In vivo Ca^{2+} imaging analysis of pancreatic β-cells and islets using transgenic mice expressing a high-sensitivity ratiometric Ca^{2+} indicator

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Pancreatic β-cells release insulin in a Ca^{2+}-dependent pulsatile manner to control blood glucose levels. Although the Ca^{2+} signaling mechanism in β-cells has been extensively studied using *in vitro* and *ex vivo* preparations, its analysis in living animals remains challenging. Therefore, while β-cell activities *in vivo* are under the influence of the autonomic nervous system, various hormones and other bioactive substances, Ca^{2+} responses of β-cells under physiological conditions have not been clarified. We here report a method to monitor and analyze *in vivo* β-cell Ca^{2+} activities using a transgenic mouse line expressing a genetically encoded ratiometric Ca^{2+} indicator, YC-Nano50. Using the method, we visualized β-cell Ca^{2+} signals in laparotomized mice under anesthesia, and observed synchronized Ca^{2+} oscillations in β-cells within individual islets. Furthermore, we succeeded in monitoring Ca^{2+} activities in multiple islets simultaneously, which may clarify the basis for a pulsatile insulin secretion. Further studies in living animals using the new method is expected to help elucidate the mechanism of insulin secretion and the etiology of diabetes.