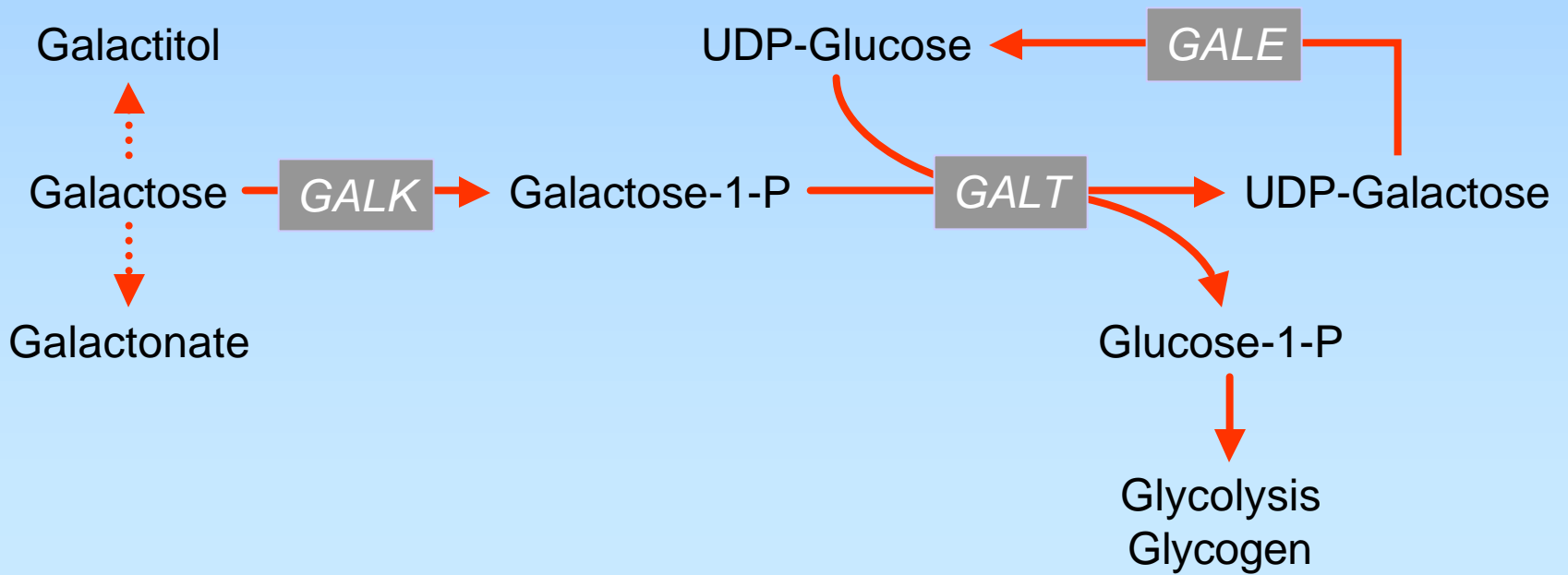


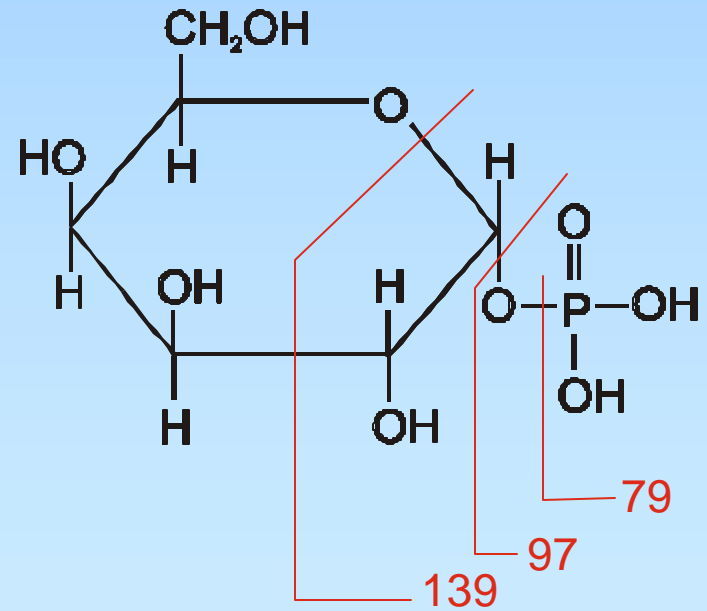
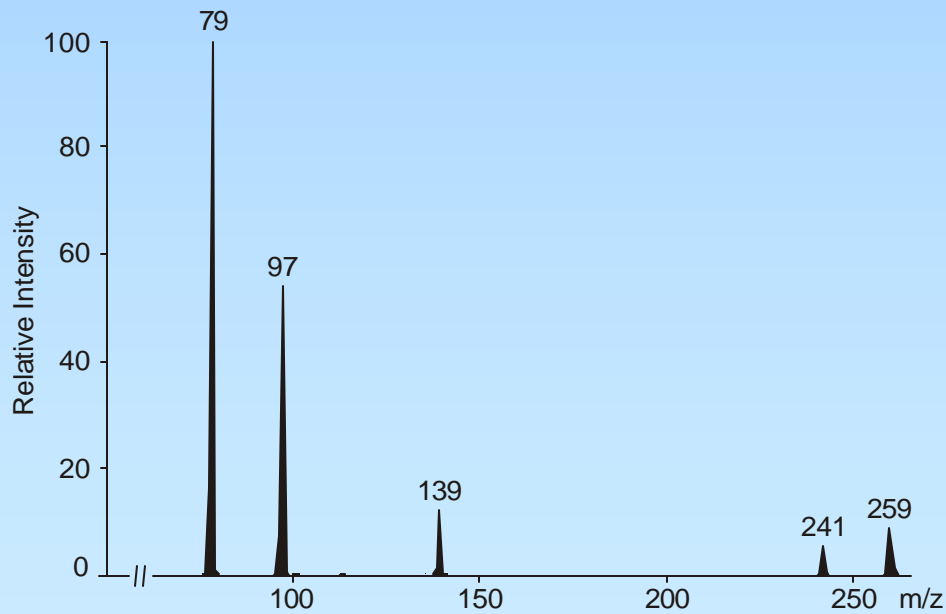
Galactosemia Screening Using Tandem Mass Spectrometry

Henrik Simonsen, MD, PhD
