ERNDiM

ERNDiM

Quality Assurance in Laboratory Testing for IEM

DPT Czech Republic participants' meeting

Petr Chrastina

Thursday 9th October 2025

Annual Report 2024

ERNDiM

Quality Assurance in Laboratory Testing for IEM

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Diagnostic Proficiency Testing
Centre: Czech Republic

Final Report 2024

prepared by
Petr Chrastina

Note: This annual report is intended for participants of the ERNDIM DPT Czech Republic scheme. The contents should not be used for any publication without permission of the Scientific Advisor.

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1. Geographical distribution of participants

Seventeen laboratories from 13 countries have participated in the Diagnostic Proficiency Testing scheme in 2024, for details see the below table:

Country	Number of participants
Austria	1
Croatia	1
Cyprus	1
Czech Republic	1
Denmark	1
Finland	1
Germany	5
Latvia	1
Lithuania	1
Malaysia	1
Portugal	1
Slovakia	1
Switzerland	1

[1] If this report is not Version 1 for this scheme year, go to APPENDIX 1 for details of the changes made since the last version of this document.

2. Design and logistics of the scheme including sample information

The scheme has been designed and planned by Petr Chrastina as Scientific Advisor and coordinated by Alessandro Salerma as scheme organiser (sub-contractor on behalf of CSCQ), both appointed by and according to procedures laid down the ERNDIM Board.
CSCQ dispatches DPT EQA samples to the scheme participants and provides a website for on-line submission of results and access to scheme reports. Existing DPT and Urine MPS scheme participants can log on to the CSCQ results submission website at:
https://cscq.hcuge.ch/cscq/ERNDIM/Initial/Initial.php

2 surveys	Round 1: patients A, B and C
	Round 2: patients D, E and F

Origin of patients: All six urines were obtained from patients with known diagnoses. Four urine samples have been provided by the scheme organizers and one sample has been provided by Department of Clinical Biochemistry of University Children's Hospital in Bratislava. The common sample was from DPT Center Switzerland (distributed in all five DPT schemes).

In 2024 the samples have been heat-treated and apart from the common sample A were re-analyzed in our department after receiving the samples from CSCQ (samples were shipped via courier at ambient temperature to mimic possible changes that might arise during transport). In all five samples prepared and checked by us the typical metabolic profiles were preserved after heat treatment.
Mailing: samples were sent by DHL, FedEx or the Swiss Post at room temperature.

3. Tests

Analyses of amino acids, organic acids, mucopolysaccharides, oligosaccharides and purines/pyrimidines were required in 2024.

4. Schedule of the scheme

Sample distribution by CSCQ	07 February 2024
Start of analysis of Survey 2024/1	12 March 2024
Survey 2024/1 – results submission	02 April 2024
Survey 2024/1 – report	14 May 2024
Start of analysis of Survey 2024/2	03 June 2024
Survey 2024/2 – results submission	01 July 2024
Survey 2024/2 – report	05 August 2024
Annual meeting of participants	03 September 2024
Annual report 2024	January 2025

5. Results

16 of 17 labs returned results for both surveys by the deadline.

	Survey 1	Survey 2
Receipt of results	16	16
No answer	1	1

6. Web site reporting

The website reporting system is compulsory for all centres. Please read carefully the following advice:

- Selection of tests: **don't select a test if you will not perform it**, otherwise the evaluation program includes it in the report.
- Results
  - Give quantitative data as much as possible.
  - Enter the key metabolites with the evaluation **in the tables** even if you don't give quantitative data.
  - If the profile is normal: enter "Normal profile" in "Key metabolites".

Participation in 2025

Country	Number of participants
Austria	1
Croatia	1
Cyprus	1
Czech Republic	1
Finland	1
Germany	4
Latvia	1
Lithuania	1
Malaysia	1
Portugal	1
Slovakia	1
United Kingdom	1
in total	**15**

Date of results submission	2025/1	2025/2
in time	15	14
late submission	0	0
no report	**0**	**1**

Tests required in the lab or in the cluster lab

- ✓amino acids
- ✓organic acids
- ✓mucopolysaccharides
- ✓oligosaccharides
- ✓purines/pyrimidines

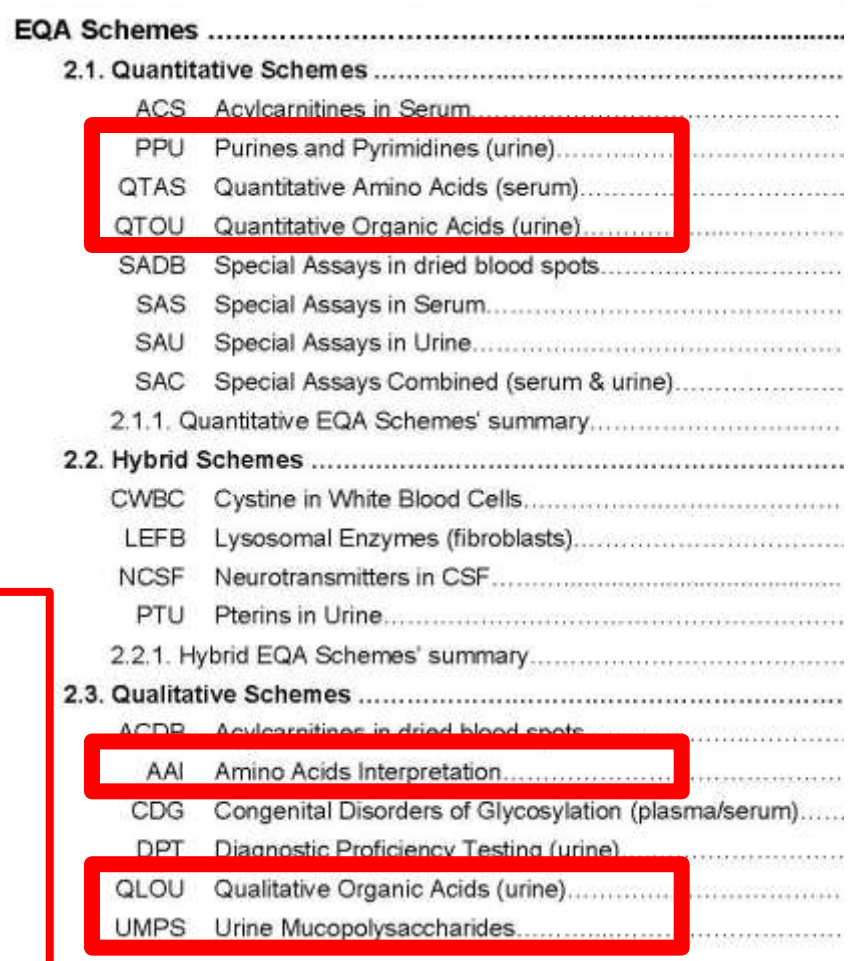
satisfactory performance

=

min. 17 points from **24**

and

no “critical error”



