating *Fbn1^{mgR/mgR}* mice. Survival was statistically evaluated using a log-rank (Mantel-Cox) test. All significant p values ($p < 0.05$) noted on figure.

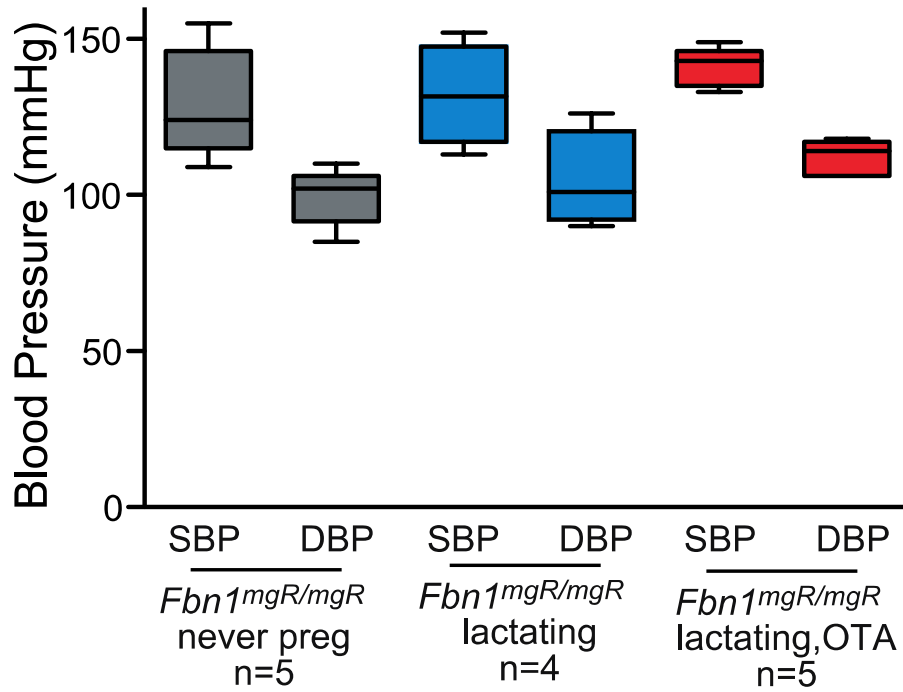


Fig. S2. Blood pressure effect in *Fbn1*^{mgR/mgR} mice. Average DBP and SBP in never pregnant (n=5), lactating (n=4), or OTA treated (n=5) *Fbn1*^{mgR/mgR} mice. The box extends from the 25th to 75th percentiles, median is denoted by the internal line, and whiskers indicate the range calculated using the Tukey method with data points outside the whiskers shown as individual points. All significant p values (p<0.05) noted on figure.

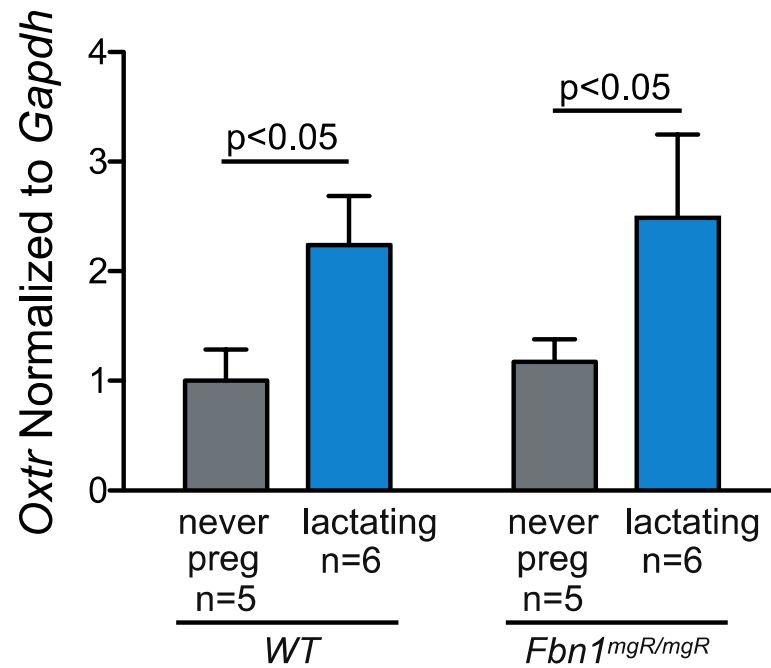


Fig. S3. OR mRNA expression in the proximal ascending aorta. Gene expression is shown for WT and *Fbn1^{mgR/mgR}* never pregnant (n=5) and lactating (n=6) mice. Data shown as mean \pm SEM, p values determined by 2-way ANOVA.

