We thank the reviewers for their time and expertise considering this study. We appreciate your insights and have made the recommended adjustments to aid in clarity of findings and in rationale for the work. The revisions include A<B<C<D<E<F. The specific requests are listed by reviewer below

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**Reviewer 1**:

This is an interesting study that examined the effect of GDF-15 deficiency on multiple pregnancy -related outcomes in GDF-15 KO mice. Suprisingly, GDF15-KO dams had no difference in pregnancy-related weight gain, food intake, insulin sensitivity and neonatal outcomes compared to WT dams, suggesting that GDF15 is not a major player in pregnancy-associated metabolic changes and pregnancy outcomes in mice. The study is well designed with multiple parameters investigated.  
A few comments to the authors:

**1. Figure 2A & B: If insulin tolerance is reduced in pregnancy why does fasting glucose tend to be lower?**

Insulin resistance and lower blood glucose, both fasting and fed, during pregnancy compared to non-pregnant mice are well-documented phenomemons1,2. A combination of placentally derived hormones, such as placental lactogens, reduced hypoglycemic counter-regulatory measures in the islet, and large feto-placental demand for glucose result in lower glucose levels for dams. We believe that our data provide strong evidence that our model is consistent with other rigorous pregnancy related glycemia studies. To address this in the manuscript, we made the following change:

Lines 198-199: “Consistent with other murine models of pregnant, fasting blood glucose in pregnant dams tended to be lower than non-pregnant females (Figure 2B, p=0.20) (35,36).”  
**2. Figure 2 D & E: If dexamethasone in drinking water reduces insulin tolerance why does fasting glucose tend to be lower?**

The poorer glycemic health and peripheral glucose disposal in response to exogenous insulin delivery is consistent with previously published work on dexamethasone treated animals from our group3. We believe the reduced glucose is a reflection of lower total body mass accretion during pregnancy with dexamethasone.

**Reviewer 2:**

The paper GDF15 knockout does not substantially impact perinatal body weight or neonatal outcomes in mice by Mulcahy et al sets out to establish how loss of GDF15 from the maternal-fetal dyad affects pregnancy and pup development. The subject of this paper is timely. The physiology and/or pathophysiology of rise in GDF15 that occurs in pregnancy is unknown, and understanding this is critical to our understanding of GDF15-GFRAL biology. As such, even though this paper predominantly presents negative findings, the core observation that loss of GDF15 does not grossly alter pregnancy-related outcomes are still of significant interest to the field. However, there are some aspects of the paper where the rationale is unclear and the findings are of much less interest. I commend the authors on their careful design of the GDF15 KO pregnancy studies.

1. **The rationale for use of dexamethasone (dex) in pregnancy to induce insulin resistance is lacking. There is no introduction of the model or its utility in the introduction. Dex is rarely given in pregnancy due to concerns related to fetal organ development, except acutely in cases where fetal lung maturation is of critical importance due to impending pre-term delivery. Insulin resistance, gestational diabetes and underlying type 2 diabetes are of broad translational relevance during pregnancy, however this is generally secondary to obesity in the human population, and as such a diet induced obese model would seem more appropriate for this study.**
2. **Specific comments relating to Fig 2: Why are the ITTs expressed as % of baseline and not mmol/l or mg/dl as as is the convention? Expressing as mg/dl would remove the need for fig 2B and 2E, and allow for interpretation of the actual glycemic state of the mice.**
3. **Fig 2C - the statistics are not clear. I believe there is likely a main effect of pregnancy and it is indeed well established that GDF15 is elevated in pregnancy, however the legend says paired t tests were used which does not make any sense in looking at the comparison marked on 2C. Dex treated dams are lighter in the second half of pregnancy, so it seems likely the results in 2E reflect body weight differences rather than anything else.**

The method used in 2C is two-way anova, assessing the effect of time of collection (ZT1 vs ZT 13) and pregnancy status. The test revealed a significant effect of pregnancy (p=0.007), but not of time (p=0.98). We changed the language of the passage from results and from the figure legend below,  
“We found that GDF15 is 49% (54 ±18.8 pg/dL) elevated in pregnant animals compared to non-pregnant mice (**Figure 2C,** p=0.007), but does not differ based on collection time (p=0.98).”   
“Figure 2C) GDF15 levels at ZT1 and ZT13 in pregnant and non-pregnant females, assessed by two way anova for effect of time and of pregnancy status.”

1. **The results text states that "Both genotypes had a rapid increase in food intake in the final week of pregnancy, with smaller increases in the Gdf15-/- dams", the lines in Fig 3E overlap completely, so this is not substantiated.**
2. **For fig 3, With regards to fig 3D, I suggest showing this as % change from delivery day - Given the higher body weight and variation in 3F around 20-25 day mark I wonder if this would account for the variability in weight loss.**
3. **For fig 5C, what is the p value? Text states p=0.05, figure legend states \*p<0.05. Given alpha is set at 0.05, p=0.05 is not actually significant.**

Thank you for pointing out that inconsistency. The p-value is 0.05, so we have removed the asterisk.

1. **Overall comments on graphs: x axis labels should be aligned with sampling timepoints within the graphs.**

We updated x-axes for insulin tolerance tests, body weight, and food intake measurements to better reflect days of collection for data.

1. **More complete labelling would be helpful.  
   I strongly applaud the authors for their use of gender neural language "expectant parents" in the discussion, but suggest "expectant gestational parents" may be more accurate and avoid confusion.**

Line: 294, “Elevated circulating levels of GDF15 have been documented in **expectant gestational parents** with normal weight status compared to those with obesity”

1. **There are a number of sentences in both the discussion and introduction that could be edited for clarity of thought.**