

Supporting Information

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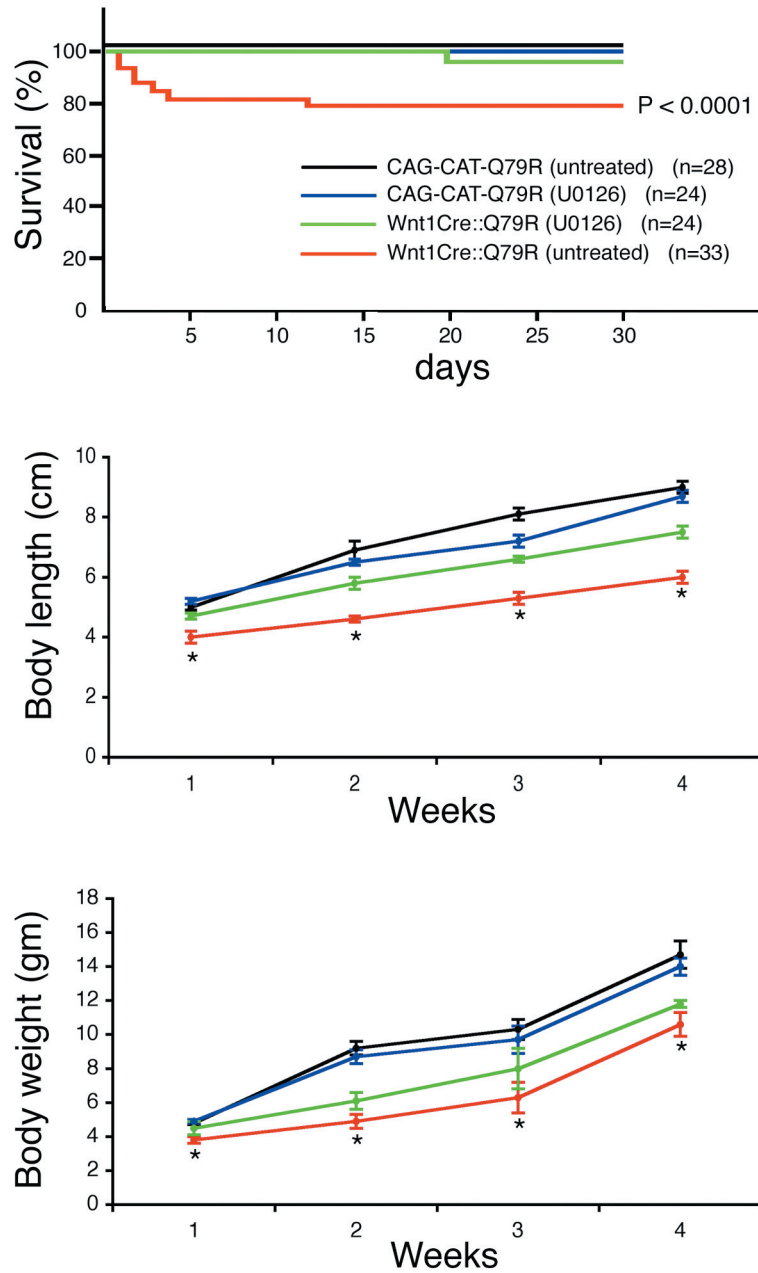


Fig. S1. Selective activation of ERK1/2 in Q79R-expressing frontal bones. A survey of potential pathways that could be activated by SHP2 Q79R was made. Activation of apoptosis was also analyzed by titrating for cleaved caspase 3. Only ERK1/2 was activated, as measured by increased phosphorylation.

