Why do beta cells stop releasing insulin in type 2 diabetes?

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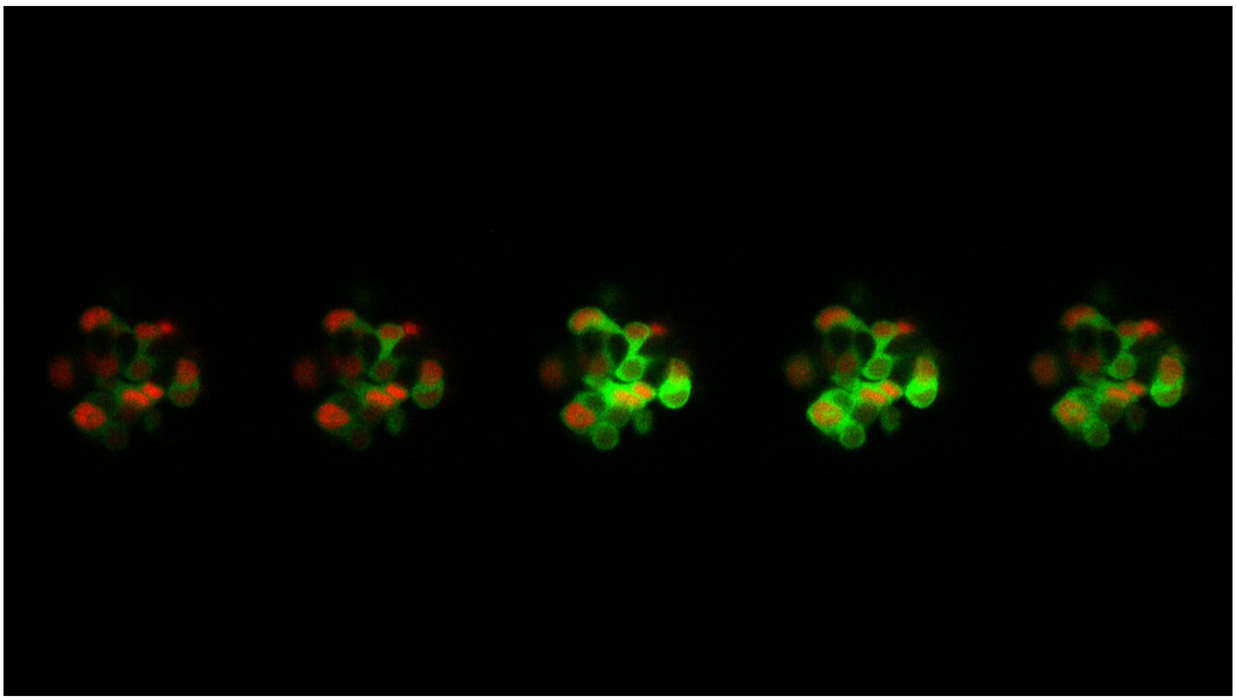


