In conclusion, the leptin-deficient ob/ob mouse is a new animal model that develops both large motor and sensory fiber and small sensory fiber PDN and responds to pathogenetic treatment. The results support the role for increased aldose reductase activity in functional and structural changes of PDN in type 2 diabetes. Publication types. Research Support, Non-U.S. Diabetic mice (db/db) and control mice (db/m) were randomly divided into four groups. We induced endothelial leptin resistance in rat aortic endothelial cells through treatment with palmitic acid (0.3 mM) or knockdown of leptin receptor (Ob-Rb), which resulted in the increase of suppressor of cytokine signaling 3 expression, the decrease of Ob-Rb expression, and signal transducer and activator of transcription 3 (STAT3) phosphorylation at Tyr705. We found that these indicators of leptin resistance were reversed by knockdown of ASM or by the selective ASM inhibitors amitriptyline (AMI) and imipramine (IMI). Supplementation of ceramide inhibited Ob-Rb expression and STAT3 phospho Animal models of human type 2 diabetes, ob/ob mouse and db/db mouse, have been extensively studied on the effects of leptin on glucose homeostasis and body weight. Ob/ob mice present with hyperphagia, extreme obesity and hyperglycemia due to mutated, biologically inactive leptin and revert to normoglycemia and normal body weight by exogenous leptin injection and leptin gene-treatment. Leptin treatment profoundly reduced food intake from 10 ± 1.5 g/day in untreated hyperphagic diabetic mice to 2.8 ± 0.8 g/day. The leptin-treated mice lost 2.5 g of body weight and 76% of body fat during the 12 days, whereas the saline treated mice lost 2.0 ± 1.7 g of body weight in 12 days, 57% of which was body fat [24]. Mouse and its ineffectiveness in the db/db mouse. Perhaps most importantly, they compared injection of Ob protein into the cerebral ventricle and found this route to be more effective than the intraperitoneal route of administration, demonstrating the primary action on central neuronal networks that play an important role in feeding behavior and energy balance. Lipodystrophic mice, lacking white adipose tissue and therefore having very low leptin levels, have a similar phenotype to the ob/ob mouse. They are hyperphagic, insulin resistant, and diabetic. Metabolic abnormalities of the ob/ob mouse...