

The role of the apical complex in controlling cell proliferation and cell survival

Cerebral cortical development depends upon tightly controlled cell fate and cell survival decisions that generate a functional neuronal population, but how these processes are coordinated is not well understood. To investigate the role of the apical, ventricular surface in directing proliferation and survival during cortical development, we disrupted the apical surface of the developing neuroepithelium by conditionally deleting the scaffolding protein Pals1, an evolutionarily conserved apical complex polarity protein (Kim et al., 2010). Pals1 is normally highly expressed in cortical progenitor cells. We found that *Pals1* knockout in progenitors causes premature differentiation of early-born neurons that is followed by their rapid cell death, leading to the loss of nearly the entire cerebral cortex.

The loss of Pals1 blocks essential cell survival signals in newly differentiating cells, including the mammalian target of rapamycin (mTOR) pathway, which has previously been associated with

polarity proteins (Massey-Harroche et al., 2007; Pinal et al., 2006; von Stein et al., 2005). Conversely, activation of the mTOR signaling pathway by elimination of a negative regulator, Tuberous sclerosis complex subunit 2 (Tsc2), partially restores the Pals1 medial cortex, suggesting a genetic interaction between the two signaling pathways.

Surprisingly, *Pals1* conditional knockout mice survive into adulthood and retain an impressive repertoire of behaviors, despite the near absence of their cerebral cortex. Taken together, our findings identify a new connection between the apical complex and mTOR signaling that couples cell fate and cell survival during cortical development.

~ Maria K Lehtinen, PhD

Reference: The apical complex couples cell fate and cell survival to cerebral cortical development. Kim S, Lehtinen MK, Sessa A, Zappaterra MW, Cho SH, Gonzalez D, Boggan B, Austin CA, Wijnholds J, Gambello MJ, Malicki J, LaMantia AS, Broccoli V, Walsh CA. *Neuron*. 2010 Apr 15;66(1):69-84.

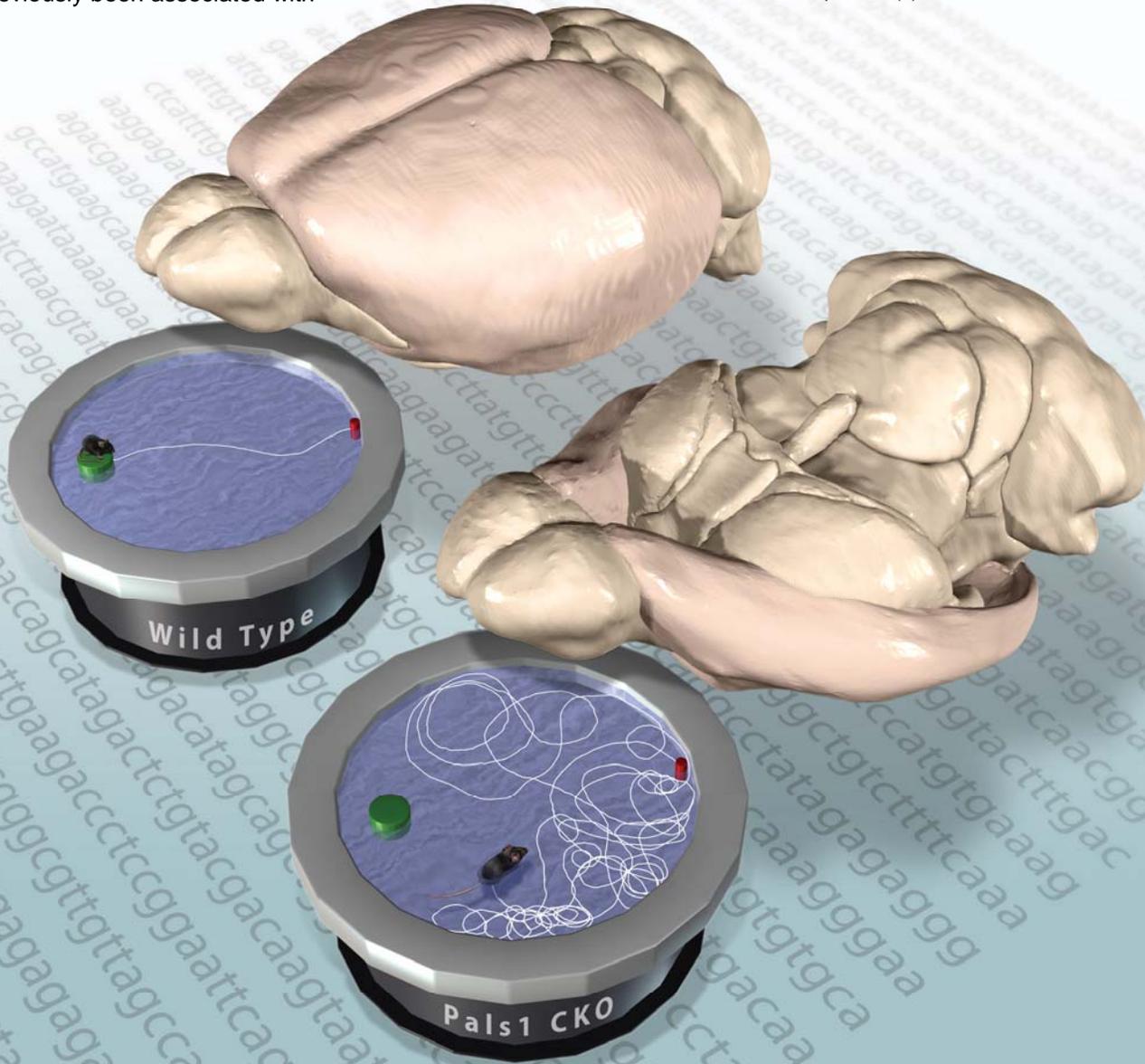


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