

Supplementary Table 4: KEGG Pathways significantly associated with differentially expressed genes in the islets of NOD mice at each age (P<0.05)

10 day old	
Pathway name	P-value
Cocaine addiction	5.53E-04
Glucagon signaling pathway	6.36E-04
Signaling pathways regulating pluripotency of stem cells	7.20E-04
ECM-receptor interaction	2.66E-03
Proteoglycans in cancer	2.86E-03
Human papillomavirus infection	3.55E-03
Amphetamine addiction	4.24E-03
Longevity regulating pathway	4.67E-03
PI3K-Akt signaling pathway	4.99E-03
Adipocytokine signaling pathway	8.51E-03
Mannose type O-glycan biosynthesis	1.22E-02
Prostate cancer	1.34E-02
Cholinergic synapse	1.34E-02
Focal adhesion	1.41E-02
Gastric cancer	1.42E-02
Hepatocellular carcinoma	1.51E-02
Insulin secretion	1.58E-02
mTOR signaling pathway	1.65E-02
Endocrine resistance	1.71E-02
Basal cell carcinoma	1.88E-02
Ras signaling pathway	2.12E-02
Rap1 signaling pathway	2.31E-02
MAPK signaling pathway	2.38E-02
cAMP signaling pathway	2.91E-02
Human T-cell leukemia virus 1 infection	2.99E-02
Hepatitis B	3.09E-02
Amyotrophic lateral sclerosis (ALS)	3.44E-02
Viral carcinogenesis	3.50E-02
Central carbon metabolism in cancer	3.51E-02
Breast cancer	3.60E-02
Long-term depression	3.63E-02
Folate biosynthesis	4.29E-02
Melanogenesis	4.50E-02
Prion diseases	4.53E-02
Protein digestion and absorption	4.64E-02

4 week old	
Pathway name	P-value
Olfactory transduction	1.12E-08
Antigen processing and presentation	6.53E-05
Fat digestion and absorption	2.58E-04
Glutamatergic synapse	4.11E-04
Autoimmune thyroid disease	5.82E-04
Cell adhesion molecules (CAMs)	1.20E-03
Type I diabetes mellitus	1.30E-03
Endocrine and other factor-regulated calcium reabsorption	1.98E-03
Longevity regulating pathway	5.98E-03
Type II diabetes mellitus	6.46E-03
Necroptosis	7.67E-03
Vitamin B6 metabolism	8.08E-03
MAPK signaling pathway	8.74E-03
Maturity onset diabetes of the young	9.75E-03
Glycine, serine and threonine metabolism	9.75E-03
Ovarian steroidogenesis	1.01E-02
GABAergic synapse	1.03E-02
Regulation of lipolysis in adipocytes	1.25E-02
Cysteine and methionine metabolism	1.30E-02
Cocaine addiction	1.41E-02
Calcium signaling pathway	1.61E-02
Neuroactive ligand-receptor interaction	1.69E-02
Mucin type O-glycan biosynthesis	2.54E-02
Allograft rejection	2.63E-02
Taurine and hypotaurine metabolism	2.84E-02
Gastric acid secretion	2.91E-02
Glycosphingolipid biosynthesis - lacto and neolacto series	3.04E-02
Morphine addiction	3.19E-02
Graft-versus-host disease	3.23E-02
Glycerolipid metabolism	3.27E-02
Hematopoietic cell lineage	3.47E-02
Aldosterone synthesis and secretion	3.53E-02
Taste transduction	3.72E-02
Pancreatic secretion	3.76E-02
Hepatitis B	4.17E-02
Cellular senescence	4.18E-02
cAMP signaling pathway	4.54E-02
mRNA surveillance pathway	4.66E-02
Oxytocin signaling pathway	4.68E-02

