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Titel des Beitrags:
In vivo functional requirement of the mouse Ifitm1 gene for germ cell development, interferon mediated immune response and somitogenesis.

Abstract:
The mammalian Interferon induced transmembrane protein 1 (Ifitm1) gene was originally identified as a member of a gene family highly inducible by type I and type II interferons. Based on expression analyses, it was suggested to be required for normal primordial germ cell migration. The knockdown of Ifitm1 in mouse embryos provided evidence for a role in somitogenesis. We generated the first targeted knockin allele of the Ifitm1 gene to systematically reassess all inferred functions. Sperm motility and the fertility of male and female mutant mice are as in wild type littermates. Embryonic somites and the adult vertebral column appear normal in homozygous Ifitm1 knockout mice, demonstrating that Ifitm1 is not essential for normal segmentation of the paraxial mesoderm. Proportions of leucocyte subsets, including granulocytes, monocytes, B-cells, T-cells, NK-cells, and NKT-cells, are unchanged in mutant mice. Based on a normal immune response to Listeria monocytogenes infection, there is no evidence for a dysfunction in downstream IFN? signaling in Ifitm1 mutant mice. Expression from the Ifitm1 locus from E8.5 to E14.5 is highly dynamic. In contrast, in adult mice, Ifitm1 expression is highly restricted and strong in the bronchial epithelium. Intriguingly, IFITM1 is highly overexpressed in tumor...
epithelia cells of human squamous cell carcinomas and in adenocarcinomas of NSCLC patients. These analyses underline the general importance of targeted in vivo studies for the functional annotation of the mammalian genome. The first comprehensive description of the Ifitm1 expression pattern provides a rational basis for the further examination of Ifitm1 gene functions. Based on our data, the fact that IFITM1 can function as a negative regulator of cell proliferation, and because the gene maps to chromosome band 11p15.5, previously associated with NSCLC, it is likely that IFITM1 in man has a key role in tumor formation.