



Articles of Significant Interest in This Issue

A Twist in Our Understanding of Extracellular Signal-Regulated Kinase 3/Mitogen-Activated Protein Kinase 6 Function

The physiological functions of the atypical mitogen-activated protein kinases (MAPKs), such as MAPK6/extracellular signal-regulated kinase 3 (ERK3), remain enigmatic. The original characterization of mice with global *Mapk6* disruption 10 years ago came to the conclusion that ERK3 was essential for viability and for lung and T cell development. In this issue, two independent groups, Ronkina et al. (e00516-18) and Soulez et al. (e00527-18), report the characterization of new conditional *Mapk6* null alleles. Unexpectedly, these new deletion strategies did not phenocopy the conventional knockout; rather, they generated viable mice without significant impairments. Furthermore, a knock-in mouse with a catalytically dead ERK3 was shown to be normal (e00527-18). Genetic analysis showed that the original strategy of deletion of *Mapk6* by *lacZ* insertion caused positional off-target effects in the genome. Therefore, the previously reported essential role of ERK3 in lung and T cell development should be reevaluated. However, the new analysis does support an important role for ERK3 in MK5 regulation *in vivo* (e00516-18).