Review of: "Prolactin-induced AMPK stabilizes alveologenesis and lactogenesis through regulation of STAT5 signaling"

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This work shows that mammary AMPK regulates mammary epithelial tissue growth and differentiation, using several elegant experimental approaches, among them, generation of mammary AMPK KO mice and MEC culture. Markers of epithelial cell proliferation, tissue differentiation, PRL signaling, milk protein and lipid synthesis, and litter growth were determined, resulting in a thorough study of the effects of AMPK ablation or inhibition. Although AMPK expression is induced by prolactin and shows maximum levels during lactation, the results show that AMPK limits mammary epithelial proliferation and milk production through inhibition of STAT5 phosphorylation, which seems rather paradoxical in terms of optimization of litter growth and eventually fitness. The authors state that the litters from the AMPK KO mothers were heavier than controls up to adulthood (60 days of age). Were other physiological parameters of these litters studied? What would be the evolutionary advantage of this limited restriction of mammary function? Optimization of maternal energy and nutrient utilization, by limiting mammary use of the available resources while maintaining adequate milk production and litter growth?

Although the results seem quite solid, the number of mice (3-4) used for each group, or replicates for the tissue cultures (3), are small and although the differences observed were statistically significant, the confidence in the validity of the observed differences is weak. It would be convenient to increase the n for all the experiments.

A brief description of the experimental protocol should be provided, that is, the age at which the mice were sacrificed and method of sacrifice, age at mating, and in particular, the group sacrificed at involution day 7 must be described; furthermore, were these mice allowed a normal lactation and sacrificed 7 days after spontaneous weaning, or were the pups separated from the mother at a specific day of lactation?