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Cell physiology

The leucine-rich repeat kinase LRRK2/Park8 controls regulated exocytosis in neurons and endocrine cells of the pancreas

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Endocrine cells of the pancreas share many physiological features with neurons, although they have different embryological origins. Regulated membrane fusion resulting in hormone exocytosis in endocrine cells is controlled by the same core SNARE (soluble N-ethylmaleimide-sensitive factor attachment protein receptor) fusion machinery that mediates neurotransmitter release at synapses.

The leucine-rich repeat kinase 2 (LRRK2), a protein expressed in neurons and associated with inherited Parkinson's disease, has been recently shown to interact with specific synaptic proteins and influence synaptic transmission. Given the functional similarities between neurons and endocrine cells of the pancreas, here we first verified LRRK2 expression in islet of Langerhans, and then we investigated its possible involvement in hormone release.

By means of RT-PCR and western blotting experiments, we detected LRRK2 expression in beta and alpha cell lines and in human islets of Langerhans. Using the pH-sensitive dye acridine orange as a tool to monitor exocytosis/endocytosis and elisa assays in the presence and the absence of specific LRRK2 inhibitors, we demonstrated LRRK2 involvement in the control of vesicles trafficking and hormone release in both alpha and beta cells.

Our data for the first time identified LRRK2 as a novel component of the secretory machinery of endocrine cells of the pancreas and further highlight the similarity between neurons and endocrine cells.