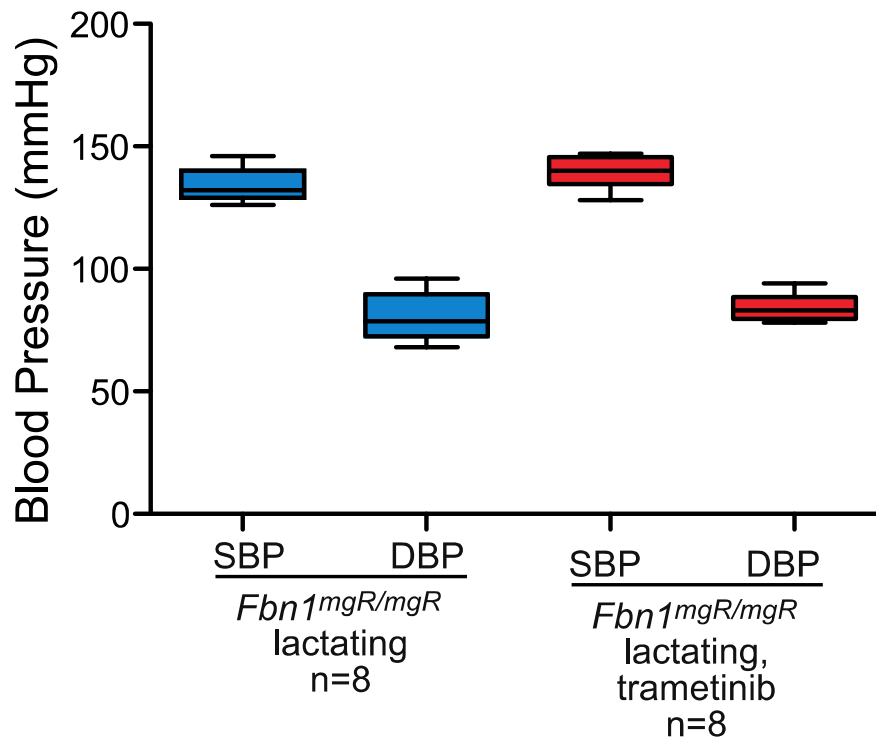


Fig. S4. Blood pressure effect in *Fbn1*^{mgR/mgR} mice. Average DBP and SBP in lactating (n=8) or OTA-treated (n=8) *Fbn1*^{mgR/mgR} mice. The box extends from the 25th to 75th percentiles, median is denoted by the internal line, and whiskers indicate the range calculated using the Tukey method with data points outside the whiskers shown as individual points. All significant p values (p<0.05) noted on figure.

Supplementary Tables

Table S1. Average aortic root and ascending aortic growth over the 7-week period spanning pregnancy and lactation in untreated mice.

