Figure S1. Transverse sections of forelimb (f) and hindlimb (h) shown in Figure 2D; m, mesonephros.

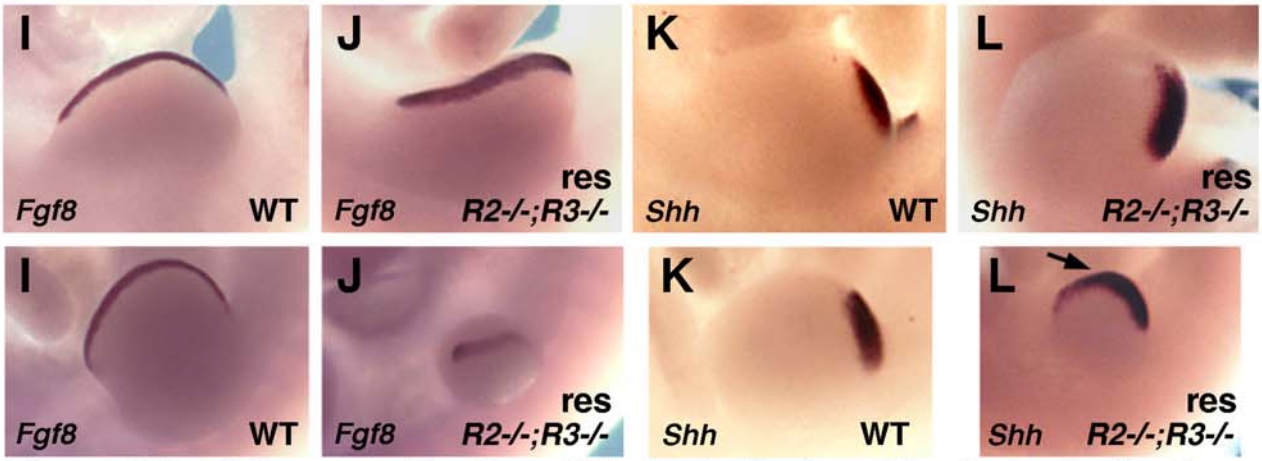

Figure S2. Higher magnification of hindlimbs (top) and forelimbs (bottom) in Figure 1I-L (anterior to left). Notice abnormal distal Shh expression in mutant forelimb (arrow).

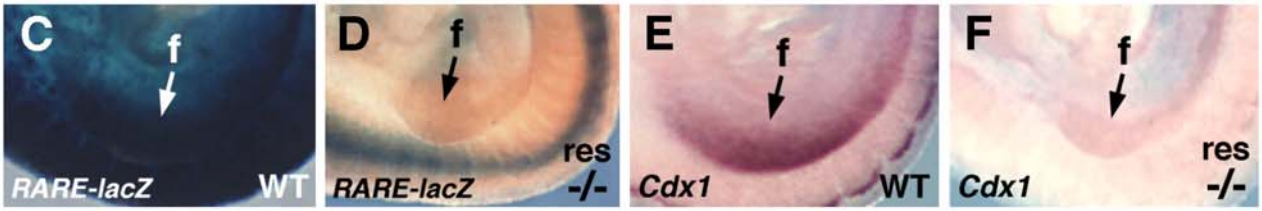

Figure S3. Higher magnification of forelimbs in Figure 2C-F (anterior to left).

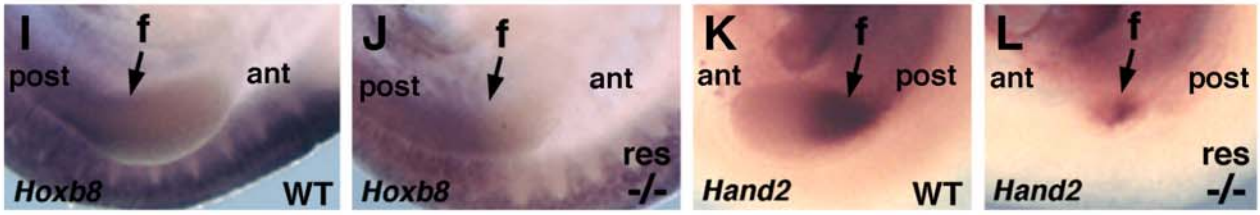

Figure S4. Higher magnification of forelimbs in Figure 3I-L.