Denmark

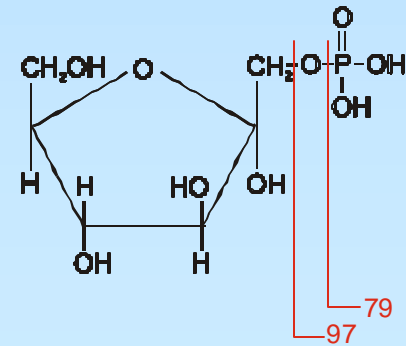
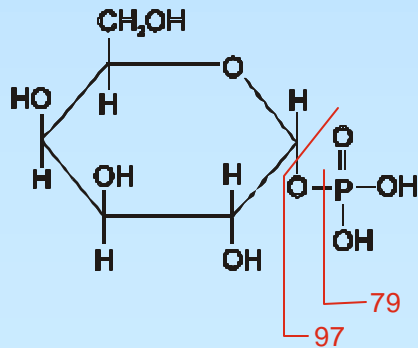
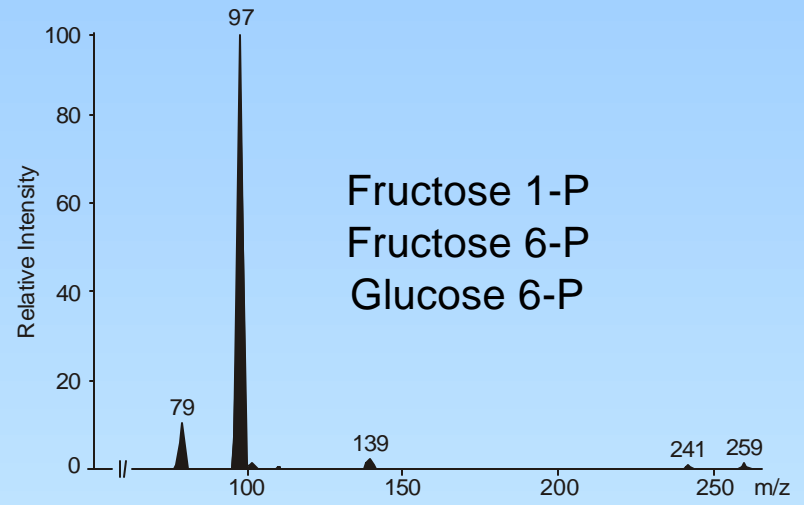
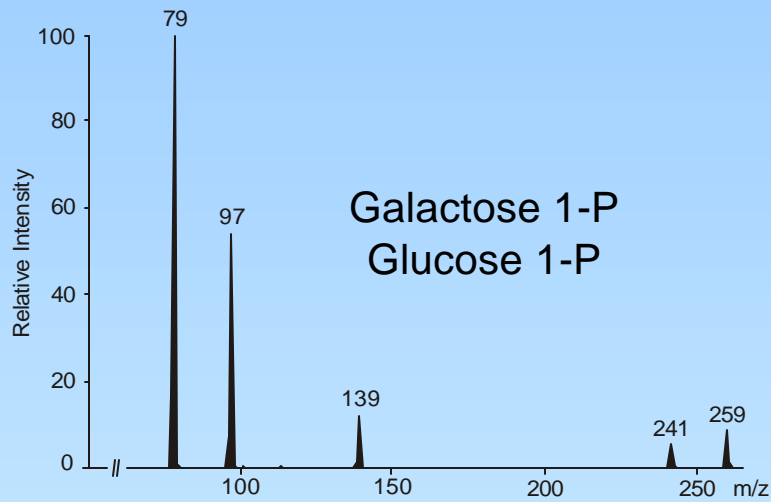
Biochemistry



