

Supplementary Information

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Abstract: The numbers of obese people and diabetic patients are ever increasing. Obesity and diabetes are high-risk conditions for chronic diseases, including certain types of cancer, such as colorectal cancer (CRC). The aim of this study was to develop a novel animal model in order to clarify the pathobiology of CRC development in obese and diabetic patients. We developed an animal model of obesity and colorectal cancer by breeding the C57BL/KsJ-*db/db* (*db/db*) mouse, an animal model of obesity and type II diabetes, and the C57BL/6J-*Apc*^{Min/+} (*Min/+*) mouse, a model of familial adenomatous polyposis. At 15 weeks of age, the N9 backcross generation of C57BL/KsJ-*db/db-Apc*^{Min/+} (*db/db-Min/+*) mice developed an increased incidence and multiplicity of adenomas in the intestinal tract when compared to the *db/m-Min/+* and *m/m-Min/+* mice. Blood biochemical profile showed significant increases in insulin (8.3-fold to 11.7-fold), cholesterol (1.2-fold to 1.7-fold), and triglyceride (1.2-fold to 1.3-fold) in the *db/db-Min/+* mice, when compared to those of the *db/m-Min/+* and *m/m-Min/+* mice. Increases (1.4-fold to 2.6-fold) in RNA levels of insulin-like growth factor (IGF)-1, IGF-1R, and IGF-2 were also observed in the *db/db-Min/+* mice. These results suggested that the IGFs, as well as hyperlipidemia and hyperinsulinemia, promoted adenoma formation in the *db/db-Min/+* mice. Our results thus suggested that the *db/db-Min/+* mice should be invaluable for studies on the pathogenesis of CRC in obese and diabetes patients and the therapy and prevention of CRC in these patients.

Keywords: C57BL/KsJ-*db/db*; C57BL/6J-*Apc*^{Min/+}; Type 2 diabetes mellitus; colon carcinogenesis; animal model

Figure S1. N9 backcross generation.