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Titel des Beitrags: Early onset of ataxia in moonwalker mice is accompanied by complete ablation of type II unipolar brush cells and Purkinje cell dysfunction.

Abstract: Transient receptor potential "canonical" cation channels (TRPC) are involved in many cellular activities, including neuronal synaptic transmission. These channels couple lipid metabolism, calcium homeostasis, and electrophysiological properties as they are calcium permeable and activated through the phospholipase C pathway and by diacylglycerol. The TRPC3 subunit is abundantly expressed in Purkinje cells (PCs), where it mediates slow metabotropic glutamate receptor-mediated synaptic responses. Recently, it has been shown that heterozygous moonwalker mice, which are a model of cerebellar ataxia, carry a dominant gain-of-function mutation (T635A) in the TRPC3 gene. This mutation leads to PC loss and dysmorphism, which have been suggested to cause the ataxia. However, the ataxic phenotype is present from a very early stage (before weaning), whereas PC loss does not appear until several months of age. Here we show that another class of cerebellar neurons, the type II unipolar brush cells (UBCs), express functional TRPC3 channels; intriguingly, these cells are ablated in moonwalker mice by 1 month of age. Additionally, we show that in moonwalker mice, intrinsic excitability of PCs is altered as early as 3 weeks after birth. We suggest that this altered excitability and the
TRPC3-mediated loss of type II UBCs may both contribute to the ataxic phenotype of these mice and that different calcium handling in PCs and type II UBCs may account for the dramatic differences in sensitivity to the moonwalker mutation between these cell types.