

ERNDIM update

Dr Mick Henderson

Chairman Executive Committee

Summary of Current Profile

Quantitative Amino Acids

Quantitative Organic Acids

Qualitative Organic Acids

Special Metabolic Assays

Purines and Pyrimidines

Acyl Carnitine

Cystine in White Blood Cells

Diagnostic Proficiency Testing schemes operated in 5 centres

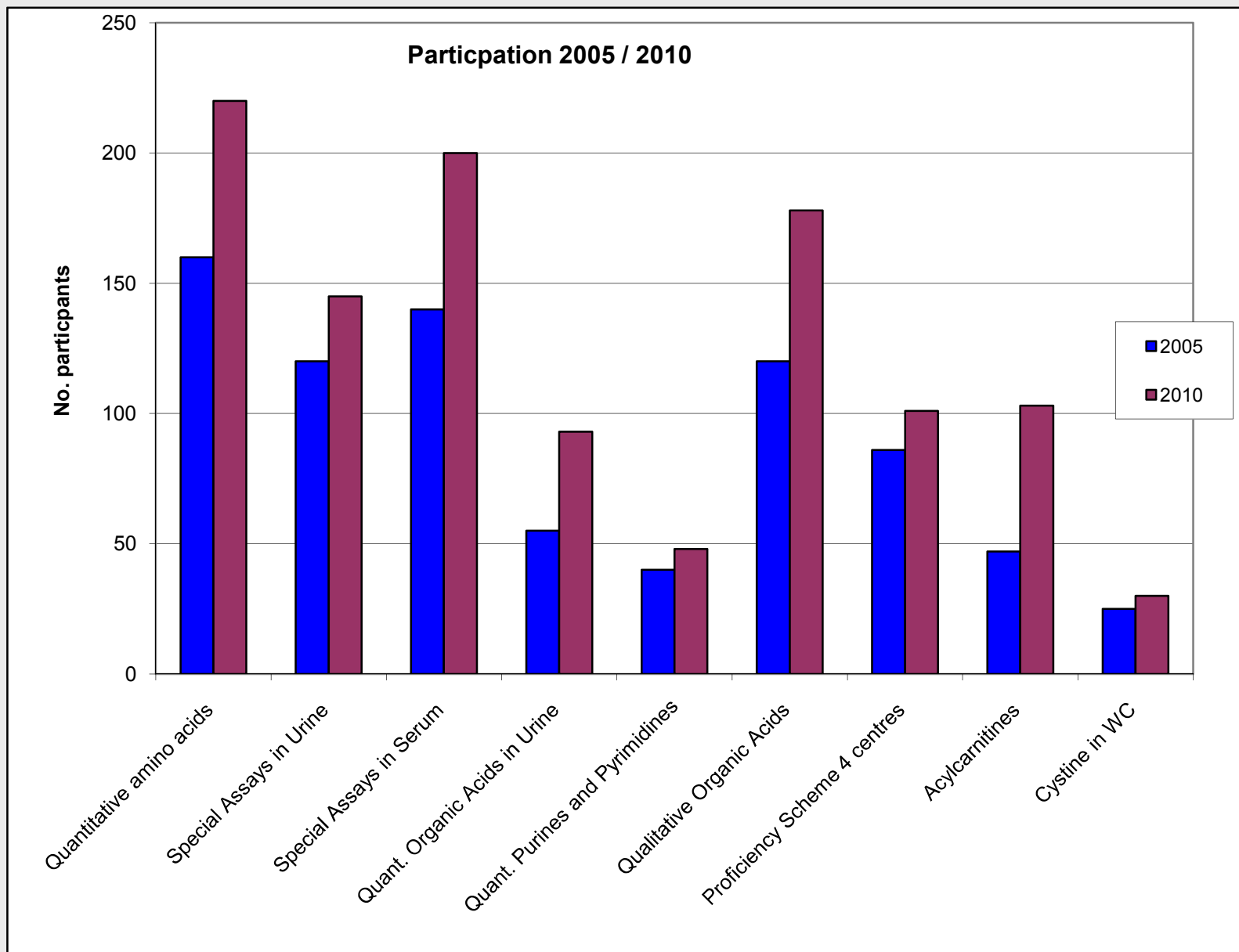
