Neural-specific ablation of the scaffold protein JSAP1 in mice causes neonatal death

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We previously identified c-Jun NH(2)-terminal kinase (JNK)/stress-activated protein kinase-associated protein 1 (JSAP1, also known as JNK-interacting protein 3) as a scaffolding factor for JNK intracellular signaling pathways. Targeted gene-disruption studies have shown that JSAP1-null mice are unable to breathe and die shortly after birth. Although neural defects might be responsible for their death, there has been no convincing evidence for this. Here we first generated genetically engineered mice carrying a loxP-flanked (floxed) *Jsap1* gene. To evaluate the validity of this deletion as a *Jsap1* conditional knockout (KO), we created mice in which the same exon was deleted in all cell lineages, and compared their phenotypes with those of the *Jsap1* conventional KO mice reported previously. The two KO lines showed indistinguishable phenotypes, i.e., neonatal death and morphological defects in the telencephalon, indicating that the conditional deletion was a true null mutation. We then introduced the floxed *Jsap1* deletion mutant specifically into the neural lineage, and found that the *Jsap1* conditional KO mice showed essentially the same phenotypes as the JSAP1-null mice. These results strongly suggest that the neonatal death of *Jsap1*-deficient mice is caused by defects in the nervous system.

Table Genotype analysis of littermates from crosses of $Jsap1^{flox/flox}$ and $Jsap1^{flox/+}$;*nes-cre* mice

Stage	No. of animals with genotype:				
	Total	*flox/flox*	*flox/+*	*flox/flox;nes-cre*	*flox/+;nes-cre*
E18.5	122	35	28	28	31
P0	56	15	19	9	13
P1	52	15	21	2	14
P2	31	9	7	0	15
Weaned	88	32	26	0	30

Reference: A. Iwanaga, T. Sato. K. Sugihara, A. Hirao, N. Takakura, H. Okamoto, M. Asano and K. Yoshioka (2007) Neurosci. Lett. 429:43-48.