Gerald J Prud'homme, J Diabetes Metab 2014, 5:10
http://dx.doi.org/10.4172/2155-6156.S1.026

OMICS Group Conferences
Accelerating Scientific Discovery

5th World Congress on
Diabetes & Metabolism
November 03-05, 2014 Embassy Suites Las Vegas, USA

The protective effects of GABA on human islet cells

Gerald J Prud'homme
University of Toronto, Canada

In previous studies we found that the administration of gamma-aminobutyric acid (GABA) prevented type 1 diabetes (T1D) in three preclinical models. Furthermore, it induced beta-cell regeneration following the streptozotocin-induced depletion of these cells. Interestingly, many of these beneficial effects were accompanied by strong anti-inflammatory and immunosuppressive activities. Thus, we observed that GABA has stimulatory effects on murine islet beta cells but, in contrast, inhibitory effects on immune cells. Because human and murine cells can respond in considerably different ways, we proceeded to analyze the effects of GABA on human cells. We found that human beta cells respond to GABA in a manner similar to the murine cells. Notably, it markedly improved the survival of islet cells in culture. It protected these cells against apoptosis induced by cytokines and immunosuppressive drugs such as rapamycin and tacrolimus (FK506). We examined several potential mechanisms and discovered that it inhibits activation of NF-kB, and we identified a likely molecular mechanism for this action. In vivo, GABA also reduced beta-cell apoptosis following human islet transplantation into immunodeficient mice, and it stimulated the proliferation of these cells. Because T1D is an autoimmune disease, we also examined the response of human immune cells. GABA exerted inhibitory effects on T lymphocytes similar to those previously reported in mice, and this was dependent on the type A GABA receptor. Importantly, as in islet cells, it suppressed NF-kB activation. We documented that it blocks one of the earliest events in T-cell activation, i.e., calcium influx.

Conclusion: GABA ameliorated human islet-cell survival considerably, and had a major inhibitory action on human immune cells. The inhibition of canonical NF-kB activation appears to be one of its most important effects, at least in the context of T1D and islet transplantation. Indeed, activation of this pathway is harmful to islet cells, and promotes autoimmune or alloreactive responses. Our findings suggest that GABA may be an effective therapeutic agent in diabetes.

prudhommeg@smh.ca