EQA Schemes

2.1. Quantitative Schemes

ACS Acylcarnitines in Serum

PPU Purines and Pyrimidines (urine)

QTAS Quantitative Amino Acids (serum)

QTOU Quantitative Organic Acids (urine)

SADB Special Assays in dried blood spots

SAS Special Assays in Serum

SAU Special Assays in Urine

SAC Special Assays Combined (serum & urine)

2.1.1. Quantitative EQA Schemes' summary

2.2. Hybrid Schemes

CWBC Cystine in White Blood Cells

LEFB Lysosomal Enzymes (fibroblasts)

NCSF Neurotransmitters in CSF

PTU Pterins in Urine

2.2.1. Hybrid EQA Schemes' summary

2.3. Qualitative Schemes

ACDB Acylcarnitines in dried blood spots

AAI Amino Acids Interpretation

CDG Congenital Disorders of Glycosylation (plasma/serum)

DPT Diagnostic Proficiency Testing (urine)

QLOU Qualitative Organic Acids (urine)

UMPS Urine Mucopolysaccharides

Web site reporting

- Selection of tests

  Don't select a test if you will not perform it, otherwise the evaluation program includes it in the report.

- Results

  Don't enter results in the "comments" window, otherwise your results will not be included in the evaluation program.

- Recommendations = **advice for further investigation**.

  Don't give advice for further investigation in "Comments on diagnosis": it will not be included in the evaluation program.

The risk is that your results will be **scored incorrectly.**

Urine samples

- at least 300 ml of urine from a patient affected with an established inborn error of metabolism
- a short clinical report
- if possible, please collect 1500 ml of urine
- the urine sample must be stored frozen
- we will organize transport with your cooperation

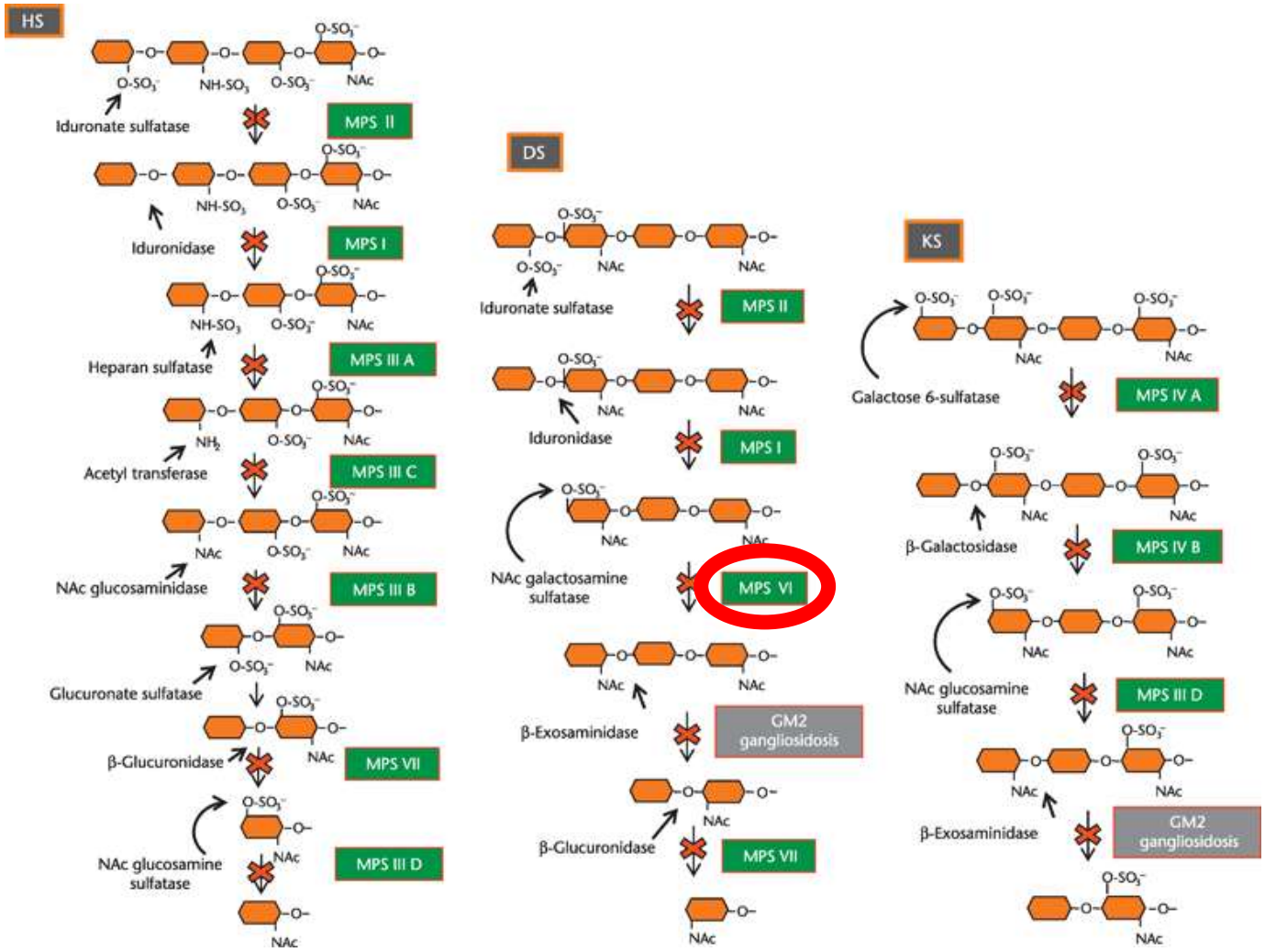
- a 20% discount on the scheme price is available to participants that donated a sample that was used as an EQA material

Sample A (common sample) mucopolysaccharidosis type VI

Clinical picture provided with the sample:

- 15-year-old boy. Dysmorphic features, scoliosis, size -1.5 SD, normal intellectual development. Under treatment.
- The sample was obtained from a 16-years old boy with mucopolysaccharidosis type VI due to arylsulfatase B deficiency.
- DPT Centre: France

Sample A (common sample) mucopolysaccharidosis type VI



Sample A (common sample) mucopolysaccharidosis type VI

- **no signs or symptoms at birth**
- **signs and symptoms often begin during early childhood**
  - skeletal abnormalities
    - macrocephaly with hydrocephalus
    - distinctive-looking facial features
    - macroglossia
    - short stature
    - joint deformities
    - dysostosis multiplex
    - spinal stenosis
  - heart valve abnormalities
  - sleep apnea
  - hearing loss or impairment
  - visual impairment
  - hepatosplenomegaly
  - frequent respiratory infections
- **treatment**
  - enzyme replacement therapy