317 participating labs
In 49 countries

New in 2010

lysosomal enzymes

congenital disorders of glycosylation

Pilot: urine MPS





Hôpitaux de Lyon

ERNDIM DPT Schemes

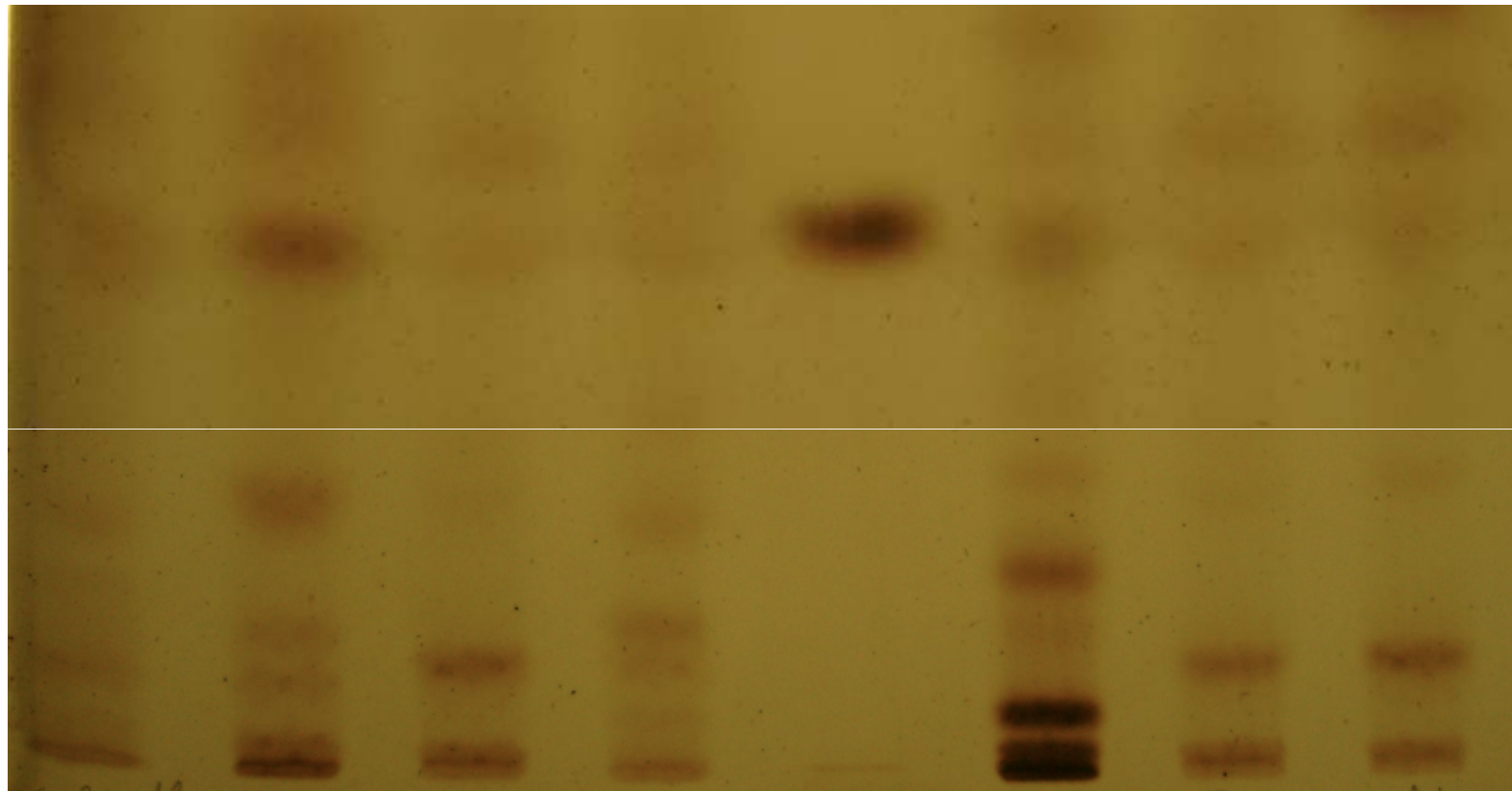
Common sample 2010

Sialidosis type I

Istanbul, 31 August 2010

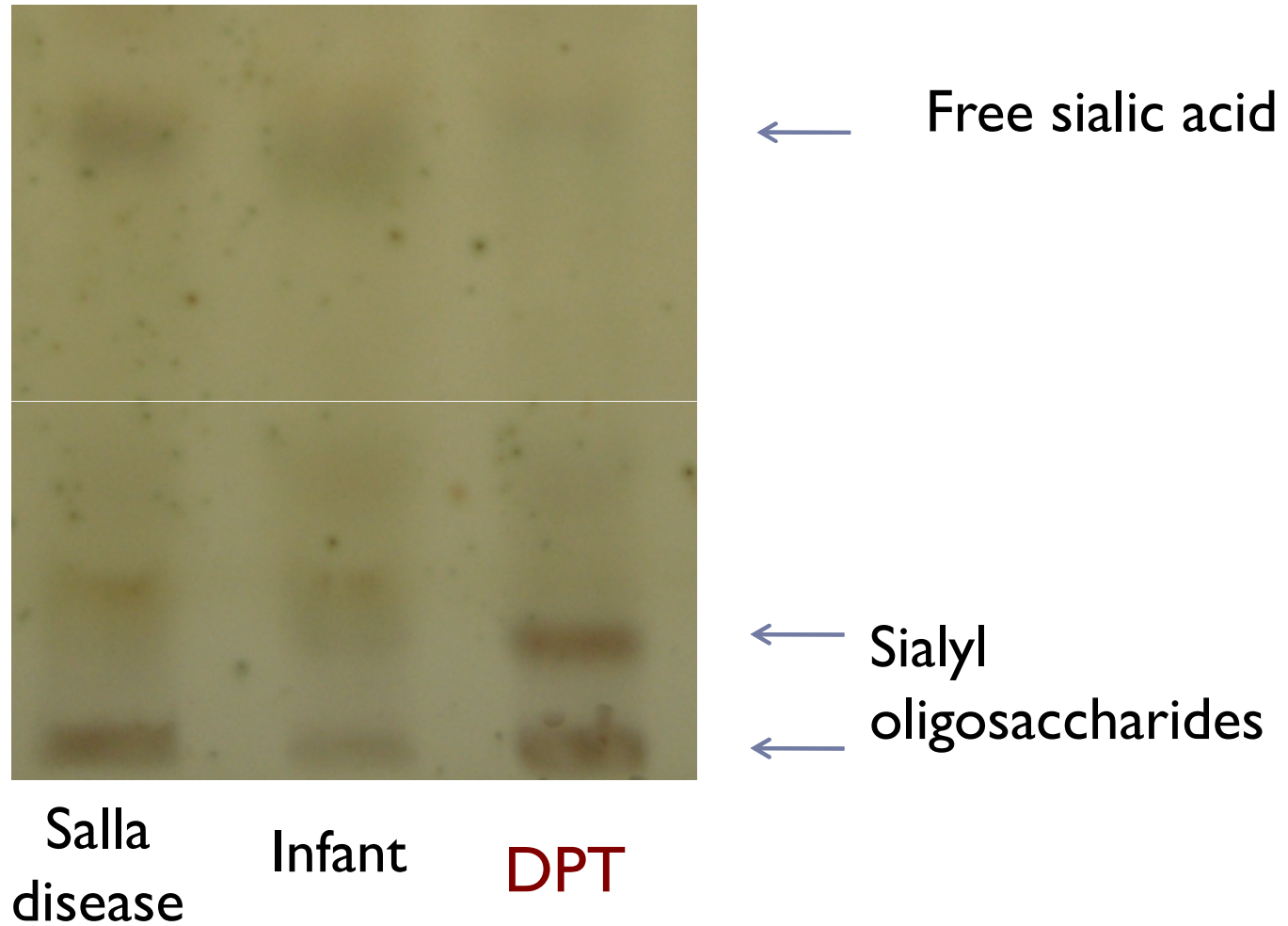
Dr Christine Vianey-Saban, CHU Lyon
christine.saban@chu-lyon.fr

