P-14*

Analysis of the effect of dextran sodium sulfate loading on the pathological development of type 2 diabetic model mice

デキストラン硫酸ナトリウム負荷が肥満２型糖尿病モデルマウスの病態進展に及ぼす影響の解析

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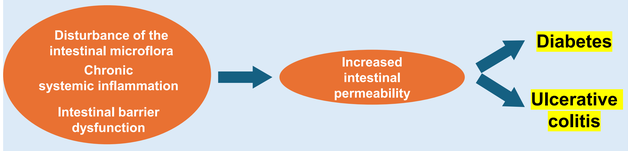
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Background and aims

Ulcerative colitis is a kind of inflammatory bowel disease (IBD).
This disease is primarily an inflammation of the intestines, often with abdominal pain, diarrhea, and bloody stools. Various mechanisms are possible, but no treatment has yet been established.

In this study, we focused on the possibility that the pathogenic mechanisms of **diabetes** and **ulcerative colitis** are similar.

The aims of this study are
1. Investigating the association between **type 2 diabetes** and **ulcerative colitis** by inducing ulcerative colitis in multiple mouse models of type 2 diabetes.
2. Searching for clues to elucidate the pathogenic mechanism of **ulcerative colitis.**



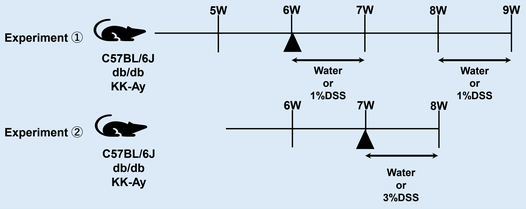
Materials and methods

Animals:
C57BL/6J mice (**C57**: normal controls)
db/db mice and **KK-Ay** mice (obese type 2 diabetes model animals)

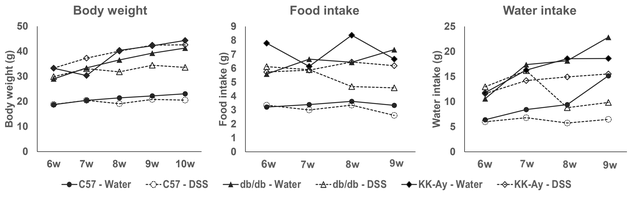
Diet: Normal chow (CE-2)

Drink:
Exp①: Water or 1%DSS solution (DSS was administered intermittently)
Exp②: Water or 3%DSS solution (DSS was administered continuously)

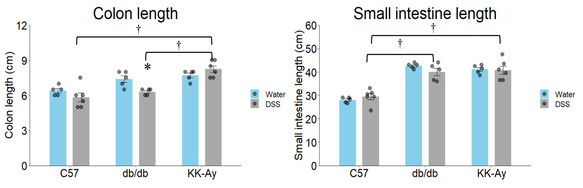
Period: 4 weeks (Experiment ①) or 1week (Experiment ②)



Results: (Experiment ①)

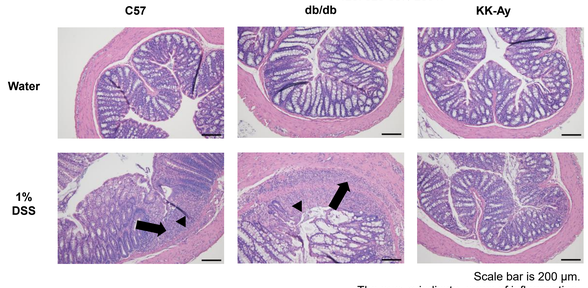


Intestine length



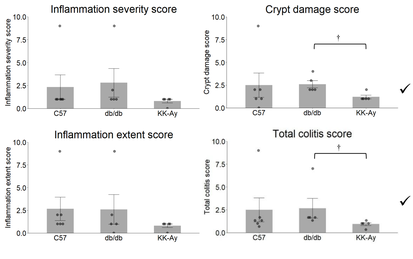
Histological images (colon tissue)

Refered to the following paper:
Williams et al., Gastroenterology 120: 925-937, 2001.



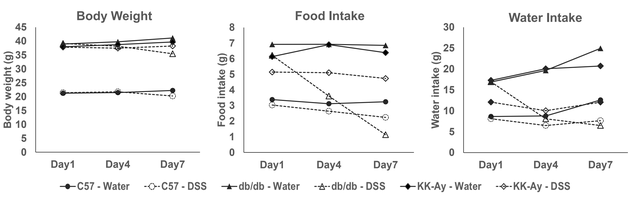
Scale bar is 200 μm.
The arrows indicate areas of inflammation.
The triangles indicate loss of crypts.