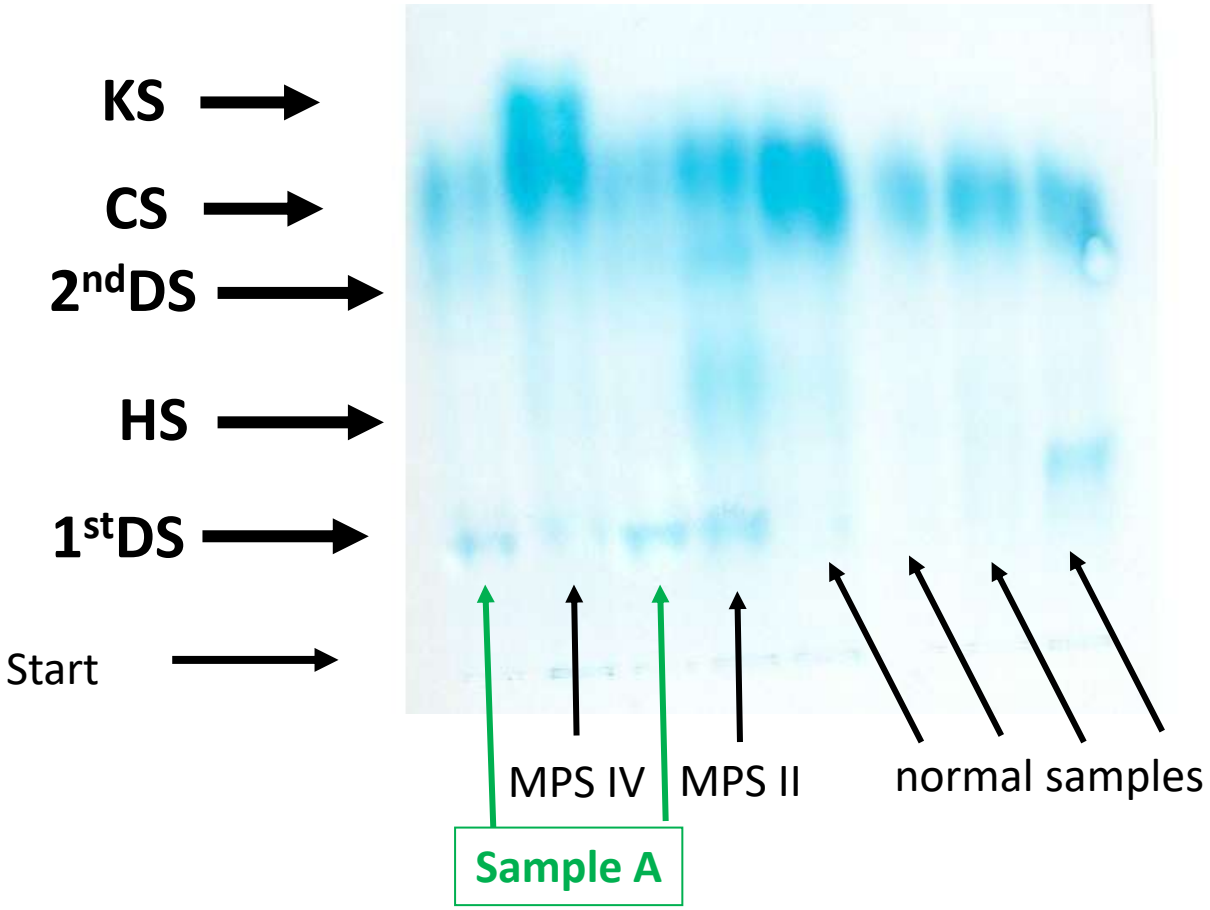
Sample A (common sample) mucopolysaccharidosis type VI

Investigation

mucopolysaccharides quantitative	**(12)**	
– increased excretion of GAG	(12)	1 point
mucopolysaccharides qualitative	**(13)**	
– dermatan sulfate	(12)	**2 points**
– keratan sulfate	(1)	0 points

Sample A (common sample) mucopolysaccharidosis type VI

Mucopolysaccharides 1-D-electrophoresis



Sample A (common sample) mucopolysaccharidosis type VI

Interpretation and recommendation

MPS VI	**(9)**	**2 points**
+ enzyme assay	**(9)**	
+ mutation analysis	**(9)**	
MPS IV	**(3)**	**1 point**
MPS VII	**(1)**	**1 point**
MPS based on clinical information	**(1)**	**1 point**
no diagnosis	**(1)**	**1 point**

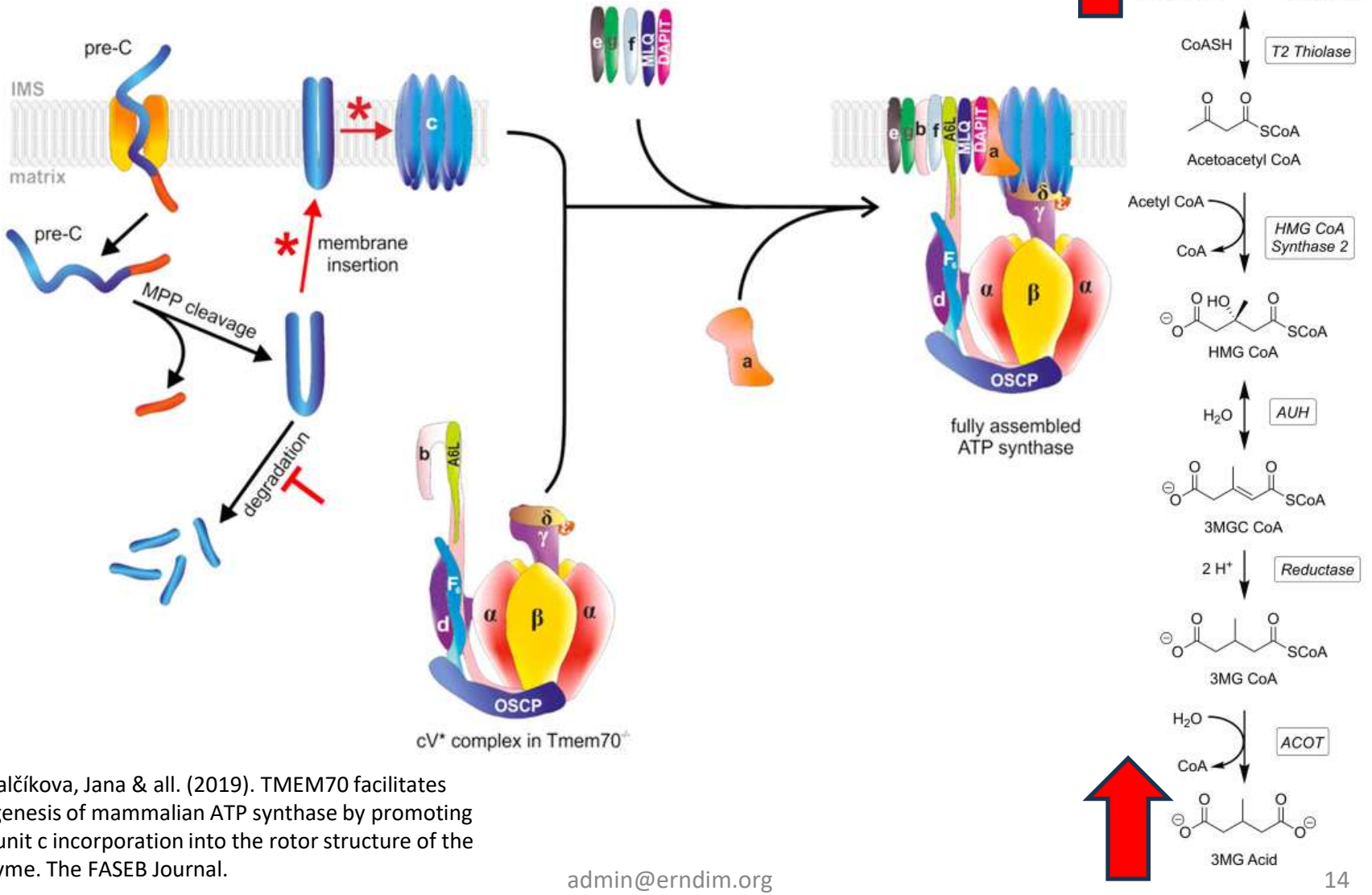
+ recommendation to carry out MPS analysis