Oligosaccharide TLC



Schindler Fuco sidosis **DPT** Apartyl glucos aminuria Lactose GM1 gangl. **DPT** Sialidosis

Sialic acid TLC



DPT centres

- ▶ Amsterdam 19 labs
- ▶ Basel 21 labs
- ▶ Lyon 21 labs
- ▶ Pragues 19 labs
- ▶ Sheffield 21 labs (3 no answer)

- ▶ Total 101 labs (98 responders)

Creatinine determination

Centre	Median	Mean	Coefficient of variation
Amsterdam	4.20	4.17	6 %
Basel	4.00	3.92	9 %
Lyon	4.21	3.96	23 %
Pragues	4.20	4.21	29 %
Sheffield	4.00	3.79	19 %
All centres	4.09	4.01	19 %

Interlab CV 2009 Special Assay urine = 6.5 % (n = 103)

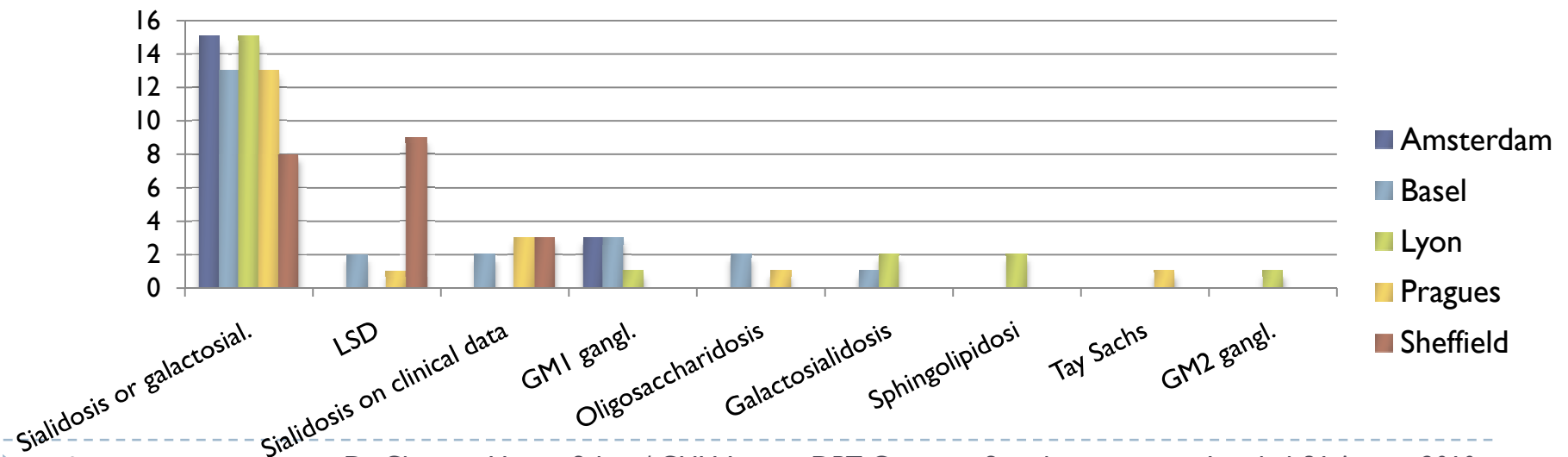
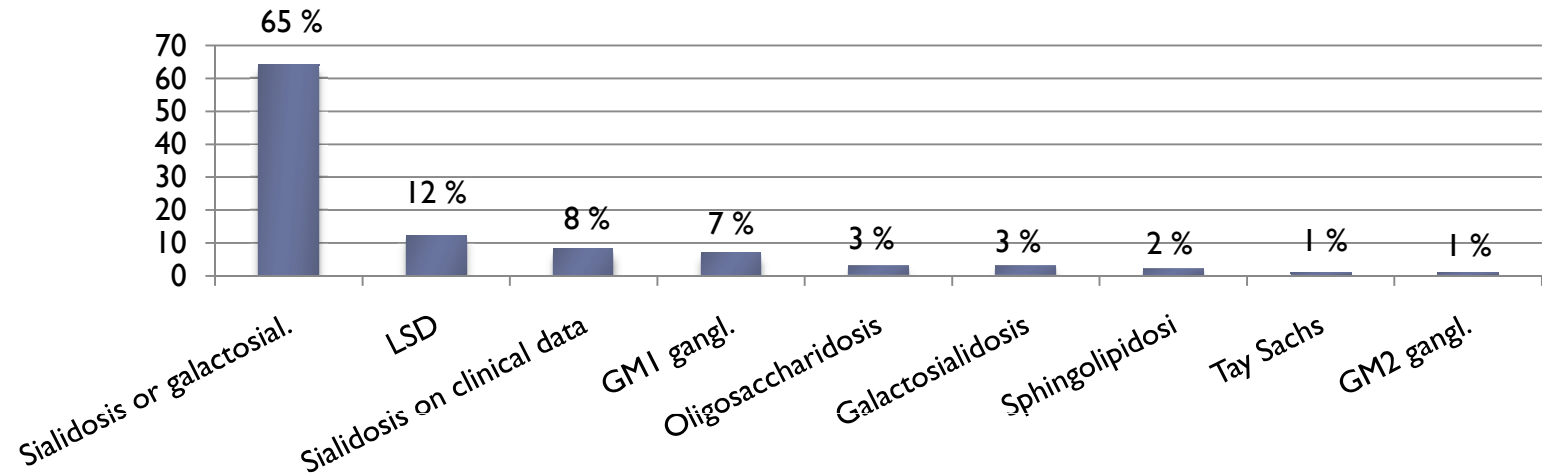
Interlab CV 2009 Quantitative organic acids = 5.8 % (n = 68)