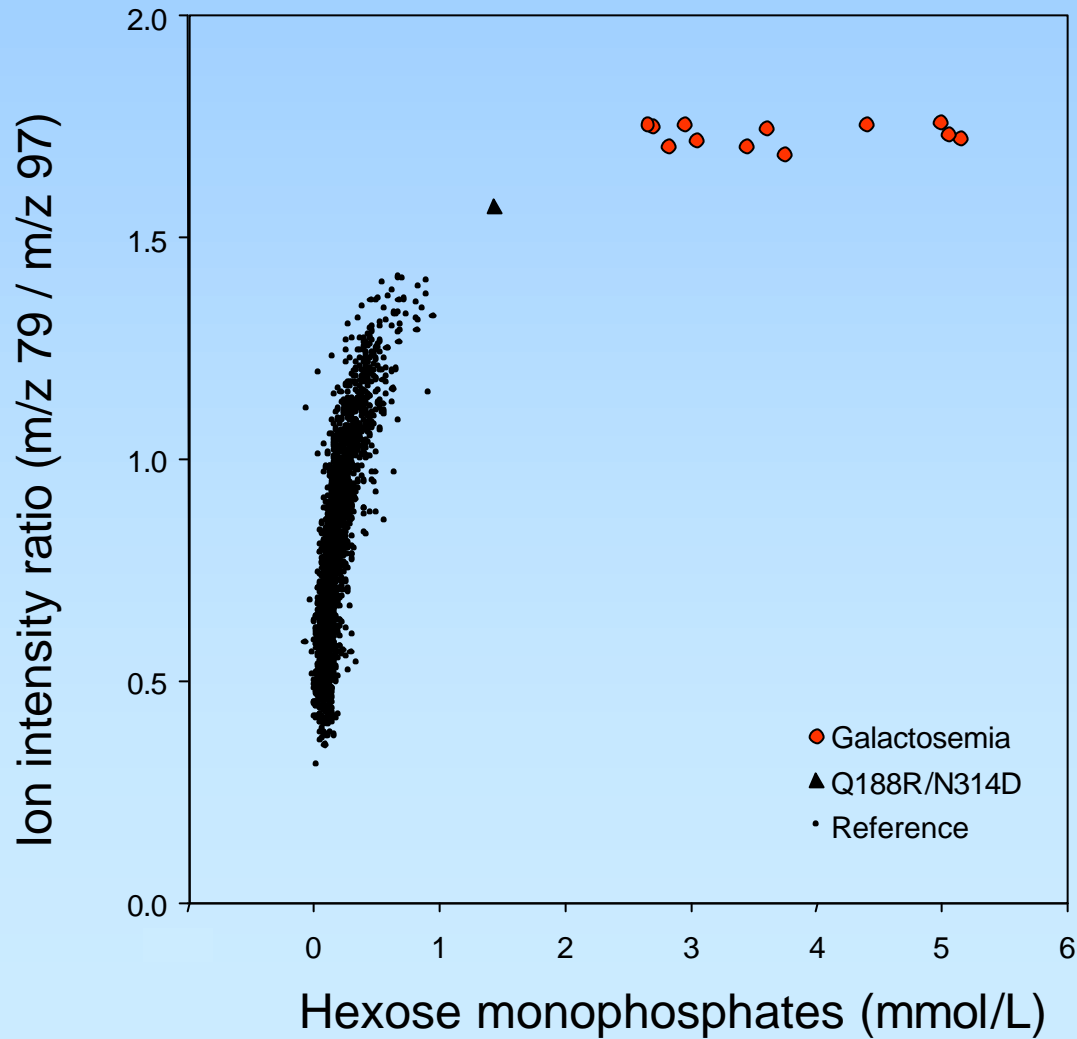
Fragmentation of galactose 1-phosphate



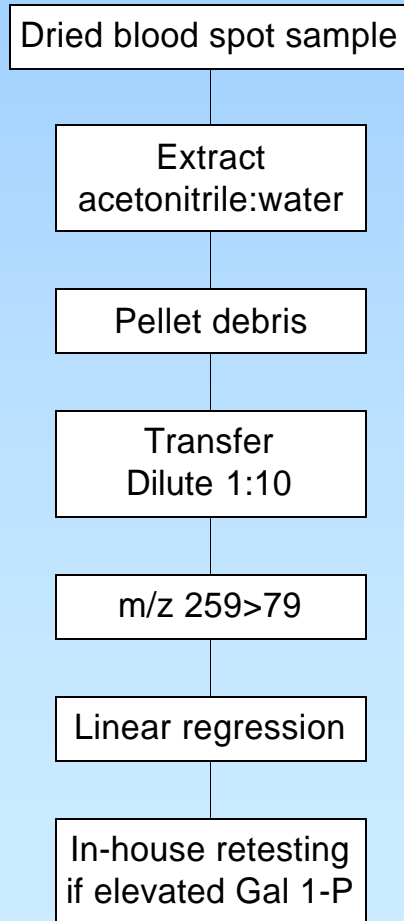
Fragmentation patterns



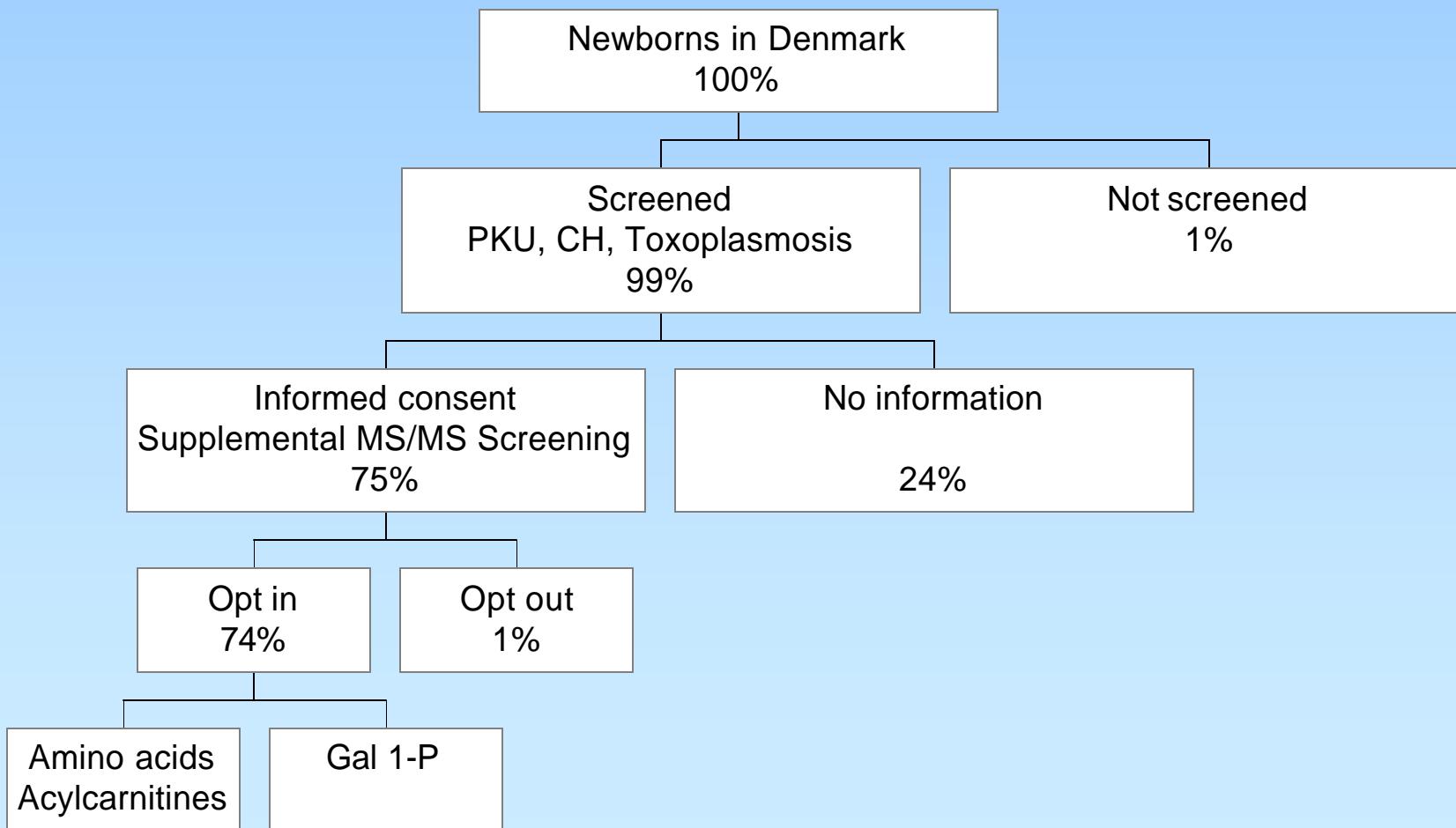
Retrospective screening



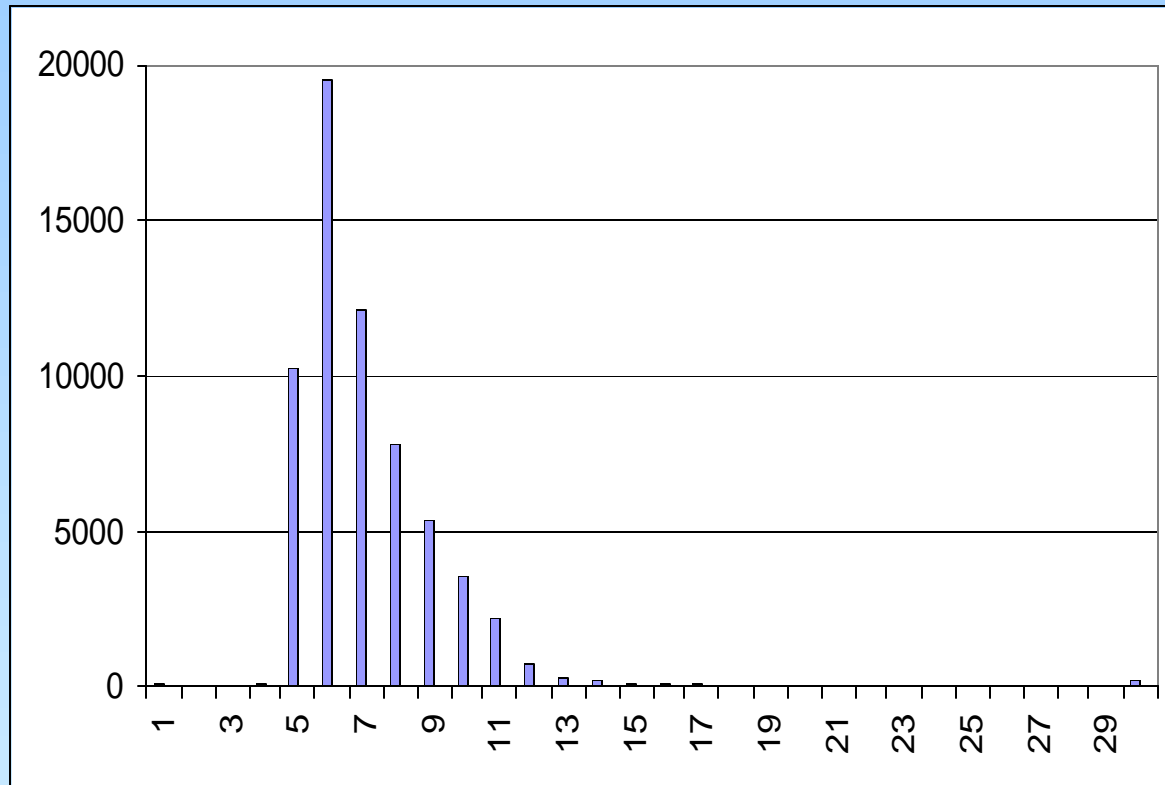