Sample B
3-methylglutaconic aciduria type IV

Clinical picture provided with the sample:

- A two-day-old newborn with cyanosis, respiratory distress and severe metabolic acidosis was presented to the emergency department. Urine was collected at the age of 1 year.
- The sample was obtained from a 1-year-old boy with 3-methylglutaconic aciduria type IV due to mutation in the *TMEM70* gene. The diagnosis was confirmed by molecular genetic analysis.

Sample B
3-methylglutaconic aciduria type IV



Kovalčíková, Jana & all. (2019). TMEM70 facilitates biogenesis of mammalian ATP synthase by promoting subunit c incorporation into the rotor structure of the enzyme. The FASEB Journal.

Sample B

3-methylglutaconic aciduria type IV

- usually present during the first year of life with neurological findings
  - psychomotor retardation
  - hypotonia
  - developmental delay
  - seizures
  - progressive spasticity
- severe failure to thrive
- cardiomyopathy, hepatic dysfunction
- eye anomalies, microcephaly
- deafness, dysmorphism
- neonatal hypoglycaemia and lactic acidosis
- treatment
  - no effective treatment

Sample B
3-methylglutaconic aciduria type IV

Investigation

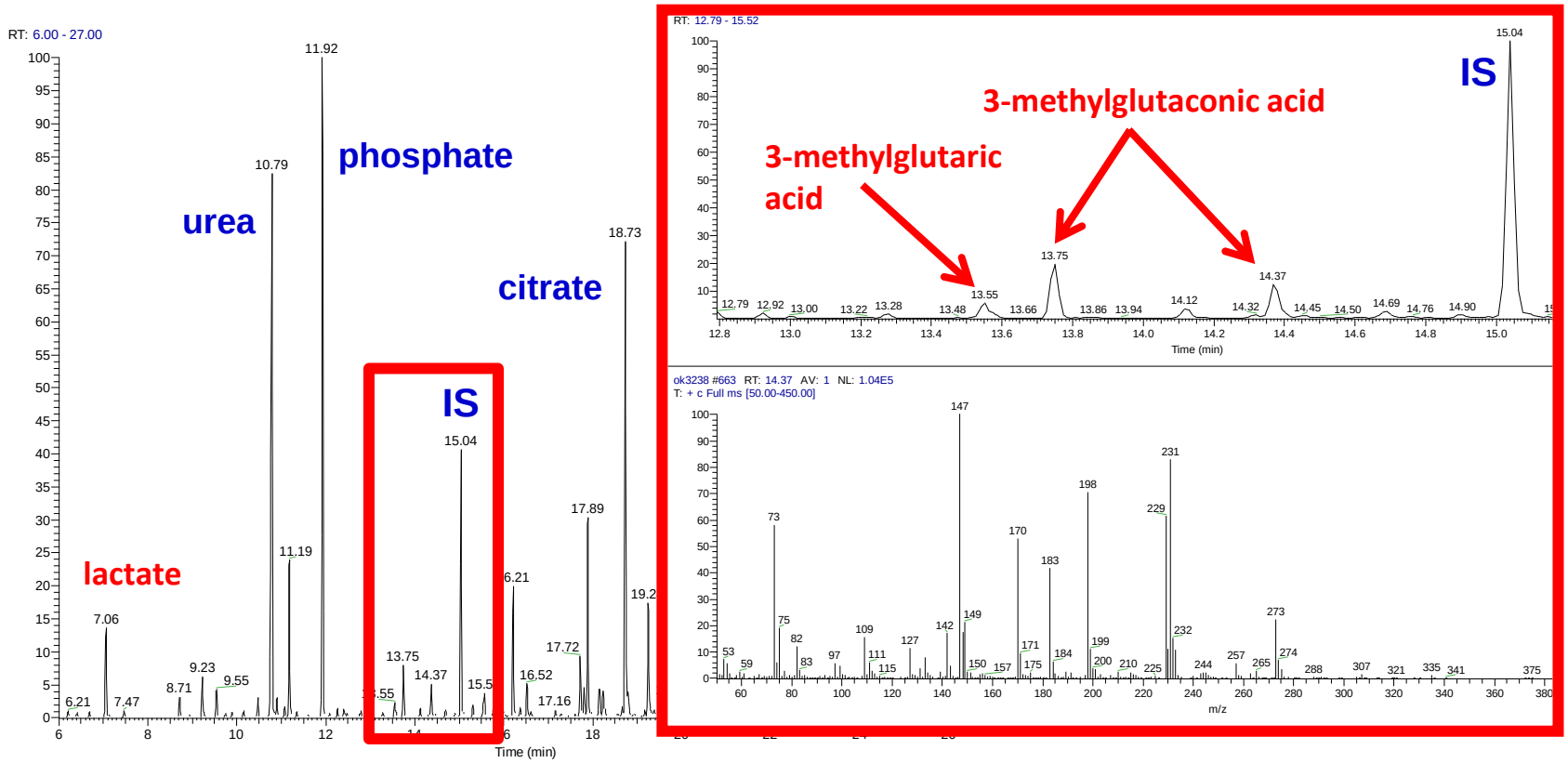
organic acids **(15)**

- 3-methylglutaconic aciduria (14) 2 points

- increased excretion of 2-hydroxyglutaric acid and lactic acid (1) 0 points
  - ❖ **tentative critical error**