Oligosaccharides determination

DPT centre	Number of labs	Test performed	%
Amsterdam	19	17	89 %
Basel	21	15	71 %
Lyon	21	20	95 %
Pragues	19	18	95 %
Sheffield	18	8	44 %
Total	98	78	80 %

Interpretation of results

All centers



Conclusions

- ▶ Oligosaccharide assay should be more widely available
- ▶ When an abnormal oligosaccharide profile is observed, the assay has to be repeated with urine samples from patients with known disorder(s) on the same plate. Scheme organizers can provide urine samples of such patients
- ▶ The ERNDIM QAP for mucopolysaccharides should be extended to oligosaccharides

Websites

- DPT schemes will move to website (CSCQ) results entry in 2011
- Website for quantitative schemes (SKML) revamped last year
- New material added to the main website



www.erndim.org

Erndim - Windows Internet Explorer

http://www.erndim.unibas.ch/

File Edit View Favorites Tools Help

Erndim



HOME About ERNDIM ERNDIM Participants Organisation Training & Education
Directory of Laboratories E-MAIL LINKS Meetings & Reports

ERNDIM is synonymous with quality control of laboratory measurements within the field of the study of inborn errors of metabolism. ERNDIM was founded in 1994 with its legal base in Maastricht, The Netherlands. The full name of ERNDIM, the "European Research Network for evaluation and improvement of screening, Diagnosis and treatment of Inherited disorders of Metabolism" reflects the original ideals and vision of its founders.

Performance Assessment Paper

A [paper](#) describing in detail ERNDIM's policy for assessment of performance in our EQA schemes is now mounted on this website.

ERNDIM meeting 2009

The meeting took place in Basel on October 22-23 and has been very successful with around 100 participants.

The **presentations** are now available on this website under "meetings and reports". Please follow the links in the meeting program.

Training of laboratory scientists

The SSIEM academy training meeting for clinicians and for laboratory workers took place on 4-5th October 2010 in Manchester. For full details see: <http://www.ssiem.org/ssiemacademy.asp>.

For course materials of the previous training meetings which took place 2008, 2009 and 2010 log in as SSIEM member at:
[Academy 2008](#)
[Academy 2009](#)
[Academy 2010](#)

For general aspects of training visit the section titled [European Training Schemes for Scientists](#) in the Training and Education section.

Next year's training meeting will take place in Amsterdam, date yet to be decided.

Newsletter Spring 2010

Dear Colleagues,
There continues to be a number of important changes taking place in our EQA schemes and the organisation of ERNDIM. Please see our latest newsletter for updates on: New Schemes; Website for DPT results entry; Resources available from our ERNDIM website; Pilot Schemes; Plea for urine Samples for DPT distributions; Training Days and Scientific Meeting October 2009; SSIEM Academy 2010; ERNDIM participants meeting 2010; Accreditation of ERNDIM; The EuroGenTest Project; European Society for Human Genetics Quality Committee. For more information read the [Newsletter 2010](#).

Neue Seite 1 - Windows Internet Explorer

http://www.erndim.unibas.ch/Meeting_Rep/09_oct_basel/menu_basel_09.htm

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Neue Seite 1

ERNDIM Meeting, October 22 – 23, 2009

SESSION 1: Diagnostic approaches

- [Brian Fowler: Opening](#)
- [Marianne Rohrbach: Clinical approach to Diagnosis of Lysosomal Storage Diseases](#)
- [O. van Diggelen: ERNDIM EQA scheme for Lysosomal Enzymes](#)
- [Dirk Lefeber: -Diagnosis of Congenital disorders of Glycosylation](#)

-ERNDIM EQA scheme for CDG

- [Matthias R. Baumgartner: Clinical presentation and diagnostic difficulties of Glycogen storage diseases](#)

SESSION 2: Future Developments in Genetic Testing / EQA

- [Brian Fowler: ERNDIM and the Eurogentest Project](#)
- [David Barton: EMQN and EQA in molecular genetic testing](#)
- [Orly Elpeleg: Homozygosity mapping as a primary diagnostic tool: LIPN1-mutations as the major cause of recurrent rhabdomyolysis](#)

SESSION 3: Novel Disorders and Biochemical Diagnosis

- [Brian Fowler: State of art of intracellular cobalamin defects: CbID, CbIF](#)
- [Valeria Tiranti: A final solution to the ethylmalonic acid syndrome](#)
- [Wim Kulik: The application of UHPLC-separation of acylcarnitines prior to MS/MS detection](#)

Common ERNDIM meeting

- [Mick Henderson: Chairman's update](#)
- [Brian Fowler: Common DPT sample](#)
- [Nenad Blau: Neurotransmitter disorders: clinical presentation, when to test](#)
- [Simon Heales: Analysis of neurotransmitters](#)

Internet 100%

EQAcom2: Welcome - Windows Internet Explorer

https://baal.hcuge.ch/cscq/ERNDIM/Initial/Initial.php



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Google EQAcom2: Welcome

Quality Control Center Switzerland

ERNDIM PROFICIENCY TESTING SCHEMES

European Research Network for evaluation and improvement of screening,
Diagnosis and treatment of Inherited disorders of Metabolism



Access to PT-WEB

- [Login](#)
- [Main page](#)
- [Recommendations](#)

Contact person

- [Contact the CSCQ](#)
- [Send an e-mail to the](#)
- [CSCQ](#)
- [FAQ](#)

Links

- [ERNDIM-Quantitative](#)
- [ERNDIM-Web site](#)
- [CSCQ Web site](#)
- [Acrobat Reader](#)

Welcome to ERNDIM Web submission application

The ERNDIM Web submission application allows DPT scheme participants to enter their results using Internet. It is accessible from any Internet connection and browser.

