Ca^{2+} signaling in the pancreatic beta cell in health and disease

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The insulin secreting beta cell is situated in the pancreatic islet which is a micro-organ consisting of endocrine cells, non-endocrine cells, a rich capillary network and nerves. The dynamics of the Ca^{2+} signal has a decisive role in overall function and survival of the pancreatic beta cell and is regulated by a sophisticated interplay between factors generated within the islet structure as well as by blood borne factors. However, information regarding in vivo beta cell Ca^{2+} signaling is scarce. The objective of our present research is to get novel insights into Ca^{2+} handling in the pancreatic beta cell under normal conditions and in diabetes within the living organism. For this purpose we have developed a unique imaging platform where we transplant islets into the anterior chamber of the eye (ACE) and use the cornea as a natural body window for functional in vivo microscopic imaging. In my presentation I will discuss the ACE as an in vivo, non-invasive, imaging site for measuring Ca^{2+} dynamics longitudinally in three dimensions and at single cell resolution. Taking the advantage of the fact that the pancreatic islet represents an entire micro-organ and of our novel in vivo imaging technology, we can now for the first time delineate the molecular regulation of Ca^{2+} signaling with cellular resolution in the living organism in an intact organ. I will also discuss some aspects of the CaV3.1 channel, the CaVα2δ1 subunit and the Cavβ3 subunit in beta cell Ca^{2+} homeostasis in health and disease. This not only leads to a better understanding of beta cell Ca^{2+} signaling but will also allow us to identify novel drugable targets enabling more effective and specific pharmacological treatment strategies for diabetes and its resulting severe complications.