Diabetic Complications Consortium

Sponsor: Georgia Regents University

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Application Title: The Effect of High-Fat Diet on Diabetic Bladder Dysfunction in Type 2 Diabetes

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1. **Project Accomplishments:**
   We found that obesity worsens the bladder dysfunction in Type 2 diabetes.

2. **Specific Aim:**
   To determine if high-fat diet (HFD) in conjunction with DM2 worsens bladder dysfunction in DKO animals.

3. **Results:**
   After 10 weeks exposure of HFD, floxed control animals had significantly higher body weight than that of control animals fed standard chow (Fig.1A). Meanwhile, DKO animal exposure to HFD had lower body weight comparing to CTR+HFD (Fig. 1A). Both control animals and DKO animals exposed to HFD had significantly higher fasting glucose than CTR fed standard chow (Fig.1B). Under standard chow, bladder strips from DKO animal had significantly higher response to αβ-meATP, CCh, and neurally-mediated EFS contractions, when compared to floxed control animals (Fig. 2A,B,C). This response was independent from the presence or absence of the mucosa. In contrast, with intact mucosa, agonists and EFS induced contractions in DKO+HFD were not significantly different from contractile responses obtained from DKO fed standard chow. However, the contractile response to EFS in CTR+HFD tissue with intact mucosa was significantly higher than the response from CTR fed a normal diet (Fig.2C). In mucosa-denuded tissue, HFD had little effect on control tissue; however, for DKO+HFD animals, CCh, KCl and EFS induced contractions were significantly higher than the responses from DKO fed standard chow (Fig.3).

   We conclude that diabetic animals that are fed high fat diet develop worse bladder dysfunction than diabetic animals that are fed a normal diet.

4. **Publications:**

(1) Wang Z, et al. Aberrant P2X1R expression and ATP release contribute to bladder dysfunction in type 2 diabetes. (in preparation)

(2) Wang Z, et al. Effect of Obesity on the Development of Diabetic Bladder Dysfunction. (in preparation)

Fig. 1

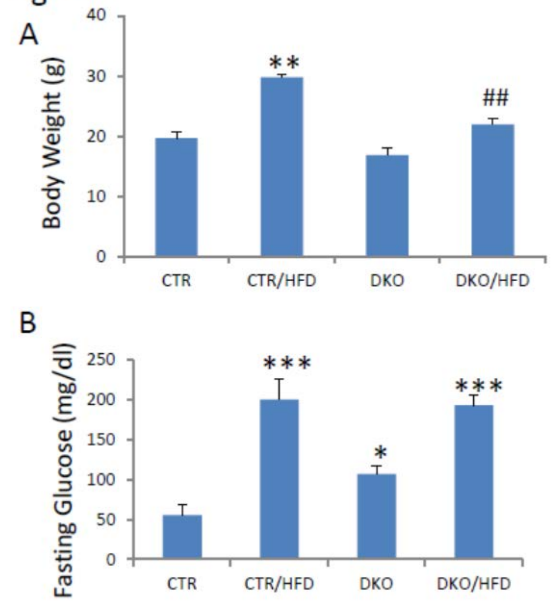

Figure 1. The body weight (A) and fasting glucose (B) level. All data are representative of at least three different experiments and are expressed as mean ± SEM, by 1-way ANOVA. * P<0.05, ** P< 0.01, compared with floxed control group; ##P<0.01, compared with CTR/HFD group.