Before using this program, you must be registered at the Quality Control Center Switzerland.

If not registered, contact the DPT scheme organizer.

If you are already registered, click [here](#) to open a session.

[More >>](#)

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Method Specification

User profile - Windows Internet Explorer

https://baal.hcuge.ch/cscq/ERNDIM/Applic/SaisieProfil.php?act=sel&id=N1-0

File Edit View Favorites Tools Help

Google User profile

Reducing substances	Test tablets	<input type="checkbox"/>	<input type="checkbox"/>	
	Spot test	<input type="checkbox"/>	<input type="checkbox"/>	
Ketoacids (DNPH)	Spot test	<input type="checkbox"/>	<input type="checkbox"/>	
Other analyte - PLEASE SPECIFY	Other	<input type="checkbox"/>	<input type="checkbox"/>	

Amino acid analysis				
Analyte	Method	Selection	Cluster Lab	User-defined method / Remarks on the pre-defined method
Amino acid screening	PC	<input type="checkbox"/>	<input type="checkbox"/>	
	HVE	<input type="checkbox"/>	<input type="checkbox"/>	
	TLC	<input type="checkbox"/>	<input type="checkbox"/>	
	TLC-2D	<input type="checkbox"/>	<input type="checkbox"/>	
	Other	<input type="checkbox"/>	<input type="checkbox"/>	
Amino acid quantitative	IEC-ninhydrin	<input type="checkbox"/>	<input type="checkbox"/>	
	IEC-other detection	<input type="checkbox"/>	<input type="checkbox"/>	
	Reversed phase HPLC	<input type="checkbox"/>	<input type="checkbox"/>	
	UPLC	<input type="checkbox"/>	<input type="checkbox"/>	
	GC/FID	<input type="checkbox"/>	<input type="checkbox"/>	
	GC-MS	<input type="checkbox"/>	<input type="checkbox"/>	
	MS-MS (no separation)	<input type="checkbox"/>	<input type="checkbox"/>	
	LC-MS/MS	<input type="checkbox"/>	<input type="checkbox"/>	
Homocyst(e)ine	Other	<input type="checkbox"/>	<input type="checkbox"/>	
	Enzymatic methods	<input type="checkbox"/>	<input type="checkbox"/>	
	HPLC- SBDF	<input type="checkbox"/>	<input type="checkbox"/>	
	HPLC-monobrombimane	<input type="checkbox"/>	<input type="checkbox"/>	
	IEC with ninhydrin	<input type="checkbox"/>	<input type="checkbox"/>	
	GC-MS	<input type="checkbox"/>	<input type="checkbox"/>	
	MS-MS (no separation)	<input type="checkbox"/>	<input type="checkbox"/>	
	LC-MS/MS	<input type="checkbox"/>	<input type="checkbox"/>	
Other	<input type="checkbox"/>	<input type="checkbox"/>		

Organic acid analysis				
Analyte	Method	Selection	Cluster Lab	User-defined method / Remarks on the pre-defined method

start ERNDIM up... [All] paed meet ... 2 Novell G... Perf Assess... User profile... Microsoft P... TVTTerm - [...] WSA- User... 14:5



Quality Control Center Switzerland

ERNDIM PROFICIENCY TESTING SCHEMES

European Research Network for evaluation and improvement of screening,
Diagnosis and treatment of Inherited disorders of Metabolism



Logged in on 2011-01-14 14:48:33

Survey

→ [09-07-D5](#)
[09-05-D5](#)

Options

[Logout](#)
[Back](#)

Results entry

Survey **09-07-D5** - Laboratory **21**

Selected sample: **D**

Select sample → **D E E**

Clinical picture	3 year old male, unexplained pyrexia, failure to thrive.		
Comment			
Treatment			
	Sex: M	Age (diag): 3 Year(s)	Age (pres.): 3 Year(s)

Step 1 : Selection of used analytes/methods

[Selection](#)

Step 2 : Analytical results input

1. Pre-investigations (0/0)
2. Amino acids (0/0)
3. Organic acids analysis (0/0)
4. Purines and Pyrimidines (0/0)
5. Lysosomal storage diseases (0/0)
6. Special assays (0/0)

Step 3 : Interpretation input

Interpretation

Step 4 : Further lab investigations

Recommendations

Step 5 : Proof reading

Poor Performance

- We have a poor performance policy and have started issuing warning letters to participants.
- Initially for DPT schemes but will apply to all
- The European Society of human Genetics has a Quality Committee in which all the major genetic lab Eqa providers collaborate.
- Initiative to harmonise definition of poor performance in process



ERNDIM Office

- Progress has been made, scientific administrator interviews have been conducted (December)
- Postholder will
 - Replace Malcolm's office functions
 - Work towards accreditation
 - Facilitate and promote training events and resources
- Additional plan to commission *someone else* to administer accounts



Dated Thursday, 16 September 2010
2010

SERVICE LEVEL AGREEMENT

BETWEEN

CENTRAL MANCHESTER
UNIVERSITY HOSPITALS NHS FOUNDATION TRUST (CMFT)

AND

European Research Network for evaluation and improvement of screening,
Diagnosis and treatment of Inherited disorders of Metabolism (ERNDIM)



1. Background - ERNDIM

ERNDIM was established in 1994 with funding from the European Commission. Its remit is to promote and improve quality in biochemical genetics testing in the European Union through the provision of External Quality Assessment (EQA) schemes and a growing commitment to providing training for laboratory scientists. ERNDIM is administered by an Executive Committee which is governed by the ERNDIM Board. The various EQA schemes are co-ordinated by the SAB (Scientific Advisory Board). The network is collaborating with the molecular genetics organisation, EMQN to provide office and administrative functions. The Foundation is governed by its Memorandum and Articles dated 5 September 1994. The legal base of ERNDIM is Maastricht, The Netherlands. The financial affairs of ERNDIM are administered from the office of the Association for Clinical Biochemists, Tooley Street, London.



