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# Heart failure mutation

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Heart failure is a major cause of death in the developed world and a growing health-care concern. In the February 28 Science Schmitt *et al.* report the discovery of a mutation in patients suffering from inherited dilated cardiomyopathy with refractory congestive heart disease (*Science* 2003, **299:**1410-1413). A dominant missense mutation (Arg→Cys) was found at residue 9 in phospholamban (PLN). Phospholamban is a 52 amino-acid transmembrane phosphoprotein that regulates the $Ca^{2+}$ ATPase pump (SERCA2a). Schmitt *et al.* generated transgenic mice expressing the mutant $PLN^{R9C}$ in the heart and observed biventral cardiac dilation and progressive cardiomyopathy resembling the human symptoms. Tissue culture experiments demonstrated that the $PLN^{R9C}$ mutant form trapped protein kinase A (PKA), which led to inhibition of the phosphorylation of wild-type $PLN^{WT}$ protein and delayed decay of $Ca^{2+}$ transients. Manipulating $Ca^{2+}$ handling and/or PLN activity may provide a therapeutic opportunity for treating human heart disease.

# References

1. Recent advances in understanding the genetic etiology of congenital heart disease.

2. *Science*, [http://www.sciencemag.org]

3. Phospholamban and cardiac contractility.