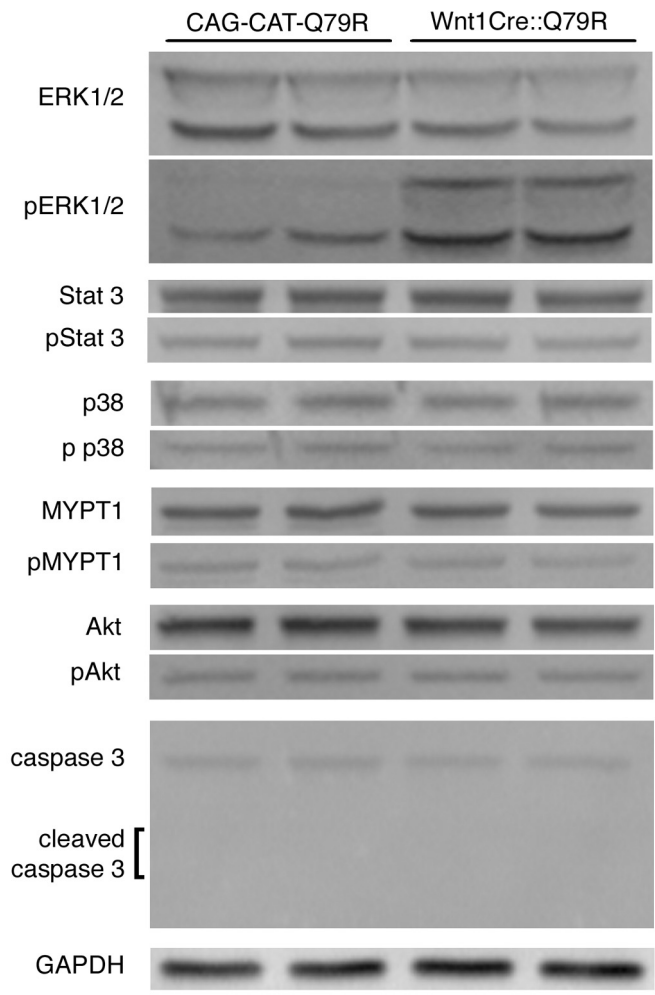


Fig. 52. Morbidity and mortality in Wnt1Cre::Q79R mice. Shown are survival, body length, and weight of the Wnt1Cre::Q79R mice compared with the CAG-CAT-Q79R control animals. U0126-treated cohorts are also shown, and abrogation of ERK1/2 hyperphosphorylation significantly decreased phenotypic presentation of growth defects and decreased mortality. Measurement of the body length and weight was performed on the third day of each week. *, $P < 0.05$, Wnt1Cre::Q79R vs. CAG-CAT-Q79R mice.

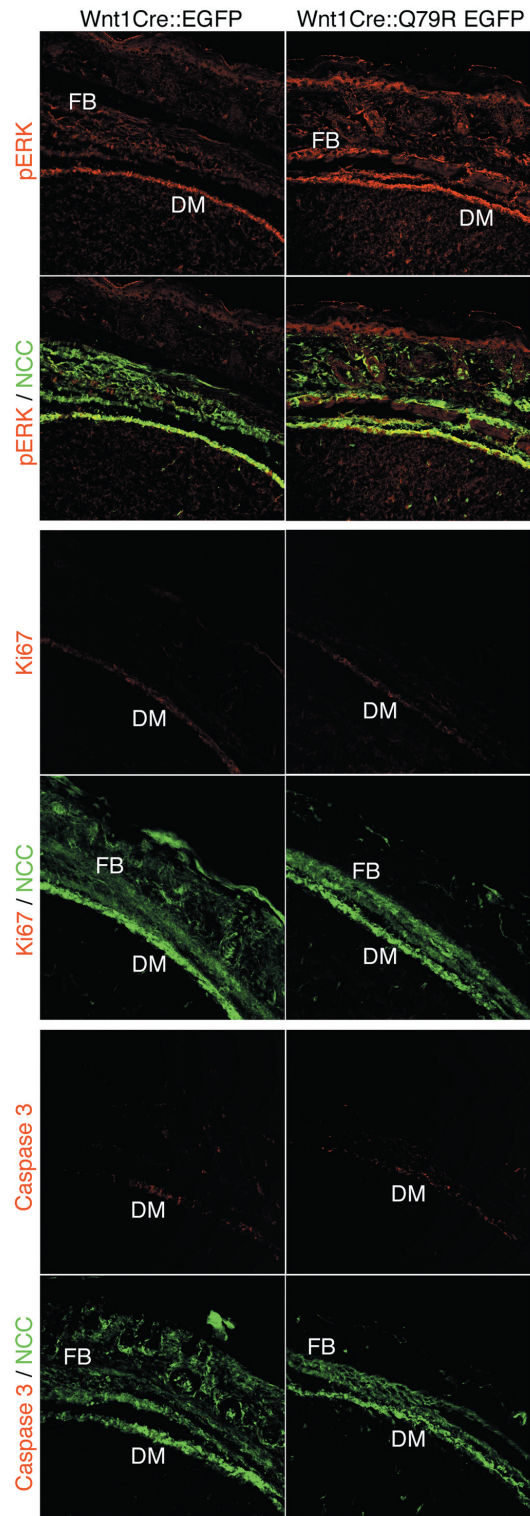


Fig. S3. Immunostaining of the frontal bone (FB) and DM in E15.5 embryos. Shown are sections that include the FB and DM: all sections were derived from E15.5 embryos, treated identically, and analyzed by immunohistochemistry using the indicated antibodies. Despite the hyperphosphorylation in the FB and DM of the Wnt1Cre::Q79R EGFP mice, cell proliferation as measured by Ki67 staining and activation of apoptosis (staining for activated caspase 3) are unchanged as compared with control Wnt1Cre::EGFP mice.

Table S1. ERK1/2 inhibition restores normal bone growth parameters

Parameter	Untreated		U0126	
	CAG-CAT-Q79R (n = 9)	Wnt1Cre::Q79R (n = 13)	CAG-CAT-Q79R (n = 12)	Wnt1Cre::Q79R (n = 12)
Length (mm)	22.36 ± 0.21	18.52 ± 0.19	22.33 ± 0.26	20.10 ± 0.22*
Width (mm)	10.87 ± 0.14	11.45 ± 0.29	10.76 ± 0.07	10.81 ± 0.06
Inner canthal distance (mm)	4.41 ± 0.13	6.26 ± 0.29	4.17 ± 0.08	4.37 ± 0.10*
Nasal bone width (mm)	2.62 ± 0.17	2.87 ± 0.08	2.54 ± 0.03	2.61 ± 0.05
Mandibular bone length (mm)	12.81 ± 0.21	11.15 ± 0.29	12.73 ± 0.21	12.30 ± 0.15*
Mandibular bone width (mm)	8.76 ± 0.16	9.05 ± 0.20	8.88 ± 0.06	8.96 ± 0.06
Frontal bone height (mm)	3.38 ± 0.17	5.52 ± 0.31	3.18 ± 0.05	3.38 ± 0.07*

**P* < 0.05 vs. untreated Wnt1Cre::Q79R measurements.