Title: Longitudinal study of the GLUcagon REsponse to hypoglycemia in children and adolescents with new-onset type 1 DIAbetes (GLUREDIA study): characteristics and predictive biomarkers

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Aims: To longitudinally assess alpha-cell response to hypoglycemia in pediatric patients with new-onset type 1 diabetes (T1D) and compare it with that of healthy subjects.

Methods: Using an insulin-induced hypoglycemia test (IIHT), we assessed 23 T1D patients at 0-, 6-, 12-, and 18-months post-diagnosis and compared them with a control group of eight healthy first-degree relatives (FDR). The IIHT involved a subcutaneous insulin dose calibrated to induce hypoglycemia, with blood samples collected at baseline and during stage 2 hypoglycemia (<54 mg/dL) to evaluate glucagon, cortisol, catecholamines, vasopressin, and growth hormone levels.

Results: In the control group, stage 1 hypoglycemia (<70 mg/dL) was consistently asymptomatic and triggered a significant increase in glucagon secretion (1.92 ± 1.06 pmol/L, p<0.001), followed by spontaneous glycemic correction. In contrast, the T1D group experienced stage 2 hypoglycemia with impaired alpha-cell response throughout the 18-month follow-up (0.64 pmol/L ± 2.43; p=0.15). At 0- and 12 months, glucagon response was nonsignificant, while a transient restoration was observed at 6 months (2.00 pmol/L ± 3.03; p<0.001), followed by a paradoxical suppression at 18 months (-1.63 pmol/L ± 1.43; p<0.001). Basal glucagon levels remained stable across all time points and did not differ between the two groups.

Conclusion: These findings highlight progressively impaired glucagon response in early T1D, with potential implications for hypoglycemia risk and disease management. The IIHT proved safe and reproducible. Ongoing studies, including 82 additional T1D patients (DIATAG cohort), will further refine our understanding of alpha-cell dysfunction in T1D progression. This study showed the dynamics of alpha-cell secretion in response to metabolic changes over time, providing insights into its role in glycemic regulation and disease progression.

SPEAKER BIOSKETCH - Maude BECKERS (UCL)

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CURRENT AND PAST POSITIONS:

- Paediatric Endocrinologist and Diabetologist in the Specialized Paediatrics Unit in Cliniques Universitaires Saint-Luc, Brussels, since 2023.
- PhD candidate in UCLouvain, since 2023.

EDUCATION:

- Specialization in Paediatrics in Cliniques Universitaires Saint-Luc, UCLouvain, from 2018 to 2023
- Master's in medicine in UCLouvain from 2012 to 2018

AWARDS AND HONORS:

- FNRS SD grant since 2023
- Nestle BVK/SBP Congress 2022 Prize for best long oral presentation: "INSENODIAB Study: Determinants and characteristics of insulin dose requirements in children and adolescent with new-onset type 1 diabetes". Beckers M, Bernard N, Gallo P, Bugli C, Lysy P. A. Société Belge de pédiatrie. Bruxelles. Mars 2022.
- Sandoz Scientific Award 2023 applicant. "Determinants And Characteristics Of Insulin Dose Requirements In Children And Adolescents With New-Onset Type 1 Diabetes : Insights From The INSENODIAB Study". Beckers M, Polle O, Bernard N, Gallo P, Lysy P.
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OTHER RELEVANT PROFESSIONAL ACTIVITIES AND ACCOMPLISHMENTS:

Scientific Committees

- Associated member in BELSPEED, since 2025.

Academic responsibilities

- Pathologies pédiatriques : Endocrinologie in ISEI, Brussels, since 2022
- Anamnèse et examen clinique pédiatrique in UCLouvain Medical School, Brussels, since 2022
- Principe des essais cliniques in UCLouvain (Public Health Master's), in 2022-2023.

NAME, SURNAME: Philippe Antoine Guy LYSY (Clinique Universitaire Saint Luc)

TITLE: MD, PhD, M.Sc.

CURRENT AND PAST POSITIONS:

- Head of Specialized Pediatrics Service, Cliniques universitaires Saint-Luc, Brussels, Belgium (2020–present)
- Pediatric Endocrinologist and Diabetologist, Cliniques universitaires Saint-Luc, Brussels, Belgium (2011–present)
- Group Leader, Diabetes and Hormones Lab, EDIN, Institut de Recherche Clinique et Expérimentale (IREC), UCLouvain, Brussels, Belgium (2011–present)
- Clinical Professor, UCLouvain (2018–present)
- Postdoctoral Fellow, Joslin Diabetes Center, Harvard Medical School, Boston, USA (2009–2011)
- Visiting Doctor, Joslin Pediatric Clinic & Massachusetts General Hospital, Harvard Medical School, Boston, USA (2009–2011)

EDUCATION:

- PhD, UCL Brussels, 2008
- MSc in Health Sciences, UCL Brussels, 2008 (Magna cum laude)
- MD, UCL Brussels, 2003 (Summa cum laude)
- Master in Pediatrics, UCL Brussels, 2009
- Pediatric Endocrinology, UCL Brussels, 2011
- Certificate in Thyroid Ultrasound, Université de Liège, 2015

AWARDS AND HONORS:

2005	The Samy Cadranel Grant, BeSPGHAN.
2009-2010	BAEF Research Fellowship (honorary, full fellowship declined as received ESPE Research fellowship).
2009-2011	ESPE Research fellowship.
2009	Pfizer Educational Grant.
2014	ABD Annual Prize of Diabetology.
2016	Honor Medal of Académie Royale de Médecine de Belgique.
2017	ESPE Young Investigator Award.
2017	Prix ABD 2017 Suzanne et Jean Pirart.
2018	STEM CELLS Translational Medicine Young Investigator Award (Best 2016 publication).
2018	BVK / SBP Research Grant.
2019	ESPE Henning Andersen Prize.
2023	Belgian Endocrine Society lecture Award.

Multiple national and international research grants and prizes (FNRS, ISPAD, BELSPEED, Helmsley, Innoviris, etc.)

OTHER RELEVANT PROFESSIONAL ACTIVITIES AND ACCOMPLISHMENTS:

- President, Belgian & Luxembourgish Society for Pediatric Endocrinology and Diabetes (BELSPEED) (2020-2025)
- Member, Program Organizing Committee, European Society for Paediatric Endocrinology (ESPE) (2020-2023)
- Member, Boards of ABD, BVK/SBP, and BAoP
- Clinical and teaching contributions at UCLouvain (medical, pharmacy, and pediatric postgraduate programs)
- Research focus on type 1 diabetes, β-cell biology, and pediatric endocrinology; >70 peer-reviewed publications, h-index 23 (Scopus), >3200 citations (Google Scholar)
- Involved in international capacity-building programs in pediatric endocrinology across Francophone Africa