Sample B
3-methylglutaconic aciduria type IV

GC/MS analysis of organic acids



Sample B

3-methylglutaconic aciduria type IV

Interpretation and recommendation

3-methylglutaconic aciduria type IV	(4)	2 points
secondary 3-methylglutaconic aciduria due to mitochondrial dysfunction	(4)	2 points
+ mutation analysis	(8)	
other type of 3-methylglutaconic aciduria	(6)	1 point
glutaric aciduria type II	(1)	0 points

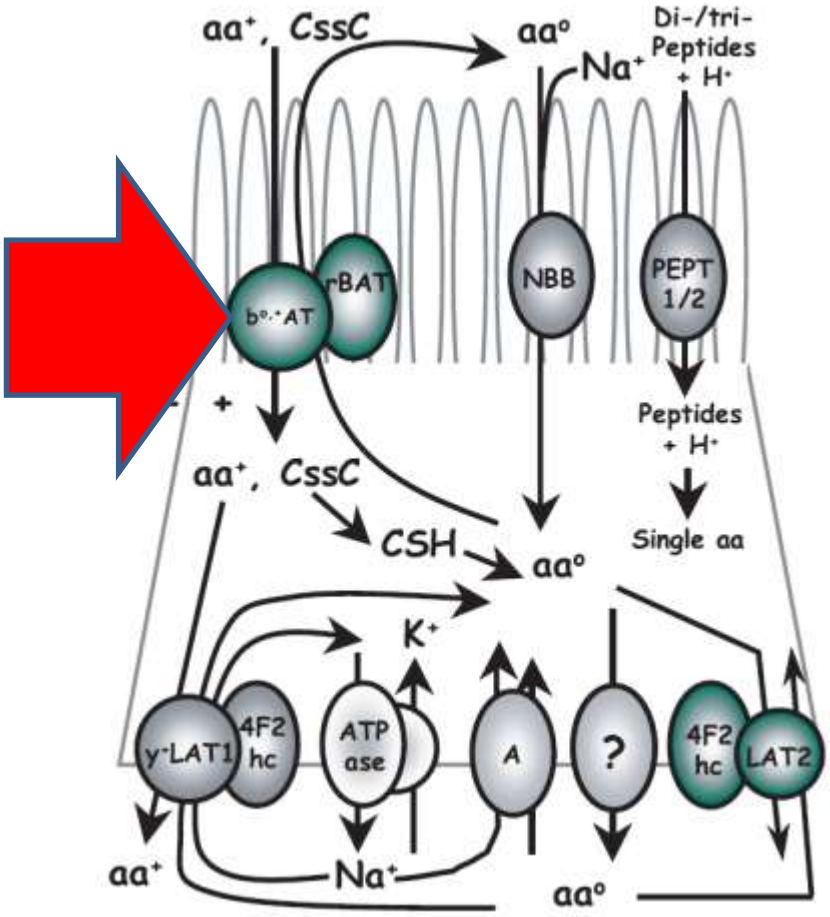
Sample C
cystinuria

Clinical picture provided with the sample:

- A 17-year-old woman presented to the emergency department with severe abdominal pain. A CT scan revealed a renal calculus. The sample was taken at the age of 17 years during the specific treatment.
- The sample was obtained from 17-years old woman with cystinuria. The diagnosis was confirmed by molecular genetic analysis.

Sample C
cystinuria

Model for the absorption/reabsorption of amino acids in an intestinal/proximal tubule epithelial cell



Sample C
Cystinuria

- **kidney stones**
  - first stone during their first two decades of life
- **treatment**
  - hydration
  - urinary alkalinization
  - thiol-based agents (tiopronin)

Sample C
Cystinuria

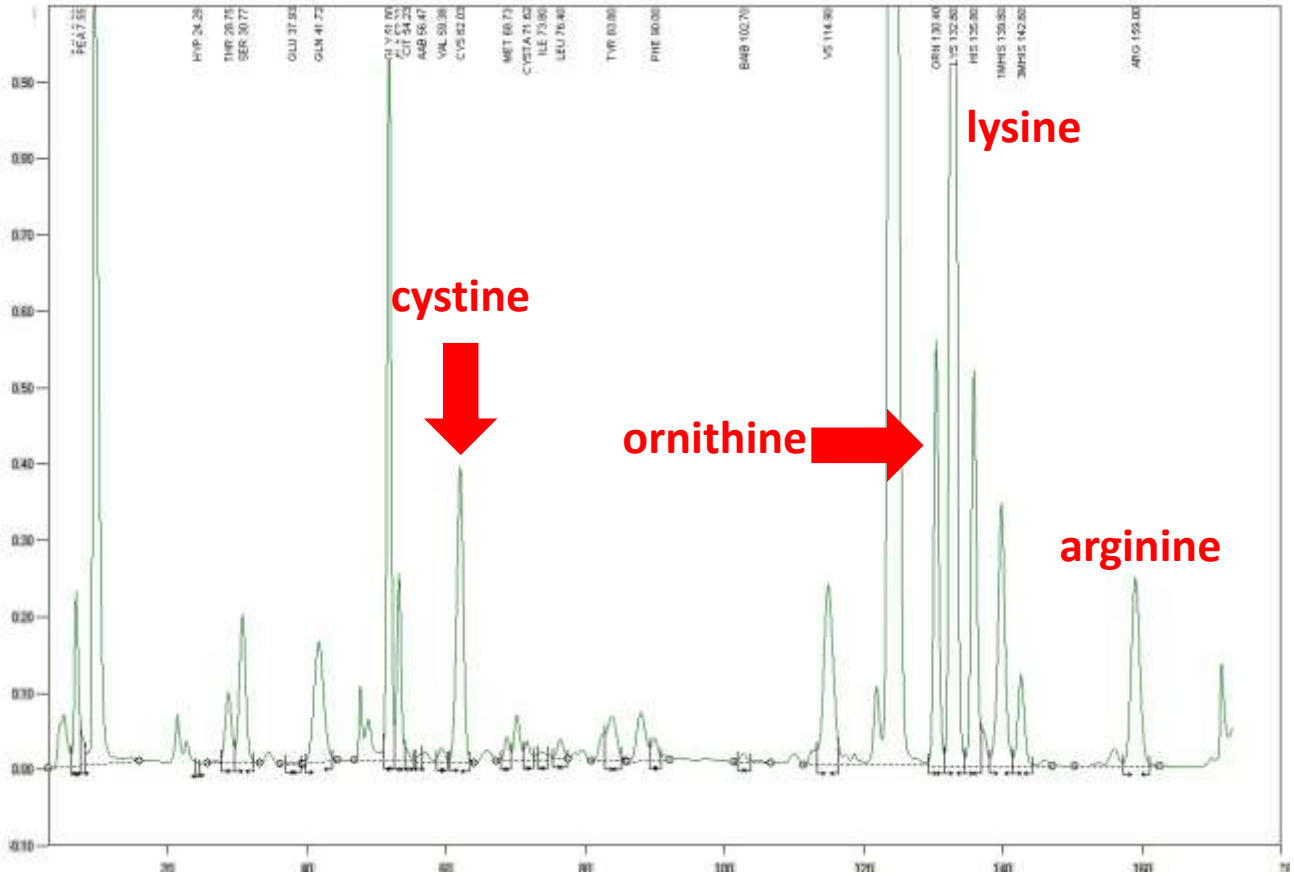
Investigation

amino acids **(15)**

- increased excretion of cystine (14) 1 point
- increased excretion of dibasic amino acids (15) 1 point

