6th ISAA, Abstract

Odyssey for islets of Langerhans, blood vessels and evolution

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My talk concerns diabetes. I first studied how insulin-producing islet B-cells are destroyed. Using isolated islets of Langerhans, streptozotocin and alloxan, representative diabetogenic agents, were found to induce islet DNA strand breaks to activate nuclear PARP, thereby depleting intracellular NAD^+ and inhibiting islet synthesis of proinsulin. What makes diabetes a terrible disease is its vasculopathy. It decreases both life expectancy and QoL. I then moved to vascular biology and conducted screen for environmental and genic accounts of diabetic vasculopathy. This screen revealed advanced glycation end-products (AGE) as the major environmental account and the receptor for AGE (RAGE) as the main cellular device that respond to AGE. RAGE-overexpressing transgenic exacerbated diabetic retinopathy and nephropathy, while RAGE-null mice never developed nephropathy. From the viewpoint of evolution, plants and insects develop hyperglycemia but without vascular derangement. Their blood sugars do not have a carbonyl moiety that elicits AGE formation. Birds occasionally show hyperglycemia, but do not suffer from vasculopathy. Animal species susceptible to diabetic vasculopathy are only mammals. What discriminates such a difference among animal species is the presence or absence of RAGE gene. Vascular RAGE was found to transport oxytocin into the brain to elicit maternal bonding behavior. Diabetes and its vasculopathy would have been beyond expectation of evolution. Diabetes abuses RAGE which was probably gifted to mammals as a device for parental bonding and nurturing.