A Phase One Insulin-Independent Glucose Regulation Cascade Study in Papio anubis Baboons

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Diabetes mellitus is a metabolic disorder resulting in the dysregulation of blood glucose (BG), affecting more than 14% of adults. BG is typically regulated by the pancreatic hormone insulin, secreted by beta cells from Islets of Langerhans. Exploring insulin independent glycemic regulation can lead to transformative therapeutics and expand treatment options. Researchers developing methods of lowering immunosuppression in porcine islet transplants for Type 1 Diabetes Mellitus induced diabetes in two Papio anubis baboons. One baboon previously underwent a total pancreatectomy followed by the islet transplant that failed to engraft. Despite complete islet ablation and failed replacement, we observed near-normal BG levels in the baboon. The aim of this Phase One study was to confirm the absence of insulin in the serum and attempt to eliminate activation of the standard insulin receptor cascade. I analyzed the serum using a C-Peptide and Insulin ELISAs to monitor endogenous and total insulin production, and results showed minimal concentration in both instances. This confirmed the absence of functional pancreatic insulin secretion. I then developed a Western Blot protocol testing for phosphorylation of the Insulin Receptor as well as AKT, a downstream signaling molecule, validated by appropriate controls. The data showed that neither protein was active in the baboon serum, enabling the elimination of the standard insulin signaling pathway. Future research will test the baboon serum for factors like hepatic production and alternate glucose regulation pathways. The implications of this project, if a novel protein is found, could be the basis of novel therapeutics for diabetes.

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