Sample C
Cystinuria

IEC-NHD analysis of amino acids



Sample C
Cystinuria

Interpretation and recommendation

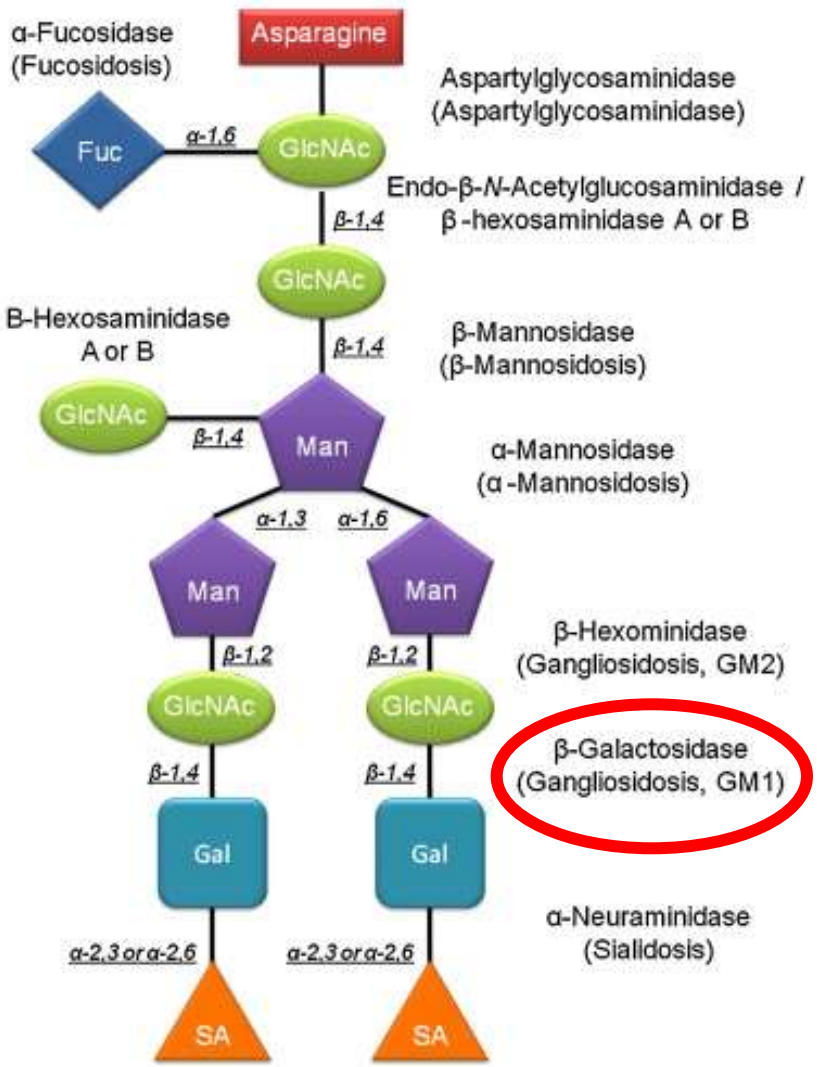
cystinuria	(14)	2 points
+ mutation analysis	(14)	
LPI	(1)	0 points

Sample D
GM1-gangliosidosis

Clinical picture provided with the sample:

- A seven-month-old boy was examined for transaminase elevation, facial dysmorphia, psychomotor retardation, and ptosis. Urine was collected at the age of 1 year.
- This sample was obtained from a 1-year-old boy with GM1-gangliosidosis due to beta-galactosidase deficiency. The diagnosis was confirmed by molecular genetic analysis.

Sample D
GM1-gangliosidosis



Sample D
GM1-gangliosidosis

- **infantile form (severe)**
  - symptoms usually develop by the age of 6 months
  - developmental delay
  - hepatosplenomegaly, cardiomyopathy and skeletal abnormalities,
  - seizures
  - red area in the eye known as a cherry-red spot, loss of vision
  - patients usually do not survive past early childhood
- **juvenile form**
  - symptoms develop around the age of 5 years
  - developmental regression but usually they do not have cherry-red spots
- **adult form**
  - most affected individuals develop symptoms in their teens
  - dystonia and abnormalities of the spinal bones
- **treatment**
  - no treatment