Training collaboration with ETAC

- 2008 one day, amino acids
- 2009 two days, organic acids
- 2010 two days, MPS, purines pyrimidines, VLCFA
 - Very popular, courses oversubscribed
 - Positive feedback



- Home
- About SSIEM
- Events
- Grants
- National Societies
- Resources
- Training
- Working Groups
- Members Area

SSIEM ACADEMY 2010

4th - 5th October 2010



- #### SSIEM ACADEMY
- Submit Application
- #### PRESENTATIONS ARCHIVE
- SSIEM Academy 2010
 - SSIEM Academy 2009
 - SSIEM Academy 2008

SSIEM ACADEMY 2010

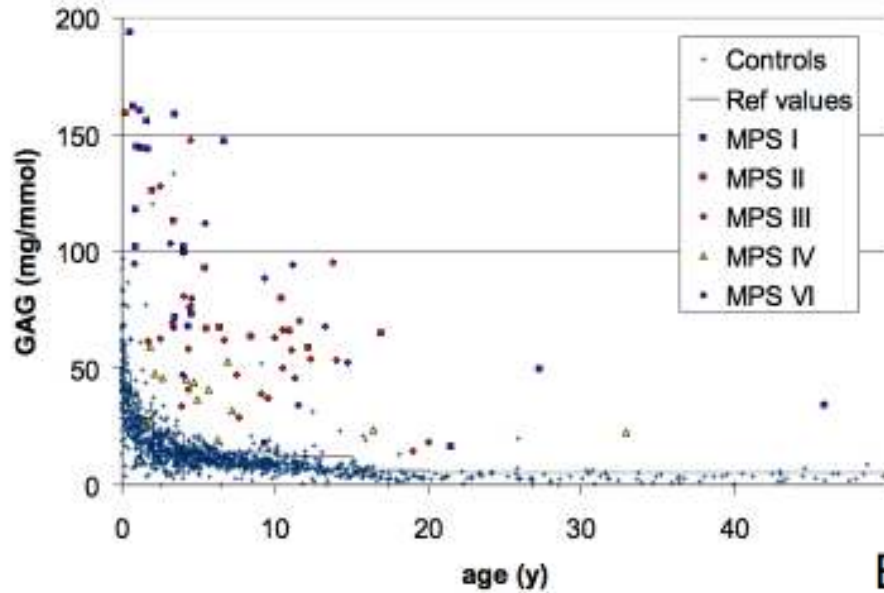
- [Laboratory Course Materials](#)
- [Clinical Course materials](#)

LABORATORY COURSE MATERIALS

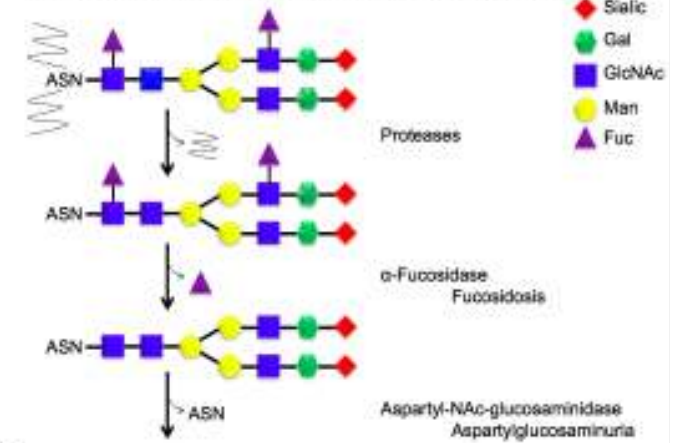
LECTURES

- [Mucopolysaccharidoses and Oligosaccharidoses](#)
Dr George Ruijter
Erasmus MC
Universitair Medisch Centrum Rotterdam
- [Peroxisomal investigation](#)
David Cheillan, Elodie Luangkhot, Christine Vianey-Saban
CHU Lyon
- [Purines and Pyrimidines](#)
Jörgen Bierau, Ph.D.
Maastricht University Medical Centre

Normal controls vs. MPS



Degradation of N-linked oligosaccharides

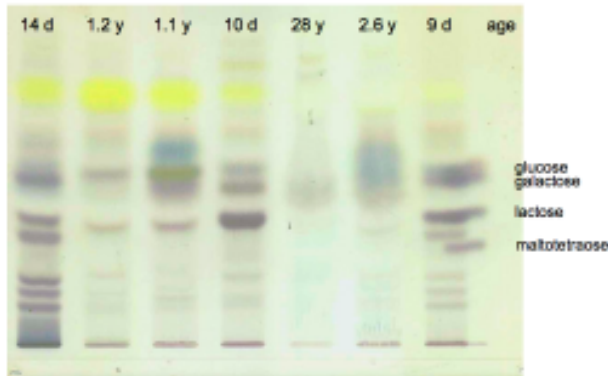


Examples disc. 1D electrophoresis (1)

