Conferencias y Simposios

SIMPOSIO 17: Falla de la célula beta

Coordinadora: Dra. Alicia Jawerbaum

Al rescate de la célula beta

Dr. Luis Flores
Centro de Endocrinología Experimental y Aplicada (CENEXA; Universidad Nacional de La Plata- Consejo Nacional de Investigaciones Científicas y Técnicas, CONICET) La Plata, Provincia de Buenos Aires, Argentina

Las células β pancreáticas están especializadas para liberar insulina ante cualquier aumento de la glucemia mediante un complejo mecanismo altamente regulado que asegura el mantenimiento de su homeostasis. Existen múltiples factores genéticos y ambientales (1) que atentan contra la integridad funcional de las células β y que son responsables de la progresión del estado normal al de prediabetes o de diabetes mellitus tipo 2 (DM2).

En la actualidad disponemos de diversas herramientas farmacológicas que pueden recuperar su función secretora, pero ninguna es capaz de recuperar su masa, por lo cual resulta fundamental prevenir su pérdida. El consumo de dietas desbalanceadas, particularmente de dietas ricas en bebidas edulcoradas con jarabe de alto contenido de fructosa (DRF), promueve la ruptura de la homeostasis metabólica y el surgimiento de un estado de insulinorresistencia (IR) que ya se manifiesta en el estadio de prediabetes (2,3).

En numerosas publicaciones nuestro grupo demostró los cambios moleculares que se presentan en las células β de ratas prediabéticas por la administración de una DRF por tres semanas (2,3), al igual que su recuperación mediante el reemplazo de dicha dieta por otra balanceada. A nivel clínico, se postula que las dietas hipercalóricas y desbalanceadas promueven un aumento de la lipogénesis de novo, desencadenando disfunciones que se explican por la llamada hipótesis de los “ciclos gemelos”. Dicha hipótesis sostiene que junto con el incremento del peso corporal que promueve IR, el aumento en el hígado de la lipogénesis de *novo* genera una mayor captación de ácidos grasos a nivel insular al afectar su función secretora y aumentar la glucemia con relativa rapidez. El estudio DIRECT (*Diabetes Remission Clinical Trial*) (4), basado en dicha hipótesis, demostró que la disminución sostenida y controlada del aporte calórico en personas obesas con DM2 (con no más de seis años de diagnóstico, IMC entre 27 y 45 kg/m^2 y sin tratamiento previo con insulina), permite recuperar la función y, posiblemente, también la masa celular β. La reversión de la DM2 sin requerimientos posteriores de medicación para mantener su homeostasis glucémica se logró en el 46% de los participantes que habían logrado perder al menos 15 kg. En conjunto, estos resultados demuestran el rol patogénico que ejercen las dietas hipercalóricas y desbalanceadas sobre las células β y la firme posibilidad de ser rescatadas tanto del estadio de prediabetes como de DM2 mediante la promoción de hábitos saludables.

Palabras clave: célula beta; diabetes.

Bibliografía:

1. Vasiljević J, et al. The making of insulin in health and disease. Diabetologia 2020; 63: 1981-1989.
2. Román CL, et al. Islet NADPH oxidase activity modulates β-cell mass and endocrine function in rats with fructose-induced oxidative stress. BBActa 2014; 1840: 3475-3482.
3. Maiztegui B, et al. VMP1-related autophagy induced by a fructose-rich diet in β-cells: its prevention by incretins. Clin. Sci 2017; 131:673-687.

4. Lean MEJ, et al. Durability of a primary care-led weight-management intervention for remission of type 2 diabetes: 2-year results of the DiRECT open-label, cluster-randomised trial. Lancet 2019; 7:344-355.

SYMPOSIUM 17: Beta cell failure

Coordinator: Dra. Alicia Jawerbaum

Rescuing the beta-cell

Dr. Luis Flores
Center for Experimental and Applied Endocrinology (CENEXA; National University of La Plata- National Council for Scientific and Technical Research, CONICET) La Plata, Province of Buenos Aires, Argentina

Pancreatic beta-cells are trained to release insulin whenever there is an increase of glycemia, through a complex mechanism which is highly regulated and ensures the maintenance of the homeostasis.

There are multiple genetic and environmental (1) factors that endanger the functional integrity of the beta-cells and are responsible for the progression from a normal state to one of prediabetes or type 2 diabetes (T2D).

Currently, we have at our disposal a diverse set of pharmacological tools that can help recover the secretory function, but none of them is able to recover the mass, which is why it is fundamental to prevent the loss in the first place.

The consumption of unbalanced diets, particularly diets rich in drinks sweetened with high-fructose corn syrup (HFCS), promotes the rupture of the metabolic homeostasis and the appearance of a state of insulin resistance (IR), which already appears in the prediabetic stage (2,3).

Our group has shown in several publications the molecular changes that occurs in the beta-cells of prediabetic rats with the administration of HFCS during three weeks (2,3), and the subsequent recovery through the replacement of said diet with a balanced one.

On a clinical level, it is claimed that high calorie and unbalanced diets promote an increase in de novo lipogenic, unchaining dysfunctions that are explained by the hypothesis of the “twin cycles”. Said hypothesis asserts that together with the increase in the body weight that promotes IR, the increase in the liver of de novo lipogenic generates a higher capture of fatty acids at an islet level, which affects the secretory function and increases glycemia relatively quickly.

The research study DiRECT (Diabetes Remission Clinical Trial) (4), based on the mentioned hypothesis, has shown that the sustained and controlled reduction of the caloric intake in obese people with T2D (with no more than 6 years since the diagnosis, a BMI between 27 and 45 kg/m2 and without a previous treatment with insulin) allows for the recovery of the function and, possibly, also the beta-cell mass.

The reversal of T2D without subsequent requirements of medication to maintain the glucose homeostasis has been achieved in the 46% of the participants that have managed to lose at least 15 kg. All together, these results show the pathogenic role that high calorie and unbalanced diets have over beta-cells and the strong possibility of being rescued from both the prediabetic stage and the T2D stage through the promotion of healthy habits.

Key words: beta cell; diabetes.

Bibliography

1. Vasiljević J, et al. The making of insulin in health and disease. Diabetologia 2020; 63: 1981-1989.
2. Román CL, et al. Islet NADPH oxidase activity modulates β-cell mass and endocrine function in rats with fructose-induced oxidative stress. BBActa 2014; 1840: 3475-3482.
3. Maiztegui B, et al. VMP1-related autophagy induced by a fructose-rich diet in β-cells: its prevention by incretins. Clin. Sci 2017; 131:673-687.

4. Lean MEJ, et al. Durability of a primary care-led weight-management intervention for remission of type 2 diabetes: 2-year results of the DiRECT open-label, cluster-randomised trial. Lancet 2019; 7:344-355.