RESEARCH STUDY OF GALACTOSAEMIA PATIENTS WHO CARRY THE S135L ALLELE

Dear Colleagues,

An international collaborative research study has been launched aimed at identifying patients with **Classic Galactosaemia (CG)** who carry the **S135L allele** in either the homozygous state, or the compound heterozygous state with another *GALT* mutation. Our goal is to document both the acute and long-term clinical outcomes of these patients and develop consensus guidelines on their management.

Background: S135L is the predominant *GALT* allele found in patients with galactosemia of African ancestry. Patients who carry an S135L-*GALT* allele have long been considered to have milder long-term outcomes due to the residual GALT enzyme activity associated with this allele. However, this understanding is based on limited evidence as most large CG cohorts reported in the literature have included very few patients with S135L.

If you take care of (or have previously cared for) pediatric and/or adult patients who carry an S135L allele, we would love to hear from you!

Project Objectives and Methodology:

- Expand what is known about the acute and long-term outcomes of galactosemia patients who carry S135L
- Compare the outcomes of patients with S135L who have, versus have not, been on dietary galactose restriction
- Questions we seek to answer: do infants with the S135L allele experience acute symptoms from milk exposure and benefit from dietary galactose restriction? If yes, is the same true for older children and adults with S135L?
- Address racial disparities in medical research by focusing on a rare genetic disorder that is predominantly found in an under-represented group (patients of African ancestry)
- Personalizing dietary treatment recommendations for a specific genotype: is there a potential benefit to dietary galactose restriction within the S135L CG population, or are we over-treating? If so, how strict should we be to prevent long-term sequalae?
- Learning the answers to these questions will help parents decide what to feed their infant or child with S135L CG; will allow for evidenced-based counseling by healthcare providers; may also help families and school systems recognize at-risk children who might benefit from early intervention at an early age
- Study Methodology:
    - Multicenter and multinational observational study; **no financial disclosures**
    - Collaborators who provide substantial usable data in support of the study will be invited to **co-author** a future manuscript/guideline
    - **Brief online survey** approved by the Emory University IRB for healthcare workers to gather information about acute and long-term outcomes, dietary galactose exposure at different ages, relevant lab results from medical records; local ethics review may also be needed
    - **No follow up** is required after initial survey completion

We appreciate your consideration. Please reach out to us if you are interested, or if you need any further clarification of our project objectives and/or methodology.

Quinton Katler, MD, MS
Atlanta, USA
Qkatler@emory.edu

Karolina M. Stepien MD, PhD
Salford, UK
karolina.stepien@srft.nhs.uk

Judith L. Fridovich-Keil, PhD
Atlanta, USA
jfridov@emory.edu