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Exploration of a Novel Behavioral Phenotype in the Interleukin-18 Receptor Knockout Mouse

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Cytokines are primarily known for their roles in inflammation and immunity; however, recent studies indicate that some cytokines (e.g. IL-1 α , IL-1 β , IL-2, IL-6) influence behavior. Our data demonstrate that interleukin-18 receptor knockout (B6.129P2-Il18r1^{tm1Aki}/J; Il18r^{-/-}) mice exhibit significant deficits relative to C57BL6/J (B6) and interleukin-18 knockout (B6.129P2-Il18^{tm1Aki}/J; IL18^{-/-}) mice in several parameters of the open field assay, which is commonly used to assess motor ability, along with learning and memory. By using a series of F1 crosses for complementation testing, we have addressed whether the phenotype is due to the ablated *Il18r* locus or to the 129P2-derived flanking region. We have shown that first day activity in the open field is significantly decreased in Il18r^{-/-} mice, and our complementation tests implicate the flanking region as being responsible for the phenotype. While Il18r^{-/-} mice appear to have a habituation deficit, this trait appears to be due to a difference in strain baseline activity rather than a learning or memory phenotype. Il18r^{-/-} mice show a significant decrease in terms of percent time spent in the center of the open field across the three consecutive days, which appears to be a dominant or additive trait. Il18r^{-/-} mice also show significantly decreased distance traveled in the center of the open field, attributable to the ablated *Il18r* locus. While our data implicate 129P2-derived genes in an activity phenotype, it also suggests that the ablated *Il18r* locus contributes to a complex anxiety-associated behavior phenotype. In addition, we show that the IL-18 ligand does not appear to have a role in these putative phenotypes. These data may suggest a novel role for the IL-18 receptor in behavior