Cardiomyocyte ErbB4 receptors are essential for neonatal cardiac hypertrophy and growth, and also maintain cardiac function in adult mouse hearts

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Activation of ErbB4 by neuregulin 1 (NRG1) promotes cardiomyocyte hypertrophy *in vitro* and proliferation in neonatal and adult mice, while application of NRG1 following myocardial infarction reduces scar size and improves function. Less is known about ErbB4 participation in cardiac hypertrophy. We evaluated the role of cardiomyocyte ErbB4 in developmental, exercise-, and angiotensin-induced hypertrophy. For adult studies, ErbB4 was deleted in αMHC-MerCreMer (cCre $Tg^{+/-}$)/ErbB4 floxed (ErbB4ff) mice at ~2 months of age with 10 injections of Tamoxifen (20 mg/kg/day). Mice were aged for up to 8 months, exposed to Angiotensin II (Ang II, 1000ng/kg/min, 14 days) or exercised (twice daily swimming, 20 min/session increasing 10 min/day to 90 min followed by 7 days at 90 min/session). Neonates (ErbB4ff or ErbB4ww) received temporal vein injections of AAV9-cTNT-eGFP-iCre (2.16×10^{11} viral particles) at p1 and were culled at p6. Three months after deletion of ErbB4 in adult hearts, contractile function was reduced *in vivo* (echocardiography, 16%) and *ex vivo* (isolated-perfused, 33%), however deletion failed to modify heart size, survival for 8 months or hypertrophy in response to Ang II or exercise. In neonates, the presence of iCre mRNA in hearts confirmed virus infection, and suppression of ErbB4 in ErbB4f/f mice was coincident with increased NRG1-alpha, and reduced body and ventricular weights. Thus, ErbB4 is critical to cardiac hypertrophy and growth in neonatal mice, and maintains adult heart function.