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Letter to Editor

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## **ACCEPTED MANUSCRIPT**

#### **Letter to Editor**

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Dipeptidyl peptidase 9 (DPP9) is a ubiquitous intracellular post-proline aminopeptidase. We made a DPP9 gki mouse and discovered that homozygotes (DPP9<sup>ki/ki</sup>) die within a day of birth (Gall, Chen et al. 2013). A recent paper in *Developmental Biology* examines this neonatal lethality, but in their own DPP9<sup>ki/ki</sup> mice. The tongue muscle is weaker than WT in their DPP9<sup>ki/ki</sup> mice (Kim, Minoux et al. 2017). Skeletal muscle is unaffected.

Kim et al concluded that the suckling defect is the primary cause of death, because they found no milk in the stomachs of DPP9<sup>ki/ki</sup> mice and showed that pups hand fed cats milk lived to 24 h. Kim et al found that body weight, tongue size, tongue surface area and the strength of nipple attachment were all diminished in their DPP9<sup>ki/ki</sup> mice compared to WT littermates, consistent with a defective tongue muscle (Kim, Minoux et al. 2017).

We contend that starvation is not the dominant cause of death, primarily because of the timing of death. Directly after birth, neonates have a normal period of starvation during the transition from maternal blood to milk derived nutrients. WT neonate mice that are not fed from birth survive for more than 24 hours. Nevertheless, a suckling defect can contribute to causes of neonate death at 12-24 hours, but for mice that die in less than 12 hours lack of milk is very unlikely to be the predominant cause of death (Turgeon and Meloche 2009). The DPP9<sup>ki/ki</sup> mice that Kim et al observed died at 12-18 hours, whereas the DPP9<sup>ki/ki</sup> neonates observed by Gall et al 2013 died within 8 to 24 hours of birth, with the majority dying within 8 - 12 hours. Thus, starvation could contribute to death but is unlikely to be the dominant cause.

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