WT, never preg		WT, lact		<i>Fbn1</i> mgR/mgR, never preg		<i>Fbn1</i> mgR/mgR, lact	
Root (mm)	Asc (mm)	Root (mm)	Asc (mm)	Root (mm)	Asc (mm)	Root (mm)	Asc (mm)
0.02	0.09	0.09	0.1	0.98	0.69	0.67	0.55
0.08	0.05	0.05	0.19	0.15	0.05	2.34	1.56
0.15	0.06	0.1	0.12	0.23	0.17	0.15	0.53
0.05	-0.11	0.11	0.03	0.34	0.78	0.17	0.41
-0.03	0.12	0.13	0.14	0.64	0.62	0.41	1.45
-0.02	-0.13	0.11	0.05	0.31	0.56	0.44	0.73
0.07	0.17	0.09	0.13	0.19	0.49	0.46	2.2
0.06	0.03	0.23	0.19	0.07	0.96	0.33	0.88
0.11	0.12	0.22	0.15	0.1	0.78	0.12	0.64
0.05	0.12	0.21	0.22	0.68	0.76	0.09	0.55
0.04	0.06	0.26	0.14	0.37	1.58	0.03	0.42
0.12	-0.01	0.24	0.31	0.19	0.34	0.04	0.71
-0.01	0.13	0.13	0.33	1.15	0.24	0.01	1.41
0.27	0.26	0.33	0.38	0.21	0.37	0.85	0.93
-0.01	0.02	0.2	0.4	0.09	0.62	0.02	0.29
0.11	0.26	0.26	0.27	0.56	1.87	1.33	0.4
0.07	0.07	0.28	0.16	0.36	0.94	0.44	0.35
0.14	0.26	0.15	0.15	0.19	0	0.45	0.65
0.06	0.04	0.31	0.27	1.61	0.3	0.4	1.44
0.09	-0.02	0.04	-0.03	0.54	0.07	0.19	1.25
0.02	0.09	0.14	0.41	0.57	1.69	-0.02	0.71
0.08	0.05	0.11	0.18	0.2	0.93	0.01	1.03
0.15	0.06	0.16	0.28	0.11	0.59	0.44	2.9
0.05	-0.21	0.2	0.15	0.1	-0.08	-0.1	0.54
-0.02	-0.13	0.18	0.22	0.22	0.5	0.22	1.55
0.07	0.27	0.09	0.11	0.31	0.35	0.1	0.78
0.04	0.02	0.17	0.34	0.13	0.46	0.51	0.46
0.13	0.13	0.18	0.19	0.19	0.45	0.46	2.2
0.09	0.04	0.2	0.1	0.18	0.12	0.16	0.88
0.2	0.21	0.22	0.09	0.16	-0.03	0.12	1.04
0	0.04			0.02	0.3	0.66	0.75
0.13	0.08			0.71	0.45	0.08	0.91
-0.02	0.11			0.1	0.16	0.03	1.64
				0.22	0.02	0.03	1.13
				-0.16	0.97	0.23	1.96
				0.43	1.57		
				0.18	0		
				0.27	0.14		
				0.2	0.88		
				0.31	0.56		
				0.45	0.91		
				0.08	0.43		
				0	0.61		
				0.1	0.58		
				0.21	1.93		
				0.99	0.69		
				0.11	0.01		
				0.32	0.52		
				0.12	0.43		
				0.11	0.58		
				0.2	0.35		
				-0.35	0.37		
				0.17	0.28		
				0.4	0.52		
				0.53	0.4		
				-0.03	0.12		
				0.2	0.4		
				0.1	0.39		
				0.04	0.62		
				0.07	0.1		

Table S2. Average aortic root and ascending aortic growth over the 7-week period spanning pregnancy and lactation in treated mice.

<i>Fbn1</i> mgR/mgR female, pups removed		<i>Fbn1</i> mgR/mgR, lact, OTA		<i>Fbn1</i> mgR/mgR, lact, hydral		<i>Fbn1</i> mgR/mgR, lact, propran		<i>Fbn1</i> mgR/mgR, lact, trametinib	
Root (mm)	Asc (mm)	Root (mm)	Asc (mm)	Root (mm)	Asc (mm)	Root (mm)	Asc (mm)	Root (mm)	Asc (mm)
0.02	1.11	0.16	-0.02	0.09	0.44	0.71	1.05	0.06	0.35
0.12	0.07	0.54	1.01	0.02	0.45	0.12	0.12	0.11	0.08
0.14	0.34	0.25	1.47	0.02	0.38	0.35	0.21	-0.09	0.2
0.22	0.68	0.19	0.3	0.33	0.62	0.17	2	0.16	0.84
0.23	1.31	0.75	1.07	-0.07	0.37	0.16	0.63	0.17	0.99
0.09	0.81	0.19	-0.07	0.16	0.35	0.02	2.11	0.05	1.33
0.11	0.26	0.21	0.77	0.9	0.38	0.16	0.82	0.03	-0.09
0.18	0.66	0.46	0.38	0.6	0.77			0.03	1.37
0.29	0.4	0.42	-0.05	0.11	0.3			0.3	2.07
0.01	0.54	0.2	0.64	0.29	0.48			0	0.53
0.15	0.12	0.23	0.19	0.41	0.41			0.06	1.03
0.02	0.54	0.18	0.28	0.66	0.69			0.2	0.57
0.07	0.05	0.18	-0.28	0.1	0.83			0.16	0.56
0.13	0.12	0.14	0.64	0.09	0.39			0.09	0.92
-0.09	0.55	0.67	0.3	-0.05	1.07			-0.04	-0.22
0.09	0.72			0.15	0.65			0.19	0.41
0.27	0.63			0.17	0.43			0.11	-0.04
-0.03	0.07			0.02	0.42			0	0.49
0.11	0.2			0.03	0.27			0.2	0.56
0.91	1.53			0	1.09			0.27	0.39
				-0.28	0.42			0.13	0.99
				0.19	1.18			1.16	1.39
				1.03	0.47			0.13	0.19
				0.03	1.19			0.28	0.65
				0.45	0.61			0.74	0.14
				0.01	0.43				
				0.9	1.01				
				0.21	0.31				