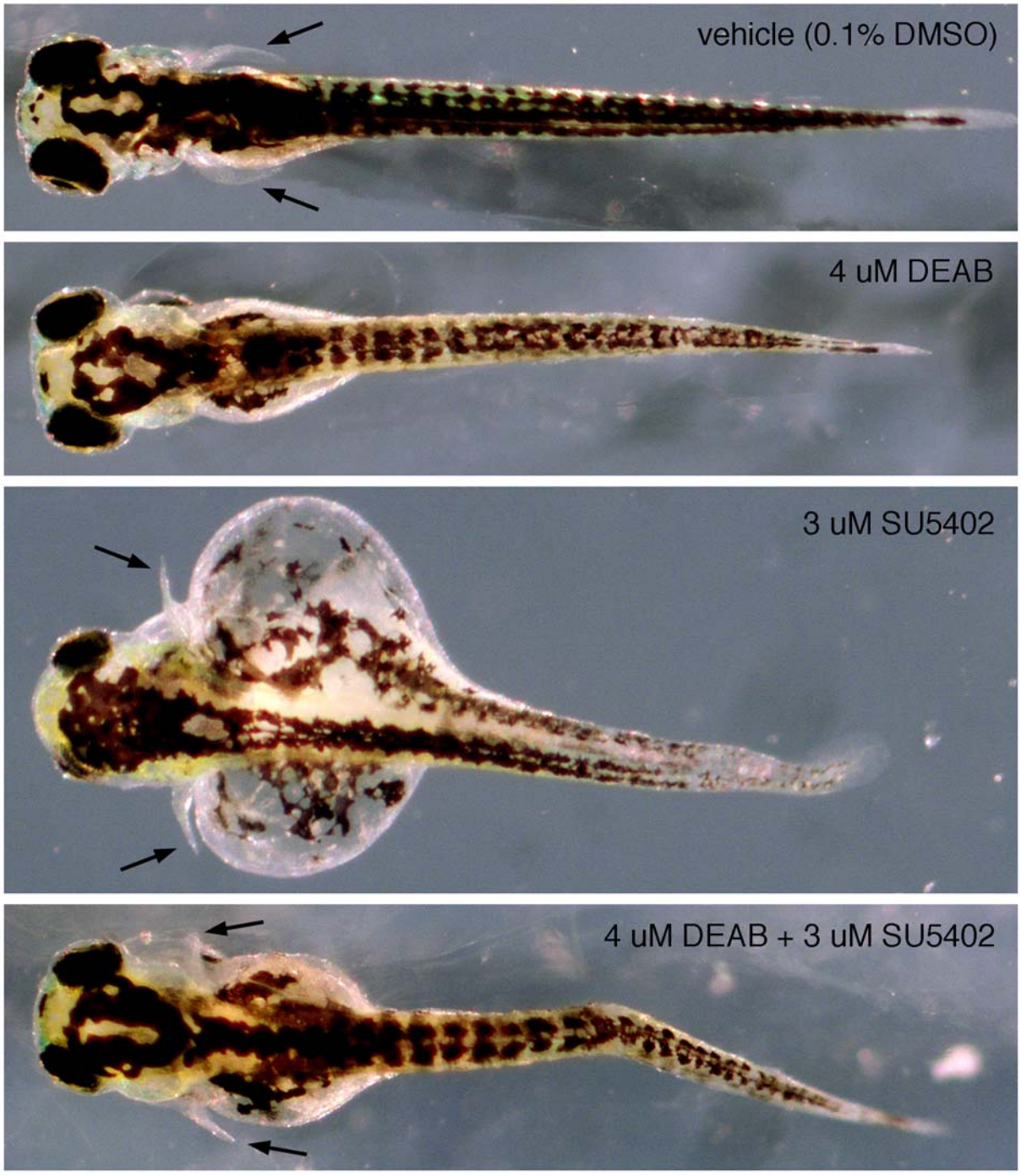

Figure S5. Rescue of pectoral fin development in RA-deficient zebrafish embryos. Zebrafish embryos were treated with diethylaminobenzaldehyde (DEAB) to inhibit RA synthesis [15] and/or SU5402 to inhibit FGF receptor signaling [27] from the bud stage (~9.5-10 hours post-fertilization [hpf]) to somite 12-13 (~15 hpf). Control embryos were treated with 0.1% dimethylsulfoxide (DMSO) which served as the vehicle for both drugs. Pectoral fins (indicated by arrows) were observed at 96 hpf. Previous studies demonstrated that 10 μM DEAB always eliminated pectoral fins [15]. Preliminary experiments were performed using doses of DEAB ranging from 1-10 μM and doses of SU5402 ranging from 3-12 μM to find the lowest dose of DEAB that would eliminate pectoral fins and still be tolerable along with SU5402. We found that DEAB in the range of 4-5 μM and SU5402 at 3 μM allowed embryos to develop to 96 hpf, plus 4-5 μM DEAB always eliminated pectoral fins. Treatment with both DEAB and SU5402 often rescued pectoral fin development, with rescued pectoral fins appearing smaller than those present in vehicle-treated embryos (see main text for numbers).