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SSIEM Academy 2010 GR

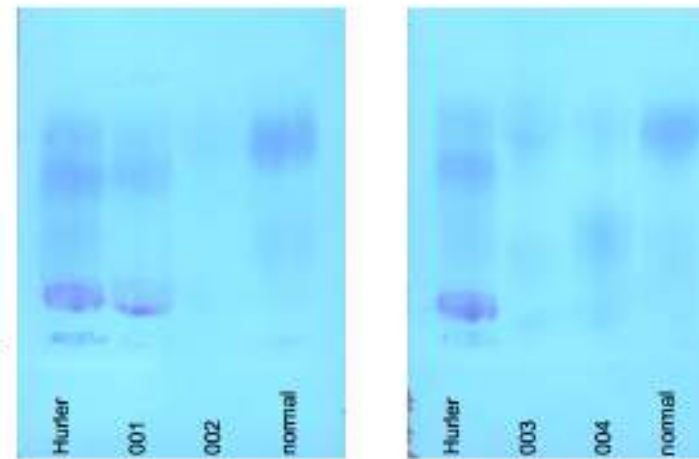
Example oligosaccharide TLC (1)



SSIEM Academy 2010 GR

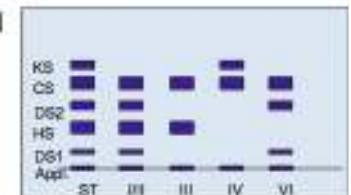


KS
CS
DS2
HS
DS1
Appl.



VI N

IV III

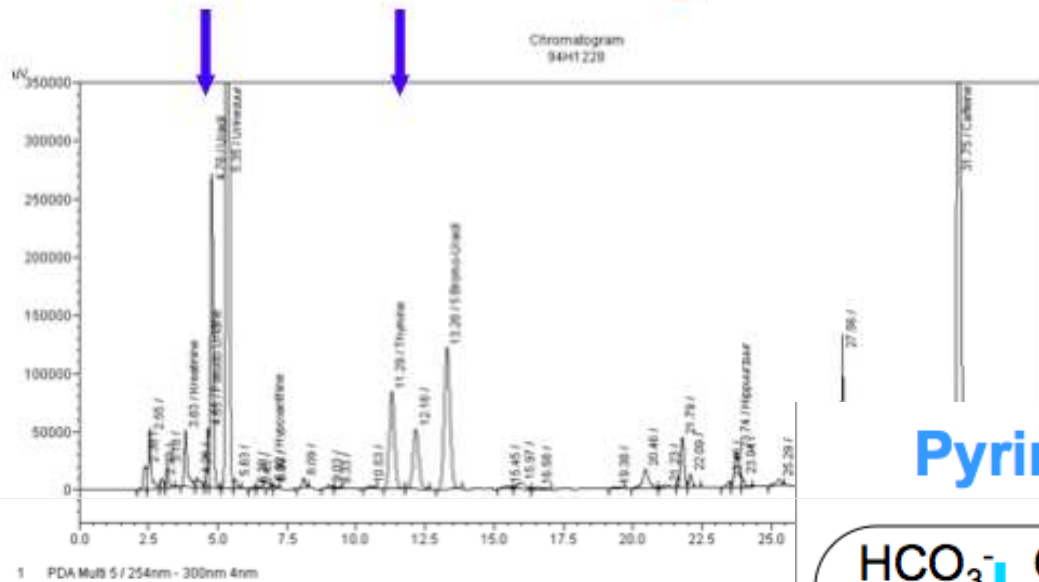


SSIEM Academy 2010 GR

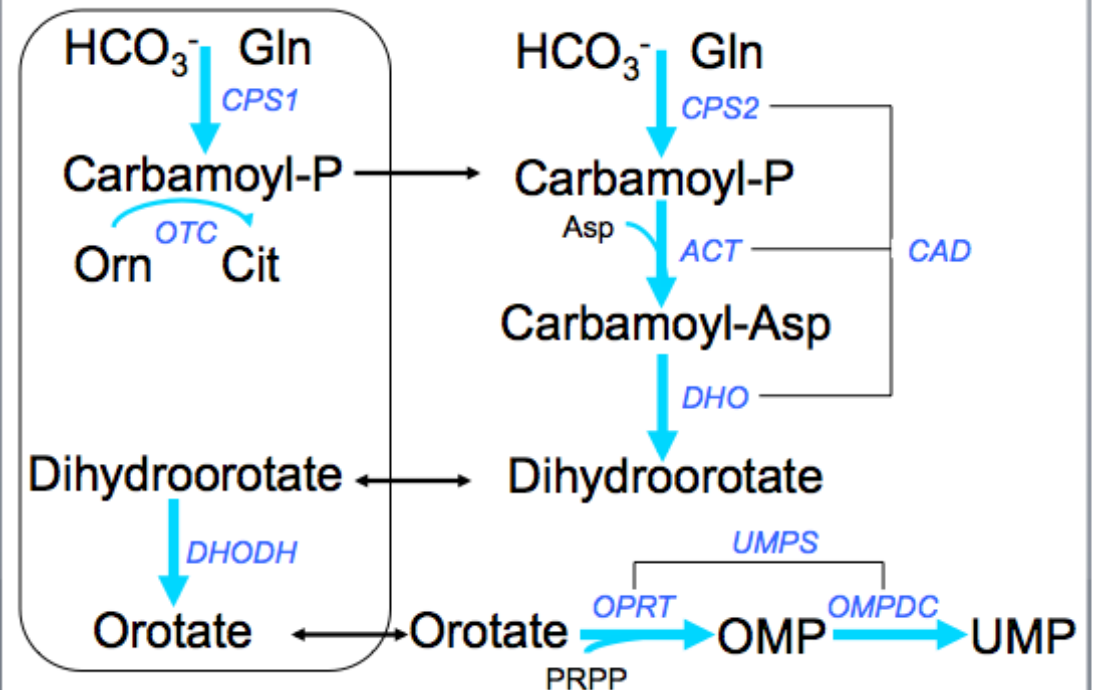
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Dihydropyrimidine dehydrogenase deficiency