Sample D
GM1-gangliosidosis

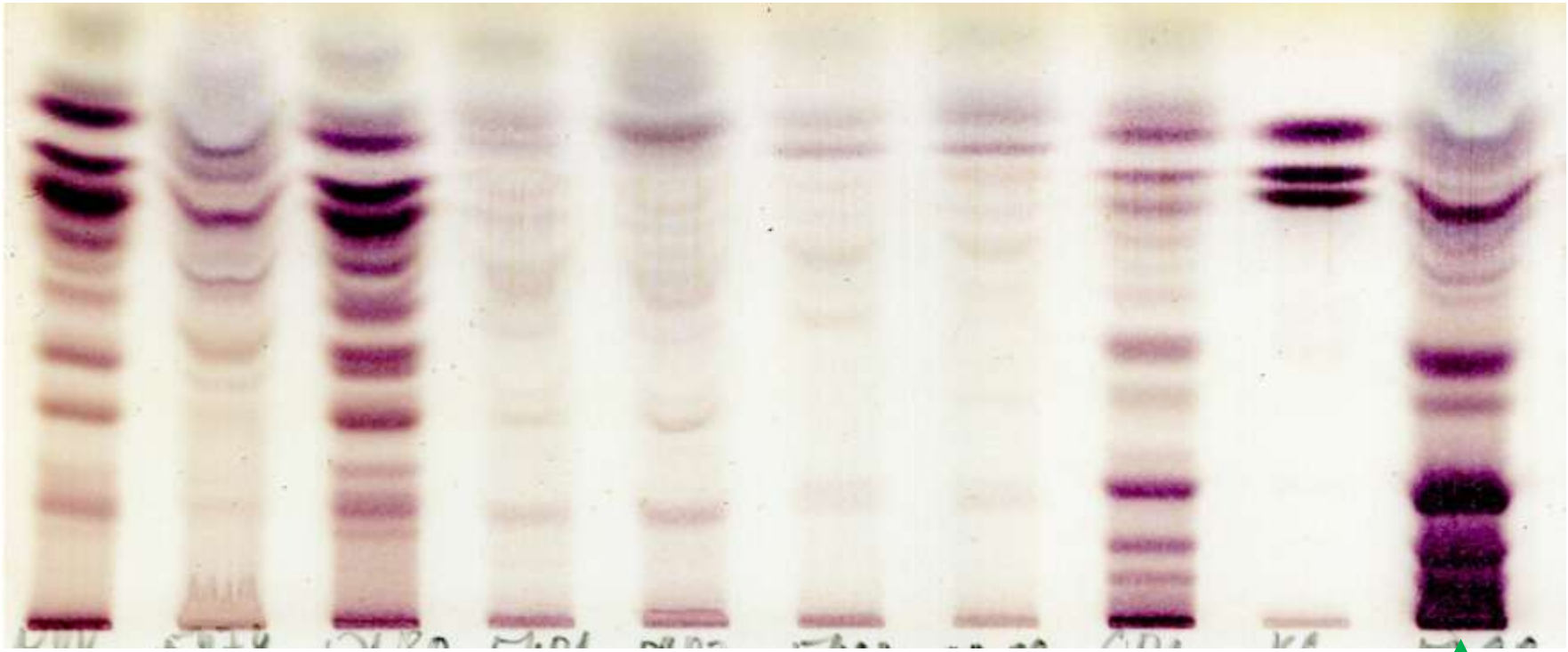
Investigation

OLS analysis **(11)**

– profile typical for GM1-gangliosidosis (11) 2 points

Sample D
GM1-gangliosidosis

OLS profile using resorcinol staining



newborn

normal samples

GM1

Sample D

Sample D
GM1-gangliosidosis

Interpretation and recommendation

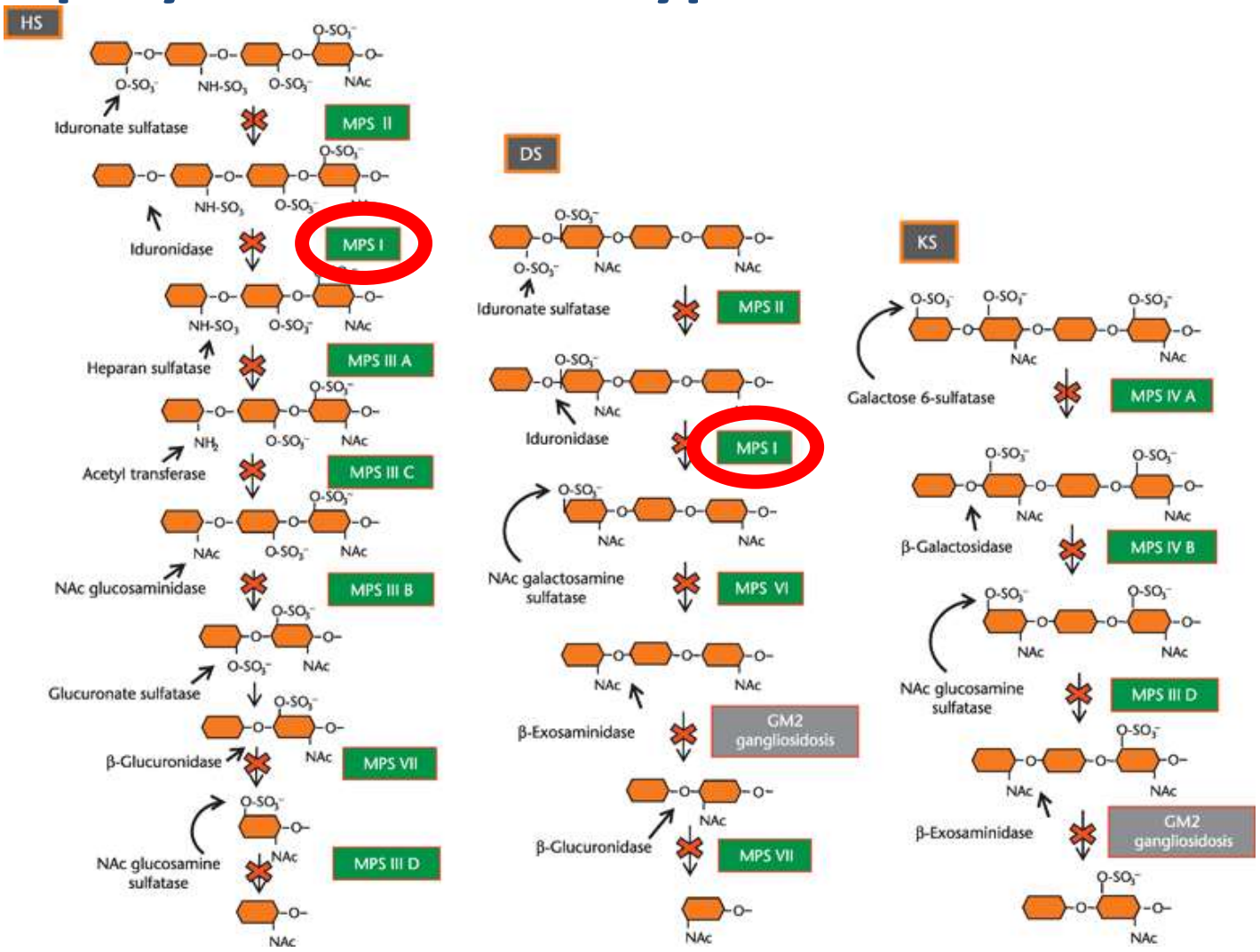
GM1-gangliosidosis	**(11)**	**2 points**
+ enzyme assay	**(11)**	
+ mutation analysis	**(11)**	
mitochondrial disorder	**(1)**	**0 points**
2-hydroxyglutaric aciduria	**(1)**	**0 points**
malonic aciduria	**(1)**	**0 points**

Sample E
mucopolysaccharidosis type I

Clinical picture provided with the sample:

- A 12-year-old boy was referred for metabolic screening because of an unknown disease of the finger joints, rheumatic origin was excluded. Urine was collected at the age of 13 years.
- The sample was obtained from a 13-year-old boy with mucopolysaccharidosis type I due to alpha-L-iduronidase deficiency, diagnosis was confirmed by molecular genetic analysis.