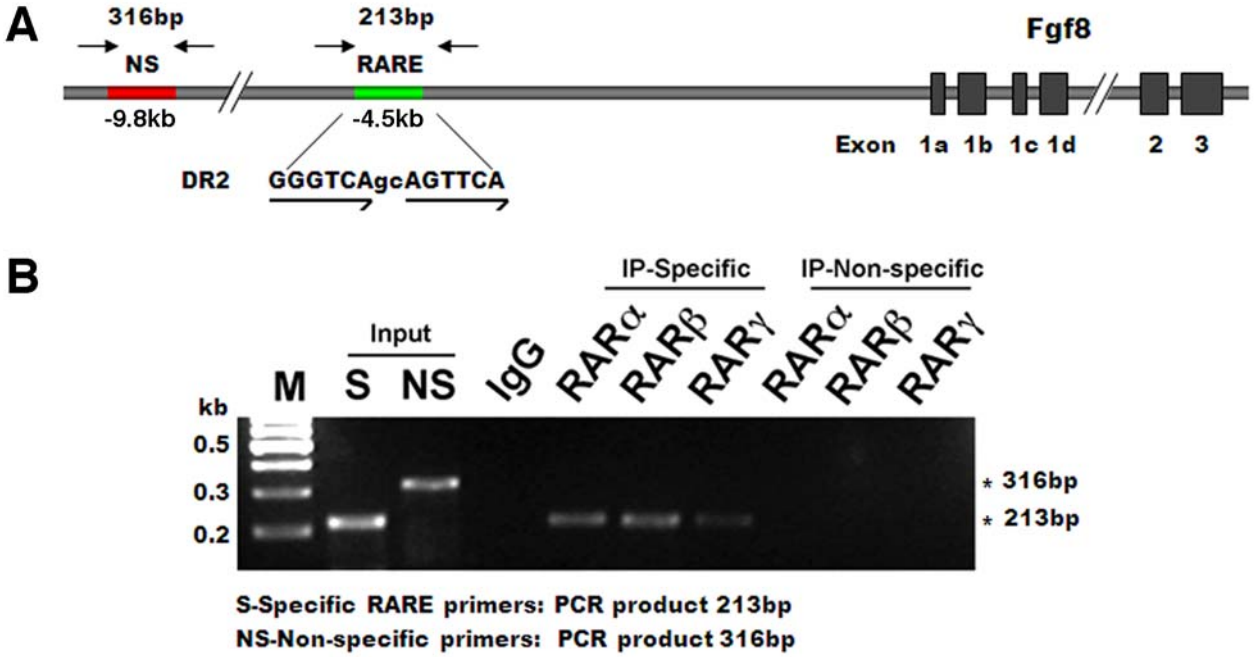

Figure S6. Recruitment of retinoic acid receptors to the mouse *Fgf8* promoter *in vivo*.
(A) Schematic representation of the mouse *Fgf8* upstream region containing the DR2 retinoic acid response element (RARE). *Fgf8* exons 1, 2 and 3 are represented as solid boxes. Exons 1a, 1b, 1c and 1d are alternatively spliced to generate eight different Fgf8 isoforms [Guo, Q. and Li, J.Y.H. (2007). Distinct functions of the major Fgf8 spliceform, Fgf8b, before and during mouse gastrulation. Development *134*, 2251-2260]. For chromatin immunoprecipitation (ChIP) assays, arrows indicate the location of primer pairs used to amplify the RARE-containing region located 4.5 kb upstream of exon 1a and a non-specific negative control region located 9.8 kb upstream.
(B) ChIP assay was performed using E8.5 mouse embryos. The cross-linked protein-DNA complexes were immunoprecipitated with anti-RAR-α, RAR-β and RAR-γ antibodies. Mouse IgG was used as a negative control. Input material and immunoprecipitates were analyzed by PCR with specific primers flanking the RARE and non-specific primers for mouse *Fgf8* promoter. PCR products were separated by 3% agarose gel electrophoresis and visualized using ethidium bromide staining. S: RARE specific primers, NS: Non-specific primers.

Experimental Procedures: Chromatin Immunoprecipitation (ChIP) was performed according to the manufacturer's ChIP protocol (Active Motif, Carlsbad, CA). Ten E8.5 wild-type mouse embryos were cross-linked with 1% formaldehyde at room temperature for 15 min. Isolated nuclei (in 750µl) were sonicated for twelve 10-s pulses on ice (to shear DNA to an average size of 500 bp) and then the sample was microcentrifuged at 13,000 rpm for 10 min. At this point, a small portion of supernatant was stored as input control. For immunoprecipitation, 150µl of sheared chromatin mixed with 3µg of either anti-RAR-α (sc-551, Santa Cruz Biotechnology), anti-RAR-β (Affinity Bioreagents), anti-RAR-γ antibodies (provided by Lorraine J. Gudas), or control IgG was used in each ChIP reaction mixed with 25 µl preblocked protein G-coated magnetic beads (Active Motifs, Carlsbad, CA) for 4 h at 4 °C. Beads were washed and eluted DNA-protein complexes were reverse cross-linked and purified. ChIP analysis was performed at least in three independent experiments. RARE specific and non-specific Primer sequences for mouse *Fgf8* used in this study were:

Fgf8 RARE-F: 5'-CAG CAC TCT GCC ATA CTG TCT TA -3'
Fgf8 RARE-R: 5'-TCT GTC AGT CTT CAG CTT GTC TG -3'

Fgf8 Non-specific-F: 5'-GTC AGT CTG CGA ATA TAG CTC AG -3'
Fgf8 Non-specific-R: 5'-CAC AGT ACC AAC AAG TGT CAC AG-3'