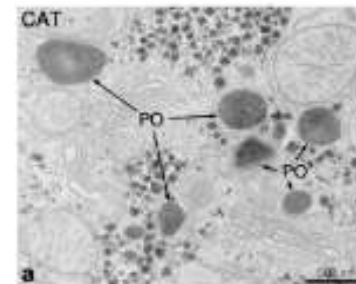


Pyrimidine *de novo* synthesis



Peroxisomes

- ▶ Subcellular organelles
- ▶ Size : 0.1 to 1 μm
- ▶ Ubiquitous distribution : abundant in liver and kidney, absent in erythrocytes
- ▶ Able to grow and divide



Cheifan, E Luangkhot, C Vianey-Saban / CHU-Lyon SSIEM Academy Manchester, 4 & 5 October 2010

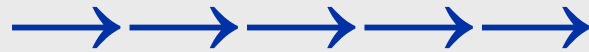
Peroxisomal disorders

Disorder	Protein, enzyme, transporter	Gene
ZSDs	Peroxisins	13 PEX genes
RDCP type 1 (Refsum)	Peroxin 7 (PTS2-receptor)	PEX 7
X-ALD	Protein ALDP	ABCD1
ACOX1 deficiency	Straight chain acyl-CoA oxidase	ACOX1
DBP deficiency	D-bifunctional protein	HSD17B4
SCPx deficiency	Sterol carrier protein	SCP2
AMACR deficiency	2-methylacyl-CoA racemase	AMACR
RDCP type 2	DHAP-AT	GNPAT
RDCP type 3	Alkyl-DHAP synthase	ADHAPS
Refsum disease	Phytanoyl-CoA-2-hydroxylase	PAHX
Hyperoxaluria type I	AGT	AGXT

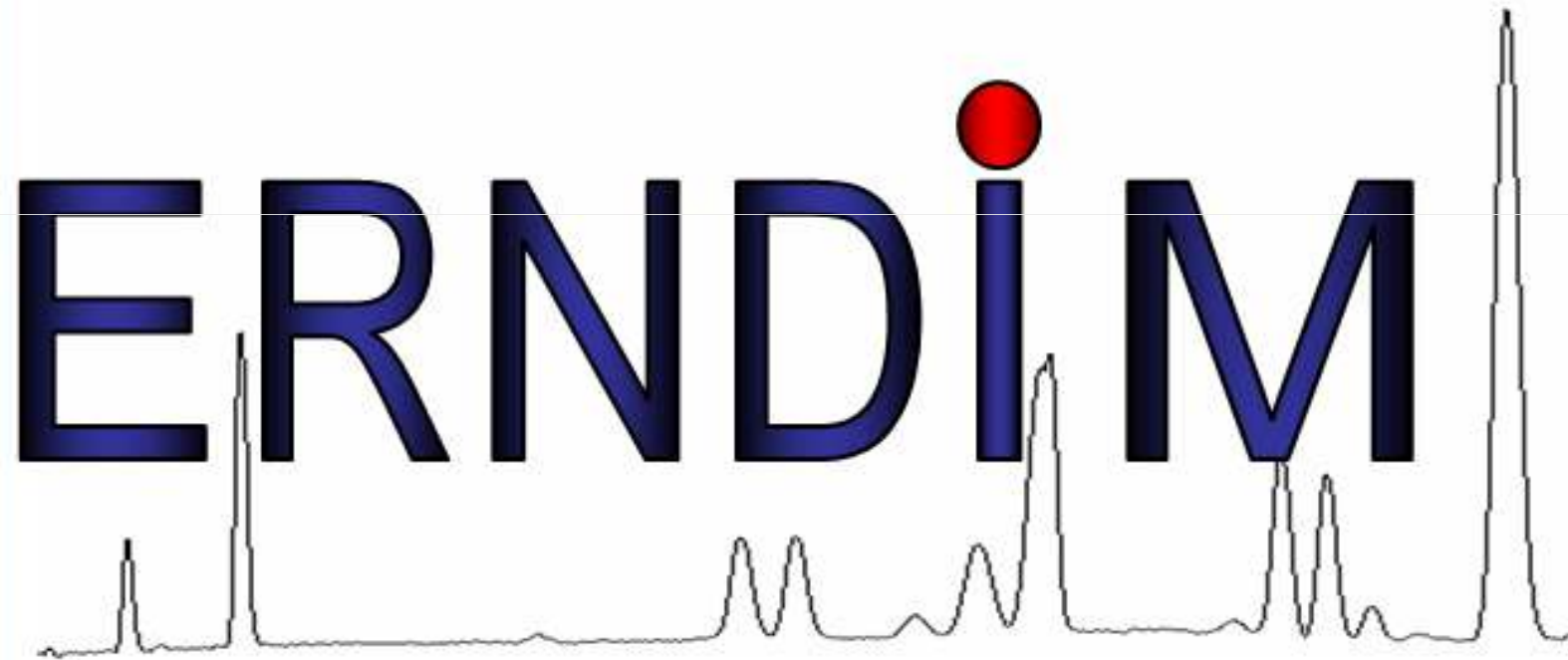
EuroGenTest

- Project officially finished last year
- Collaboration with new bid which was successful, but less funding
- Prof Brian Fowler to continue to be link from ERNDIM executive

A sneak preview of exciting news



A new logo!!



ERNDiM

The logo features the word "ERNDiM" in a bold, blue, sans-serif font. The letter "i" is lowercase and has a red dot above it. The text is set against a background of a chromatogram with several peaks of varying heights and widths. The entire logo is enclosed in a thin blue rectangular border.

Quality Assurance in Laboratory Testing for IEM