Table S3. Effect of OTA treatment on the average systolic and diastolic blood pressure.

<i>Fbn1</i> mgR/mgR, never preg		<i>Fbn1</i> mgR/mgR, lact		<i>Fbn1</i> mgR/mgR, lact, OTA	
systolic (mmHg)	diastolic (mmHg)	systolic (mmHg)	diastolic (mmHg)	systolic (mmHg)	diastolic (mmHg)
121	98	129	98	143	116
137	102	134	104	137	118
124	102	113	90	149	106
155	110	152	126	143	114
109	85			133	106

Table S4. Average OR expression in the aorta.

never pregnant		lactating	
WT	<i>Fbn1</i> mgR/mgR	WT	<i>Fbn1</i> mgR/mgR
0.2410558	1.541924	2.331098	1.536699
1.931625	1.059976	4.127545	1.052347
1.237286	0.5630537	1.884531	6.026768
0.6667373	1.709378	2.683533	1.437247
0.9232956	0.9931157	1.158455	1.823745
		1.241769	3.053058

Table S5. Effect of hydralazine or propranolol on the average systolic and diastolic blood pressure.

<i>Fbn1mgR/mgR</i> , never preg		<i>Fbn1mgR/mgR</i> , lact		<i>Fbn1mgR/mgR</i> , lact, hydral		<i>Fbn1mgR/mgR</i> , lact, propran	
systolic (mmHg)	diastolic (mmHg)	systolic (mmHg)	diastolic (mmHg)	systolic (mmHg)	diastolic (mmHg)	systolic (mmHg)	diastolic (mmHg)
132	90	131	68	104	58	109	54
128	98	141	82	104	48	112	58
141	101	120	72	111	51	118	60
129	100	121	61	104	59	99	42

Table S6. Average ERK1/2 phosphorylation in untreated mice.

WT		<i>Fbn1mgR/mgR</i>	
never pregnant	lactating	never pregnant	lactating
0.199507389	0.429927415	0.968475452	1.016613076
0.45625367	0.548196015	0.532402792	1.203883495
0.336553945	0.298314607	0.446769231	1.839694656
0.456663055	0.39197995	0.771397616	2.050344828

Table S7. Average ERK1/2 phosphorylation in treated mice.

WT		<i>Fbn1mgR/mgR</i>					
never pregnant	lactating	never pregnant	lactating	pups removed	OTA	hydralazine	
3.14908662	5.48640916	6.20333988	7.68521739	4.20368194	8.52375052	6.64315669	
2.70076816	5.9640678	6.99820144	9.25362845	6.05139186	5.45016251	6.22814983	
2.34533228	5.7009702	9.64836224	13.0657895	5.50969779	8.000819	4.63847145	
		4.29026549	9.93471954				

Table S8. Effect of trametinib on average systolic and diastolic blood pressure.

<i>Fbn1mgR/mgR</i> , lact		<i>Fbn1mgR/mgR</i> , lact, trametinib	
systolic (mmHg)	diastolic (mmHg)	systolic (mmHg)	diastolic (mmHg)
131	72	136	82
129	68	134	84
146	96	146	90
133	88	128	79
142	90	142	81
126	77	144	84
129	74	138	78
134	80	147	94

Table S9. Average ERK1/2 phosphorylation in trametinib-treated mice.

<i>Fbn1mgR/mgR</i>	
lactating	lact, trametinib
0.287155147	0.064662951
0.426111334	0.106531049
0.449943757	0.051665862
0.611052072	0.041792853
0.828813559	-0.016420361
0.411355736	