Supplementary information S1 (table) | Rho GTPase knockout mouse models

Gene	Knockout strategy	Phenotype	Reference
RAC1	Global knockout	Embryonic lethal before E9.5; germ-layer formation defects	1
RAC1	LysM-Cre myeloid cells	Defects in neutrophil recruitment, chemotaxis and actin polymerization	2
RAC1	CD19-Cre B-cell lineage	Impaired B-cell development and BCR signalling when crossed with *Rac2*-knockout mouse	3
RAC1	Mx1-Cre haematopoietic cells	Haematopoietic stem/progenitor cell engraftment defect in the bone marrow	4
RAC1	K14-CreER epidermal cells	Loss of epidermal stem cells, defects in hair follicles	5
RAC1	K5-Cre epidermal cells	Hair loss and defects in lower region of hair follicle	6
RAC1	MHC-Mer-Cre-Mer cardiomyocytes	Decreased NADPH oxidase activity, superoxide anion production; cardiac hypertrophy	7
RAC1	P0-Cre Schwann cells	Delayed axonal sorting and impaired myelination	8
	Dhh-Cre Schwann cells	Impaired radial sorting	9
RAC1	Cell permeable Cre embryonic fibroblasts	Reduced lamellipodia and decreased proliferation	10
RAC1	Foxg1-Cre forebrain	Defects in brain development and axon guidance	11

RAC1	Tie2-Cre endothelial cells	Embryonic lethal around E9.5; defects in vascular development	12
RAC2	Global knockout	Defects in neutrophil function; for example, chemotaxis and superoxide production	13
RAC3	Global knockout	Developmentally normal and viable; behavioural differences with improved motor skills	14, 15
RhoG	Global knockout	Developmentally normal and viable; mild hyper-responsiveness of B and T lymphocytes to antigen	16, 17
CDC42	Global knockout	Embryonic lethal before E7.5; embryos smaller and disorganized, often lacking primary ectoderm	18
CDC42	Mx1-Cre haematopoietic cells	Defect in quiescence and homing and retention in the bone marrow	19
CDC42	Emx1-Cre cerebral cortex	Change in fate determination of apical neural progenitor cells	20
CDC42	Foxg1-Cre telencephalic neural progenitors	Loss of apico-basal polarity of telencephalic neuroepithelium	21
CDC42	K5-Cre keratinocytes	Hair loss; increased β-catenin degradation, fate change of progenitor cells in hair follicle	22
CDC42	Nestin-Cre brain	Defect in axonogenesis	23
CDC42	Dhh-Cre Schwann cells	Inhibition in Schwann cell proliferation and radial sorting	24
CDC42	Alb-Cre hepatocytes and bile duct cells	Develop hepatocellular carcinomas	25

RhoB	Global knockout	Viable and normal development; increased susceptibility to cancer in skin cancer model	26
RhoC	Global knockout	Viable and normal development; inhibition of tumour cell motility and metastasis	27
RhoH	Global knockout	Defects in TCR signalling and T-cell differentiation	28, 29

