Figure S1: Modified representation of Kegg pathway bta04015: Rap1 signaling pathway, highlighting DEG identified in this study. Proteins encoded by genes whose expression was significantly higher in leukocytes of cows with LOW (<35 ng/ml) compared with HIGH (>100 ng/ml) IGF-1 at 14 days in milk are shown in red and those whose expression was lower are in green. Epac, RASGRP5 and RPAGEF5 (repac) are all guanine nucleotide exchange factor (GEF). These activate Rap1 and Rap2 by catalyzing the dissociation of GDP from inactive Ras proteins allowing GTP to bind and induce a conformational change that permits interaction with downstream effectors (Quilliam et al., 2002). Potential extracellular activators identified in our study included dopamine, adenosine, and several growth factors. Autotaxin, encoded by *ENPP2*, is a secreted ectoenzyme which hydrolyzes lysophosphatidylcholine to produce lysophosphatidic acid (LPA), a lipid known to be involved in immune cell signaling.