Analytical procedure



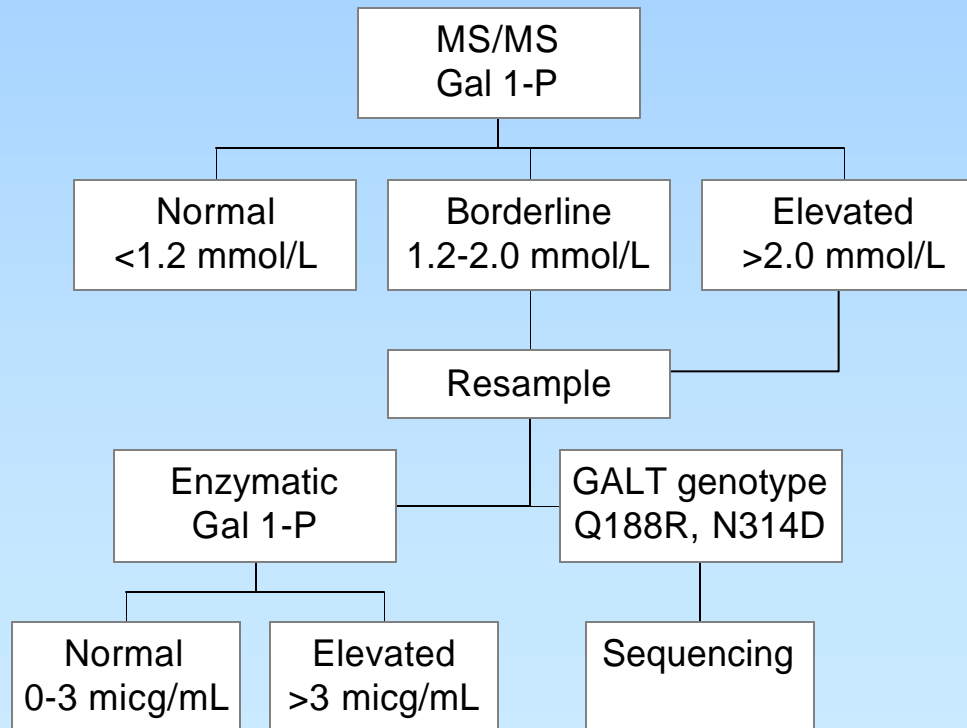
Participation



Sampling time



Diagnostic Algorithm



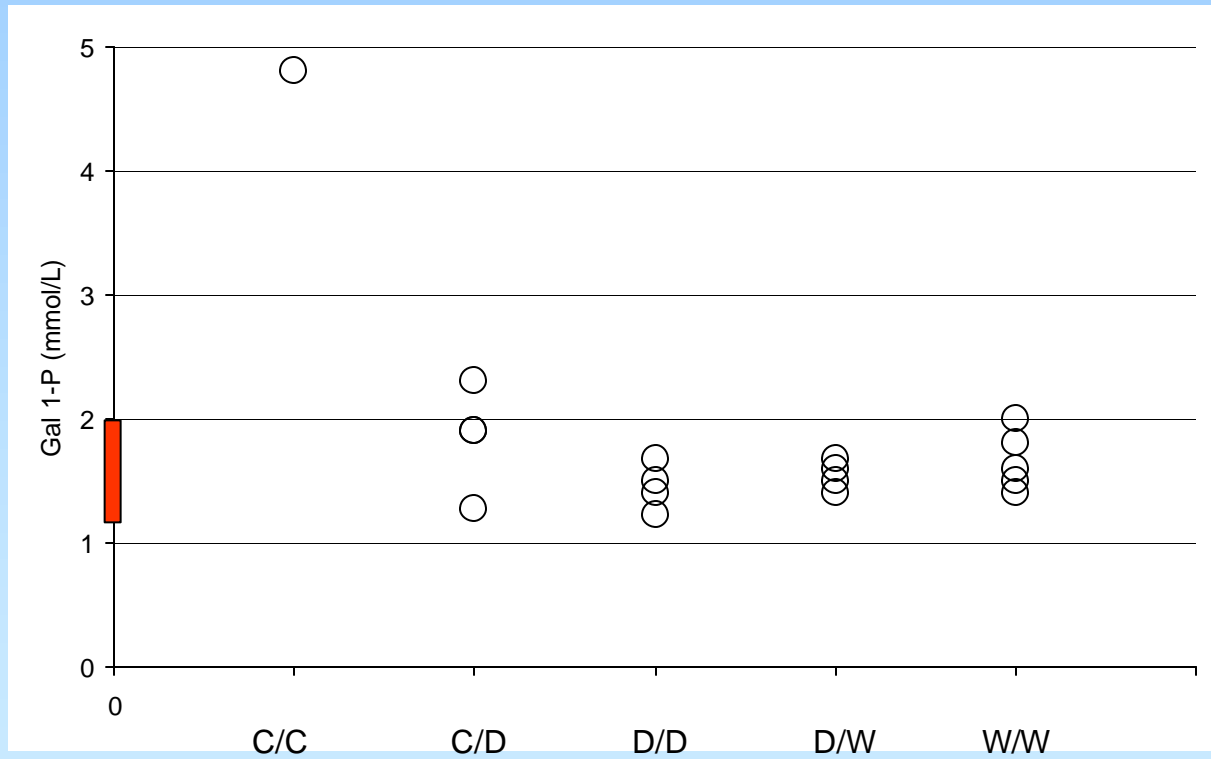
Analytical performance

- Measured samples 9613
- Technical redeterminations 94 = 1%