Histological score

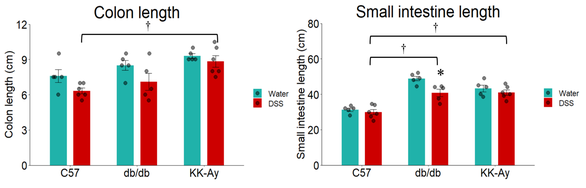


- ✓ The decrease was more pronounced in **db/db** mice (body weight, food intake, water intake, colon length).
- ✓ **db/db** mice showed the remarkable inflammation in colon tissue (crypt damage score, total colitis score).
- ✓ **KK-Ay** mice showed relatively mild inflammation compared to **C57** and **db/db**.

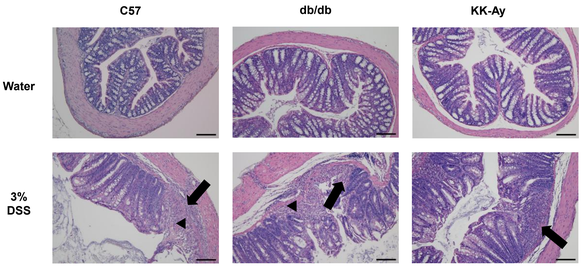
Results (Experiment ②)



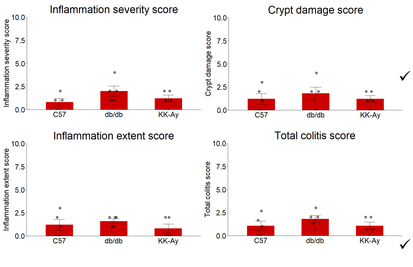
Intestine length



Histological images (colon tissue)



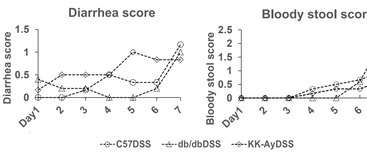
Histological score



- ✓ As in experiment ①, **db/db** mice showed a greater decrease (food intake, water intake).
- ✓ Compared to experiment ①, there is not a large clear difference between the strains, but the **db/db** mice show the most severe loss of crypts and inflammatory cell infiltration.
- ✓ **db/db** mice had the most blood in their stools.

Diarrhea and bloody stool scoring in Exp②

Diarrhea and bloody stool scoring		
score	diarrhea	bloody score
0	normal	normal
1	soft stool	blood in stool
2	disfigured diarrhea	blood in anus
3	watery diarrhea	constant bleeding



Discussion

In this experiment, it was suggested that **db/db** mice may be more susceptible to DSS-induced ulcerative colitis than **C57BL/6J** and **KK-Ay** mice.
Possible reasons for the differences include,
- Differences in genetic predisposition
- Differences in intestinal microflora (under analysis)

⇒Several pathways were found where microbial abundance was markedly different from the other two strains.

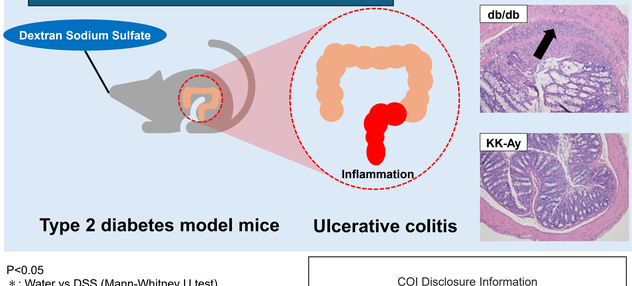
Conclusion

In this experiment, the possibility arose that **db/db** mice were more susceptible to DSS-induced ulcerative colitis than **C57BL/6J** and **KK-Ay** mice.

On the other hand, the effect of type 2 diabetic background on ulcerative colitis remains unknown at this time.

In the future, we plan to analyze the connection between the intestinal microflora and inflammation.

Summary



P<0.05
＊: Water vs DSS (Mann-Whitney U test)
†: C57DSS vs db/dbDSS or C57DSS vs KK-AyDSS or db/dbDSS vs KK-AyDSS (Kruskal-Wallis test, Steel-Dwass test)

COI Disclosure Information
Yusuke Nakata
In connection with this presentation, there is no COI to be disclosed with any companies.