New Insights into Islet Biology in Congenital Hyperinsulinism

ESPE Congenital Hyperinsulinism Family Conference
September 30th 2015

Mark Dunne, The University of Manchester
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The β-Cell in Congenital Hyperinsulinism in Infancy

Hyperactive

$\text{Ca}^{2+}$

$\Delta \Psi$

K$^+$

Insulin

Ins$^+$

Diffuse CHI
SBFSEM and Islets: Congenital Hyperinsulinism in Infancy
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SBFSEM and Islets: Congenital Hyperinsulinism in Infancy
CHI Islet; Organisation of Cells Within Islet Capillary Network
CHI Islet; Digital Reconstruction

Capillary

Red blood cells
Enlarged nuclei in CHI Islets. A normal feature, but increased in incidence in diffuse cases of CHI. Volume increase? From approx. 160 to 450 μm³.

Han et al (2015) ESPE Meeting
Ins+ Diffuse CHI

Ca^{2+} + K^+

ΔΨ

Hyperactive

The β-Cell in Congenital Hyperinsulinism in Infancy

Ins+ Insulin

Diffuse CHI
CHI Islet Cells; β-Cell, α-Cell & Capillary Vessel
CHI Islet Cells; β-Cell, α-Cell & Capillary Vessel
CHI Islet Cells; β-Cell, α-Cell & Capillary Vessel
CHI Islet Cells are **Smaller** Than Healthy Islet Cells

Control Islet Cells

- \(\alpha\)-cell
- \(\beta\)-cell

CHI Islet Cells

- \(\alpha\)-cell
- \(\beta\)-cell

Cell Volume
CHI Islet Cells are **Smaller** Than Healthy Islet Cells

- Control Islet Cells: 15% α-cell, 24% β-cell
- CHI Islet Cells: 17% α-cell, 30% β-cell

Nuclear Volume
CHI Islet Cells are Smaller than Control

Control Islet Cells

CHI Islet Cells

Mitochondrial Volume

2.5 fold increase in mitochondrial density

α-cell

24%

β-cell

15%

α-cell

30%

17%
CHI Islet Cells are Smaller than Control Islet Cells

Control Islet Cells

β-cell

α-cell

CHI Islet Cells

2.5 fold increase in mitochondrial density

- Helps to explain sustained insulin release
- A contribution to hyperinsulinism?
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K^+ → Ca^{2+} → Insulin
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