- Confirmatory redeterminations 29 = 0,3%

Screening results

Gal 1-P	Gal 1-P	Mut1	Mut2	Comment
4,8	1282	Q188R	R51L	
1,3	7	Q188R	N314D	
1,9	124	R67C	N314D	
1,9	0	Q188R	N314D	
2,3	43	Q188R	N314D	
1,2	nd	N314D	N314D	Neg. Benedict
1,4	0	N314D	N314D	
1,5	nd	N314D	N314D	Normal second filterpaper screen
1,7	15	N314D	N314D	
1,4	1	wt	N314D	
1,5	1	wt	N314D	
1,6	0	wt	N314D	
1,7	nd	wt	N314D	
1,4	0	wt	wt	
1,5	2	wt	wt	
1,6	1	wt	wt	
1,8	1	wt	wt	
2,0	1	wt	wt	

Gal 1-P levels



Genotypes

	Classical	Duarte	Wild type	Sum
Classical	1	4	0	5
Duarte		4	4	8
Wild type			5	5
Sum				18

Diagnostic Performance

- Screened 96.000 (est.)
- Gal 1-P >2.0 mmol/L 1 patient + 2
- Gal 1-P 1.2-2.0 mmol/L 15

- Clinical incidence: 1 (2 y study period)
1:60.000 (42 y period)

- Sensitivity: 100% (1:1)