1. Sugihara, K. et al. Rac1 is required for the formation of three germ layers during gastrulation. *Oncogene* **17**, 3427–3433 (1998).
2. Glogauer, M. et al. Rac1 deletion in mouse neutrophils has selective effects on neutrophil functions. *J. Immunol.* **170**, 5652–5657 (2003).
3. Walmsley, M.J. et al. Critical roles for Rac1 and Rac2 GTPases in B cell development and signaling. *Science* **302**, 459–462 (2003).
4. Gu, Y. et al. Hematopoietic cell regulation by Rac1 and Rac2 guanosine triphosphatases. *Science* **302**, 445–449 (2003).
5. Benitah, S.A., Frye, M., Glogauer, M. & Watt, F.M. Stem cell depletion through epidermal deletion of Rac1. *Science* **309**, 933–935 (2005).
6. Chrostek, A. et al. Rac1 is crucial for hair follicle integrity but is not essential for maintenance of the epidermis. *Mol. Cell Biol.* **26**, 6957–6570 (2006).
7. Satoh, M. et al. Requirement of Rac1 in the development of cardiac hypertrophy. *Proc. Natl Acad. Sci. USA* **103**, 7432–7437 (2006).
8. Nodari, A. et al. Beta1 integrin activates Rac1 in Schwann cells to generate radial lamellae during axonal sorting and myelination. *J. Cell Biol.* **177**, 1063–1075 (2007).
9. Benninger, Y. et al. Essential and distinct roles for cdc42 and rac1 in the regulation of Schwann cell biology during peripheral nervous system development. *J. Cell Biol.* **177**, 1051–1061 (2007).
10. Vidali, L., Chen, F., Cicchetti, G., Ohta, Y. & Kwiatkowski, D.J. Rac1-null mouse embryonic fibroblasts are motile and respond to platelet-derived growth factor. *Mol. Biol. Cell* **17**, 2377–2390 (2006).
11. Chen, L. et al. Rac1 controls the formation of midline commissures and the competency of tangential migration in ventral telencephalic neurons. *J. Neurosci.* **27**, 3884–3893 (2007).
12. Tan, W. et al. An essential role for Rac1 in endothelial cell function and vascular development. *FASEB J.* **22**, 1829–1838 (2008).
13. Roberts, A.W. et al. Deficiency of the hematopoietic cell-specific Rho family GTPase Rac2 is characterized by abnormalities in neutrophil function and host defense. *Immunity* **10**, 183–196 (1999).
14. Corbetta, S. et al. Generation and characterization of Rac3 knockout mice. *Mol. Cell Biol.* **25**, 5763–5776 (2005).
15. Cho, Y.J. et al. Generation of rac3 null mutant mice: role of Rac3 in Bcr/Abl-caused lymphoblastic leukemia. *Mol. Cell Biol.* **25**, 5777–5785 (2005).

16. Vincent, S., Jeanteur, P. & Fort, P. Growth-regulated expression of RhoG, a new member of the ras homolog gene family. *Mol. Cell Biol.* **12**, 3138–3148 (1992).
17. Vigorito, E. et al. Immunological function in mice lacking the Rac-related GTPase RhoG. *Mol. Cell Biol.* **24**, 719–729 (2004).
18. Chen, F. et al. Cdc42 is required for PIP(2)-induced actin polymerization and early development but not for cell viability. *Curr. Biol.* **10**, 758–765 (2000).
19. Yang, L. et al. Rho GTPase Cdc42 coordinates hematopoietic stem cell quiescence and niche interaction in the bone marrow. *Proc. Natl Acad. Sci. USA* **104**, 5091–5096 (2007).
20. Cappello, S. et al. The Rho-GTPase cdc42 regulates neural progenitor fate at the apical surface. *Nature Neurosci.* **9**, 1099-1107 (2006).
21. Chen, L. et al. Cdc42 deficiency causes Sonic hedgehog-independent holoprosencephaly. *Proc. Natl Acad. Sci. USA* **103**, 16520–16525 (2006).
22. Wu, X. et al. Cdc42 controls progenitor cell differentiation and beta-catenin turnover in skin. *Genes Dev.* **20**, 571–585 (2006).
23. Garvalov, B.K. et al. Cdc42 regulates cofilin during the establishment of neuronal polarity. *J. Neurosci.* **27**, 13117–13129 (2007).
24. Benninger, Y. et al. Essential and distinct roles for CDC42 and Rac1 in the regulation of Schwann cell biology during peripheral nervous system development. *J. Cell Biol.* **177**, 1051–1061 (2007).
25. van Hengel, J. et al. Continuous cell injury promotes hepatic tumorigenesis in CDC42-deficient mouse liver. *Gastroenterology* **134**, 781–792 (2008).
26. Liu, A.X., Rane, N., Liu, J.P. & Prendergast, G.C. RhoB is dispensable for mouse development, but it modifies susceptibility to tumor formation as well as cell adhesion and growth factor signaling in transformed cells. *Mol. Cell Biol.* **21**, 6906–6912 (2001).
27. Hakem, A. et al. RhoC is dispensable for embryogenesis and tumor initiation but essential for metastasis. *Genes Dev.* **19**, 1974–1979 (2005).
28. Gu, Y. et al. RhoH GTPase recruits and activates Zap70 required for T cell receptor signaling and thymocyte development. *Nature Immunol.* **7**, 1182–1190 (2006).
29. Dorn, T. et al. RhoH is important for positive thymocyte selection and T-cell receptor signaling. *Blood* **109**, 2346–2355 (2007).