12 week old			
Pathway name	P-value	Pathway name	P-value
Cell adhesion molecules (CAMs)	4.74E-14	Rap1 signaling pathway	1.71E-04
Hematopoietic cell lineage	1.09E-10	Phosphatidylinositol signaling system	2.15E-04
Phagosome	2.24E-09	PD-L1 expression and PD-1 checkpoint pathway in cancer	2.52E-04
Cytokine-cytokine receptor interaction	1.12E-08	MAPK signaling pathway	4.54E-04
Th17 cell differentiation	1.12E-08	Regulation of actin cytoskeleton	6.70E-04
Natural killer cell mediated cytotoxicity	1.12E-08	DNA replication	7.81E-04
Systemic lupus erythematosus	1.12E-08	Kaposi sarcoma-associated herpesvirus infection	7.97E-04
Staphylococcus aureus infection	3.20E-08	Acute myeloid leukemia	1.09E-03
Primary immunodeficiency	7.79E-08	MicroRNAs in cancer	1.72E-03
Leukocyte transendothelial migration	8.06E-08	Platelet activation	1.79E-03
Chemokine signaling pathway	8.13E-08	Small cell lung cancer	2.32E-03
Human T-cell leukemia virus 1 infection	9.09E-08	Viral carcinogenesis	3.38E-03
NF-kappa B signaling pathway	3.30E-07	NOD-like receptor signaling pathway	4.24E-03
Pathways in cancer	4.61E-07	Apoptosis - multiple species	5.13E-03
Antigen processing and presentation	4.62E-07	p53 signaling pathway	6.61E-03
Inflammatory bowel disease (IBD)	6.01E-07	Homologous recombination	7.61E-03
T cell receptor signaling pathway	6.61E-07	Chagas disease (American trypanosomiasis)	8.66E-03
Osteoclast differentiation	1.13E-06	Melanoma	8.84E-03
Complement and coagulation cascades	2.09E-06	Adherens junction	1.14E-02
Pertussis	2.91E-06	Inositol phosphate metabolism	1.32E-02
Fc gamma R-mediated phagocytosis	3.17E-06	Cholinergic synapse	1.38E-02
Viral myocarditis	3.26E-06	Pancreatic cancer	1.43E-02
Tuberculosis	5.15E-06	Measles	1.49E-02
Intestinal immune network for IgA production	5.24E-06	Central carbon metabolism in cancer	1.54E-02
Apoptosis	7.53E-06	Human cytomegalovirus infection	1.65E-02
Ras signaling pathway	8.60E-06	Hypertrophic cardiomyopathy (HCM)	1.72E-02
Transcriptional misregulation in cancer	8.73E-06	Inflammatory mediator regulation of TRP channels	1.93E-02
Graft-versus-host disease	9.83E-06	Focal adhesion	1.96E-02
Allograft rejection	1.03E-05	Non-alcoholic fatty liver disease (NAFLD)	2.29E-02
Leishmaniasis	1.05E-05	Alcoholism	2.47E-02
Rheumatoid arthritis	1.14E-05	Oxytocin signaling pathway	2.58E-02
Cell cycle	1.20E-05	ECM-receptor interaction	2.76E-02
Toxoplasmosis	1.25E-05	Salmonella infection	2.77E-02
Th1 and Th2 cell differentiation	1.42E-05	Chronic myeloid leukemia	2.78E-02
Asthma	1.88E-05	Insulin resistance	2.82E-02
Human Immunodeficiency virus 1 infection	2.72E-05	Vascular smooth muscle contraction	2.94E-02
Epstein-Barr virus infection	4.37E-05	Proteoglycans in cancer	3.36E-02
Autoimmune thyroid disease	4.90E-05	AGE-RAGE signaling pathway in diabetic complications	3.44E-02
Type I diabetes mellitus	5.80E-05	TNF signaling pathway	3.57E-02
JAK-STAT signaling pathway	7.11E-05	cAMP signaling pathway	3.99E-02
PI3K-Akt signaling pathway	7.31E-05	Axon guidance	4.34E-02
Malaria	1.12E-04	Apelin signaling pathway	4.46E-02
IL-17 signaling pathway	1.29E-04	FoxO signaling pathway	4.61E-02
Fc epsilon RI signaling pathway	1.40E-04	Nicotinate and nicotinamide metabolism	4.82E-02
B cell receptor signaling pathway	1.52E-04	Dilated cardiomyopathy (DCM)	4.83E-02
C-type lectin receptor signaling pathway	1.53E-04	Base excision repair	4.91E-02
Cellular senescence	1.56E-04	Endocytosis	5.02E-02