Sample E
mucopolysaccharidosis type I



Sample E
mucopolysaccharidosis type I

- **typically, no signs or symptoms at birth**
- **signs and symptoms often begin during early childhood**
  - skeletal abnormalities
    - deformity of the lower spine
    - progressive skeletal dysplasia
    - progressive arthropathy
    - short stature
  - intellectual disability is progressive and profound
  - progressive cardiorespiratory involvement
  - hearing loss
  - corneal clouding
  - in severe cases - without treatment, death usually occurs within the first ten years of life
- **treatment**
  - hematopoietic stem cell transplantation
  - enzyme replacement therapy

Sample E
mucopolysaccharidosis type I

Investigation

mucopolysaccharides quantitative **(10)**

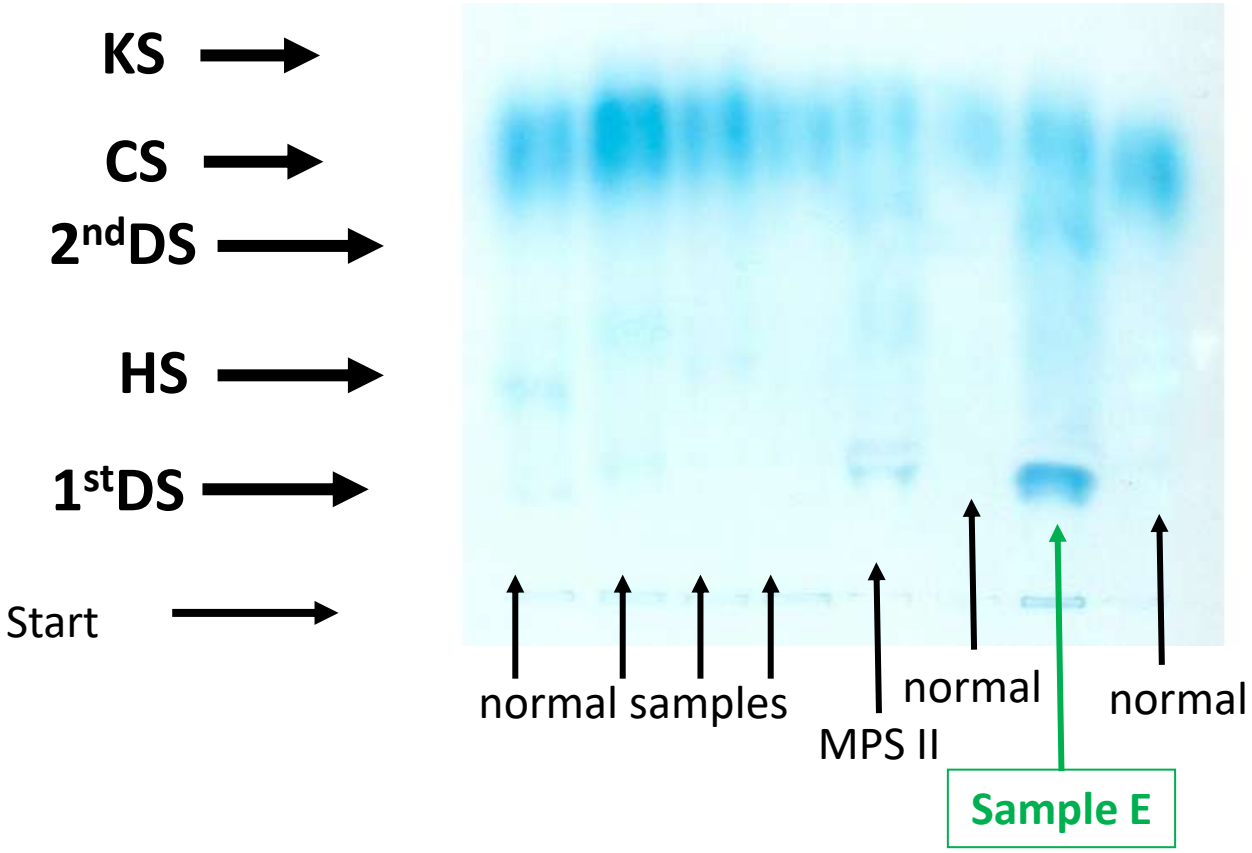
– increased excretion of GAG (10) 1 point

mucopolysaccharides qualitative **(12)**

– **dermatan sulfate** (12) **2 points**

Sample E
mucopolysaccharidosis type I

Mucopolysaccharides 1-D-electrophoresis



Sample E
mucopolysaccharidosis type I

Interpretation and recommendation

MPS I	**(11)**	**2 points**
+ enzyme assay	**(11)**	
+ mutation analysis	**(11)**	
MPS VI	**(1)**	**1 point**
no diagnosis	**(2)**	**1 point**

+ recommendation to carry out MPS analysis

Sample F
no IEM

Clinical picture provided with the sample:

- This woman was referred for hearing impairment at the age of 51. The sample was taken at the age of 51 years.
- This sample was obtained from a 51-year-old woman with no evidence of an inherited metabolic disorder, despite extensive metabolic screening.

Sample F
no IEM

Investigation

Organic acids **(14)**

- normal profile (9) 1 point
- mildly elevated lactate excretion (3) 1 point
- mildly elevated pyruvate excretion (1) 1 point

- elevated excretion of lactate and 3-methylglutaconic acid (1) 0 points

Sample F
no IEM

Investigation

Other methods

- lab analyzed at least three of the five required methods and reported a normal profile except for organic acids (10) 1 point

Sample F
no IEM

Interpretation and recommendation

no IEM	**(9)**	**2 points**
purine metabolism disorder	(1)	**0 points**
PRPS deficiency	(1)	**0 points**
BCKDK deficiency	(1)	**0 points**
alpha-mannosidosis	(1)	**0 points**
maternally inherited diabetes and deafness	(1)	**0 points**

Performance scores

Survey 2025/1 [points]	Survey 2025/2 [points]	Total point 2025
12	12	24
10	8	18
7	12	19 +TCE
12	10	22
10	12	22
11	10	21
12	12	24
8	9	17
8	4	12
11	7	18
11	12	23
12	10	22
9	7	16
12	0	12
11	9	20

satisfactory performance

=

17 points or more

and

no “critical error”

Performance scores

Sample	Diagnosis	Analytical [%]	Interpretation and recommendations [%]	Total [%]	Number of tentative critical errors
A	MPS VI	83	80	82	0
B	3-methylglutaconic aciduria type IV	93	73	83	**1**
C	cystinuria	97	93	95	0
D	GM1-gangliosidosis	79	79	79	0
E	MPS I	86	89	88	0
F	no IEM	82	64	73	0

Tentative schedule of DPT scheme in 2026

Sample distribution	**04 February 2026**
Start of analysis of Survey 2026/1	**17 March 2026**
Survey 2026/1 – results submission	07 April 2026
Survey 2026/1 – report	19 May 2026
Start of analysis of Survey 2026/2	**01 June 2026**
Survey 2026/2 – results submission	22 June 2026
Survey 2026/2 – report	03 August 2026
Annual meeting of participants	**25 August 2026, Helsinki, Finland**
Annual report 2026	January 2027

ERNDiM

THANK YOU

For Your Attention!