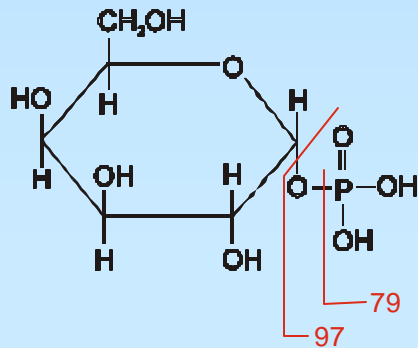
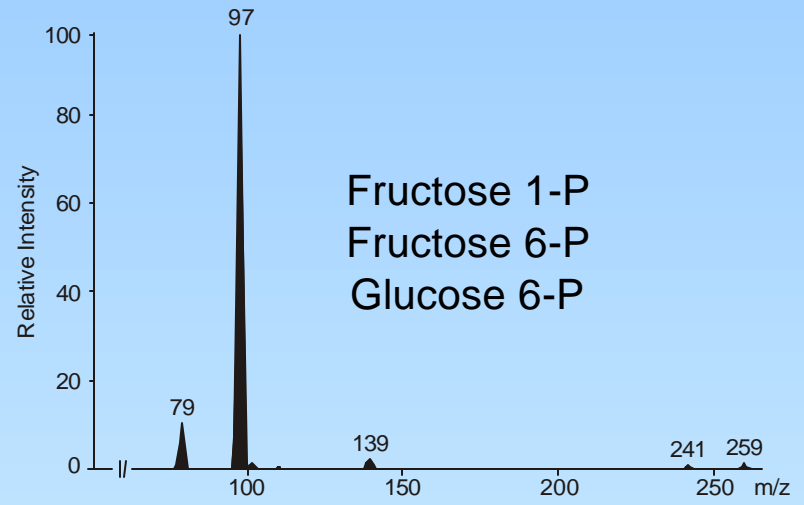
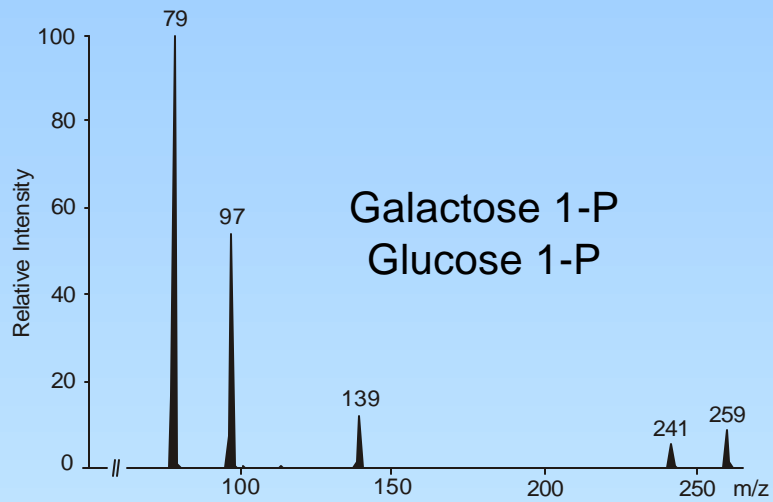
- FPR 1:6.400 (0,02%) -
1:32.000 (0,003%)

- PPV: 6% (1:18) - 33% (1:3)

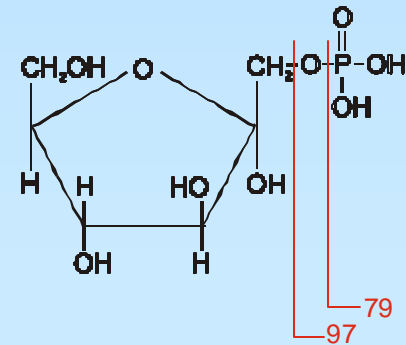
Conclusions

- MS/MS is able to detect even weak abnormalities in the GALT gene.
- High sensitivity
- Low false positive rate
- Internal standard is recommended

Fragmentation patterns



Galactose 1-P



Fructose 1-P

Kristin Skogstrand
Ulrich Glümer Jensen
Ernst Christensen
Marianne Schwartz
Allan Lund
David Hougaard
Niels Jacob Brandt
Bent Nørgaard-Pedersen
Flemming Skovby