Fig. 2

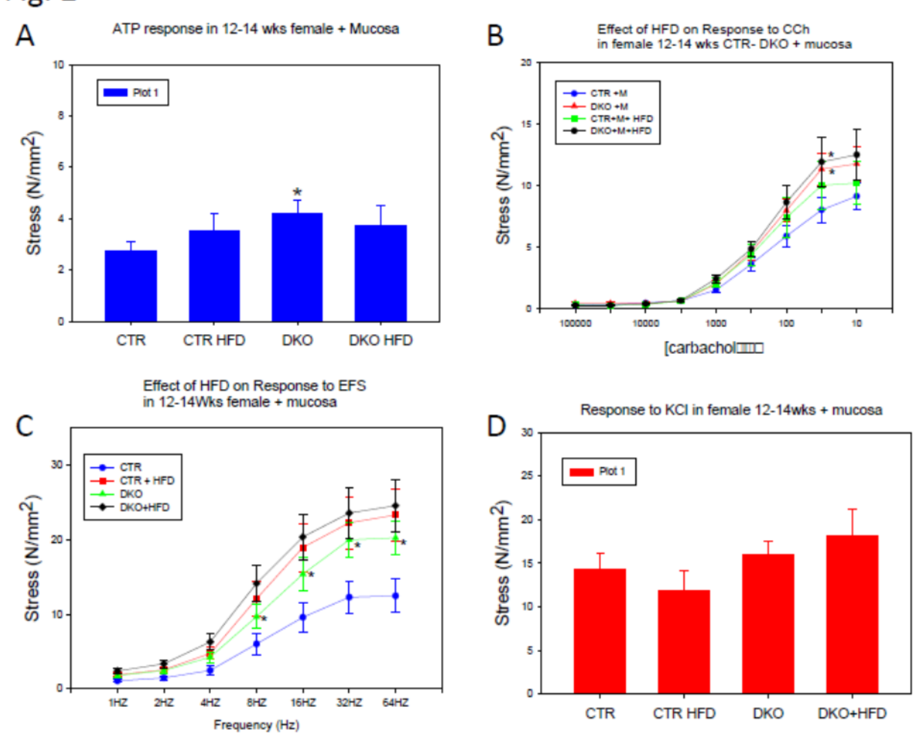

Figure 2. The stress of intact bladder strips upon different stimulations. All data are representative of at least three different experiments and are expressed as mean ± SEM, by 1-way ANOVA. * P<0.05, compared with floxed control group.

Fig. 3

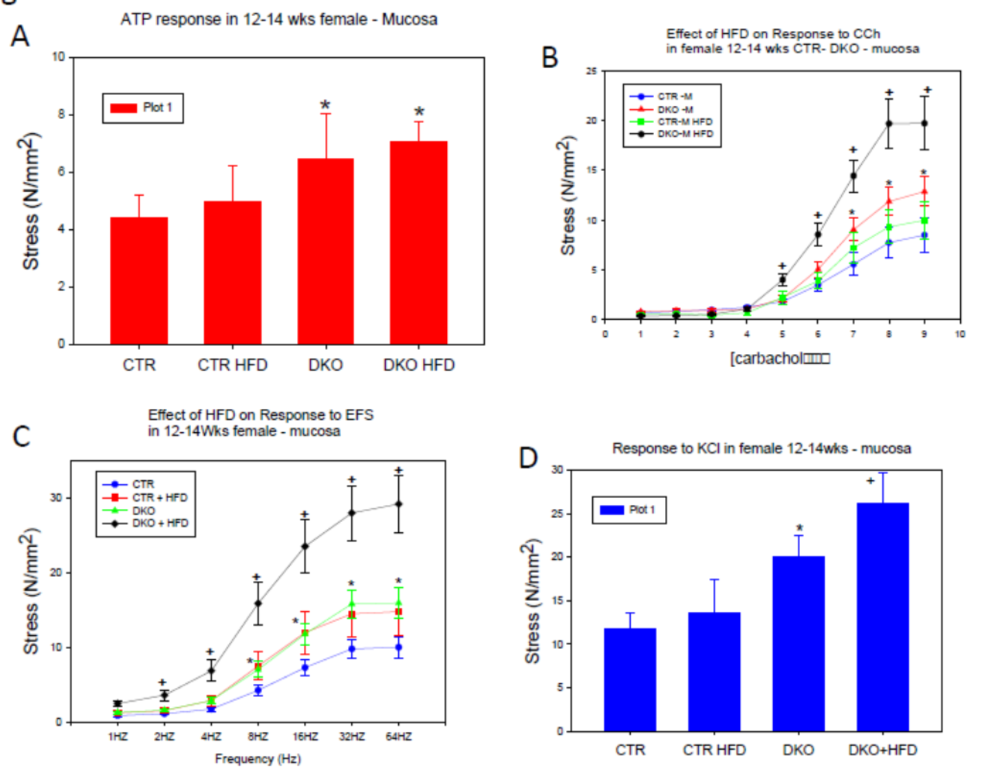

Figure 3. The stress of mucosa-denuded bladder strips upon different stimulations. All data are representative of at least three different experiments and are expressed as mean ± SEM, by 1-way ANOVA. * P<0.05, compared with urothelium-removed floxed control group; +P<0.05, compared with urothelium-removed DKO group.