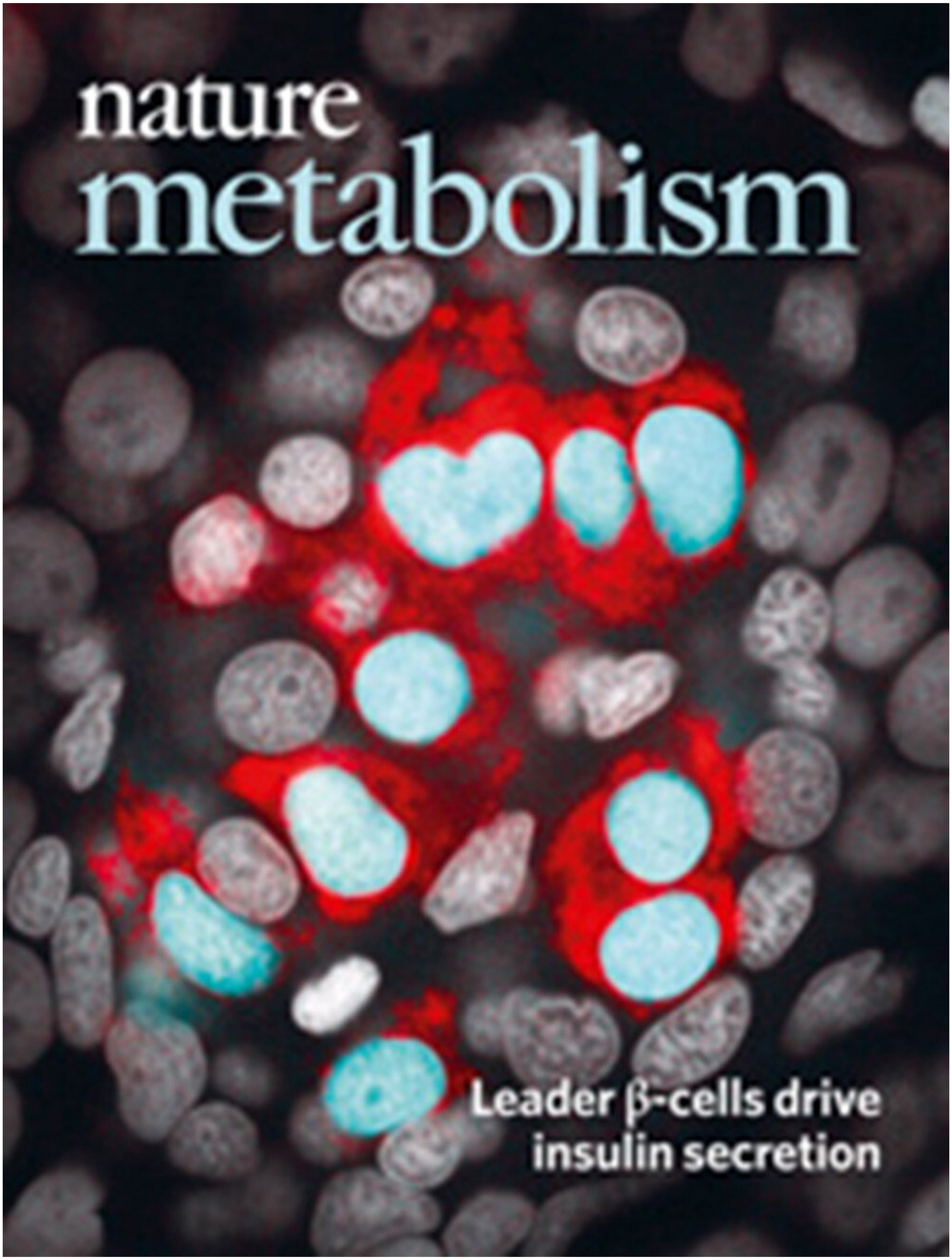
Super-connected "leader" cells coordinate insulin response and help us to understand how diabetes develops. Credit: CRTD

Due to the increasing insulin resistance of cells, patients with type 2 diabetes suffer from increased blood sugar levels with far-reaching consequences. After many years of illness, insulin production dries up and patients have to inject insulin.

What causes the lack of insulin production in people with type 2 diabetes? Researchers from the Center for Regenerative Therapies (CRTD) at the Technische Universität Dresden (TUD), together with colleagues from Imperial College London and other research institutes from the U.K., Canada and Italy, have observed notable cell interactions: The beta cells of the pancreas work as highly connected clusters known as islets, and their responses to rising blood glucose levels are coordinated by small teams of "leader cells." The scientists have published their results in *Nature Metabolism*.

Previous work from co-author Professor Guy Rutter from Imperial College London and Professor David Hodson (now at Birmingham University in the U.K.) provided evidence that this may be the case using isolated tissues. To show that this was also true in living animals including in zebrafish and mice, the research teams developed an innovative imaging technique that allowed them to observe beta cells' hierarchical relationship in vivo.

"In these model organisms, we saw that when blood glucose levels increased, the response of beta cells originated from temporally defined leader cells. When we selectively deleted the leader cells, the level of coordination in subsequent responses to glucose was disrupted," explains CRTD Ph.D. student Luis Delgadillo Silva, one of the two lead authors of the study. Mathematical analysis revealed that the leader cells have a controlling role over the islet. In addition, the researchers were able to show that some beta cells contained a unique molecular signature, which would allow them to be more metabolically active and perhaps more glucose sensitive.


nature
metabolism
Leader β-cells drive
insulin secretion

The study of Imperial College London and TU Dresden / CRTD scientists and colleagues from other research institutes from the UK, Canada and Italy is featured on the cover of the scientific journal *Nature Metabolism*. Credit: *Nature Metabolism*

Based on their findings, the scientists will now study the importance of leader cells are in the development of diabetes. "It's important for us to understand if the leader cells are vulnerable to damage as diabetes develops, and crucially, whether they can be targeted to maintain strong and healthy insulin responses to help cure the disease," explains Dr. Victoria Salem, senior clinical research fellow in the Section of Investigative Medicine at Imperial College London, who co-led the U.K. study.

"To understand better the role of leader cells in islet function, we have established a set of new tools in zebrafish, which will help us to activate or silence beta cells by shining light on them, as well as to track individual cells over time. Using these tools, we will be able to ask precisely how many cells are controlled by a leader cell and what genes determine the identity of a leader cell," says Luis Delgadillo Silva.

More information: Victoria Salem et al, Leader β-cells coordinate Ca2+ dynamics across pancreatic islets in vivo, *Nature Metabolism* (2019). DOI: 10.1038/s42255-019-0075-2

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