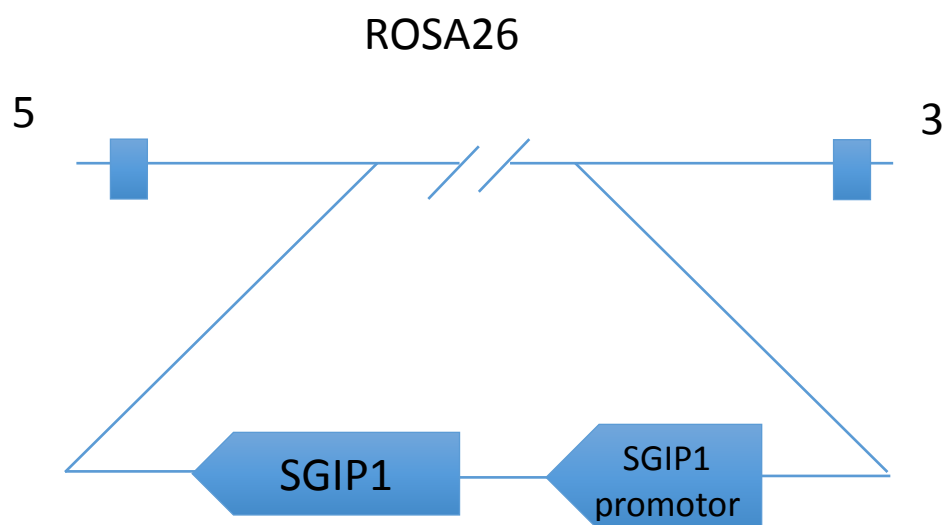


SGIP1 transgenic mice as a model of obesity and diabetes mellitus 2 (SGIP1 KI mice)

Many diseases of the nervous system, including central regulation of metabolic homeostasis, are accompanied by alterations in synaptic functions. Synaptic plasticity mediated by the endogenous cannabinoid system involves the activation of the Cannabinoid Receptor 1 (CB1R). The principles of CB1R signaling must be understood in detail for its therapeutic exploration.

Src homology 3-domain growth factor receptor-bound 2-like (endophilin) interacting protein 1 (SGIP1) is a novel Cannabinoid receptor (CB1R) interacting partner. SGIP1 prevents the endocytosis of the activated CB1R and signaling via the CB1R is altered as a consequence of the receptor's interaction with SGIP1 in a biased manner. While the CB1R mediated Gi/o-protein coupling is influenced by SGIP1 only marginally, the arrestin-associated signaling is changed profoundly. The projected studies are aimed at deciphering the consequences of SGIP1 interaction with the CB1R on its signaling at the molecular and cellular levels.

SGIP1 overexpression in *Psammomys Obesus* (Israeli sand rat) leads to an energy regulation imbalance resulting in obesity. Interestingly, the animals in their original ecosystem do not become obese. The obesity occurs only in when kept in cages with enough source of energy. Thus, in a way, this animal model is far closest to the situation of so called "civilization disease" characterized by lack of movement, inappropriate caloric input with all consequences known as metabolic syndrome.



Obř. 1. Schematic representation of the generation of SGIP KI mice via insertion into the ROSA26 locus

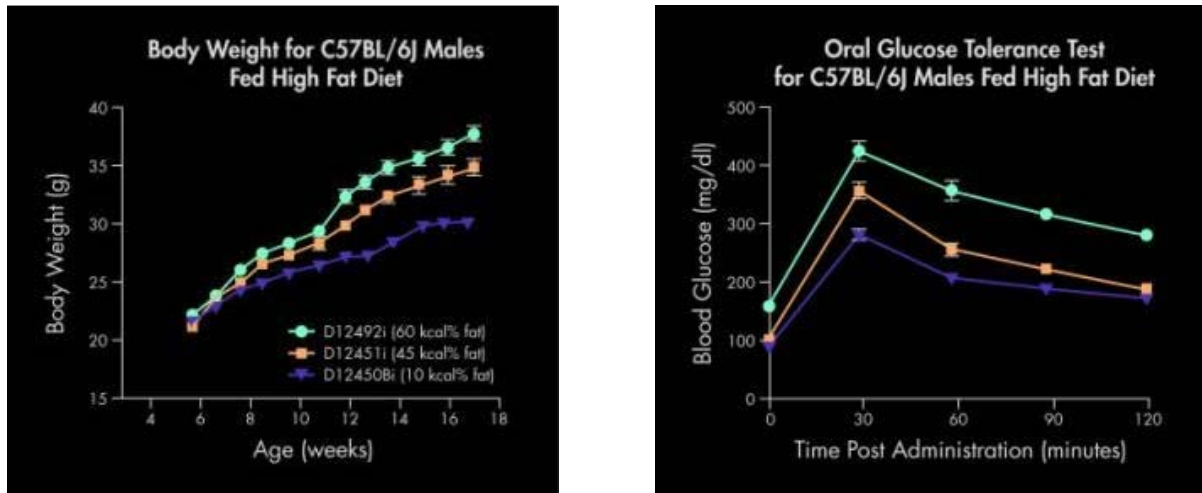


Fig. 2 Body weight development in SGIP1 KI mice (left) and glycaemia (right) upon glucose tolerance test

Most of the current problems with obesity and growing number of Diabetes Mellitus type 2 patients arise as a consequence of the life style. Animal model that reflects such situation, lean in its biotope, obese in cages resembles well this type of disorder and might thus serves as an excellent model in prediction of treatment possibilities and prevention cure.

To get more information about the mice, please contact Center for Technology Trasfer, IMG AS CR, Videnska 1083, 142 20 Praha 4, Czech Republic; Tel. (420-241 063 227 or 420-602 892 876).