EBV serology:
Simplicity through complexity

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Specific EBV serology is required, as the symptoms of clinically apparent EBV infection may be overlapping with those of many other diseases.

The serological response to EBV infections

is highly variable.

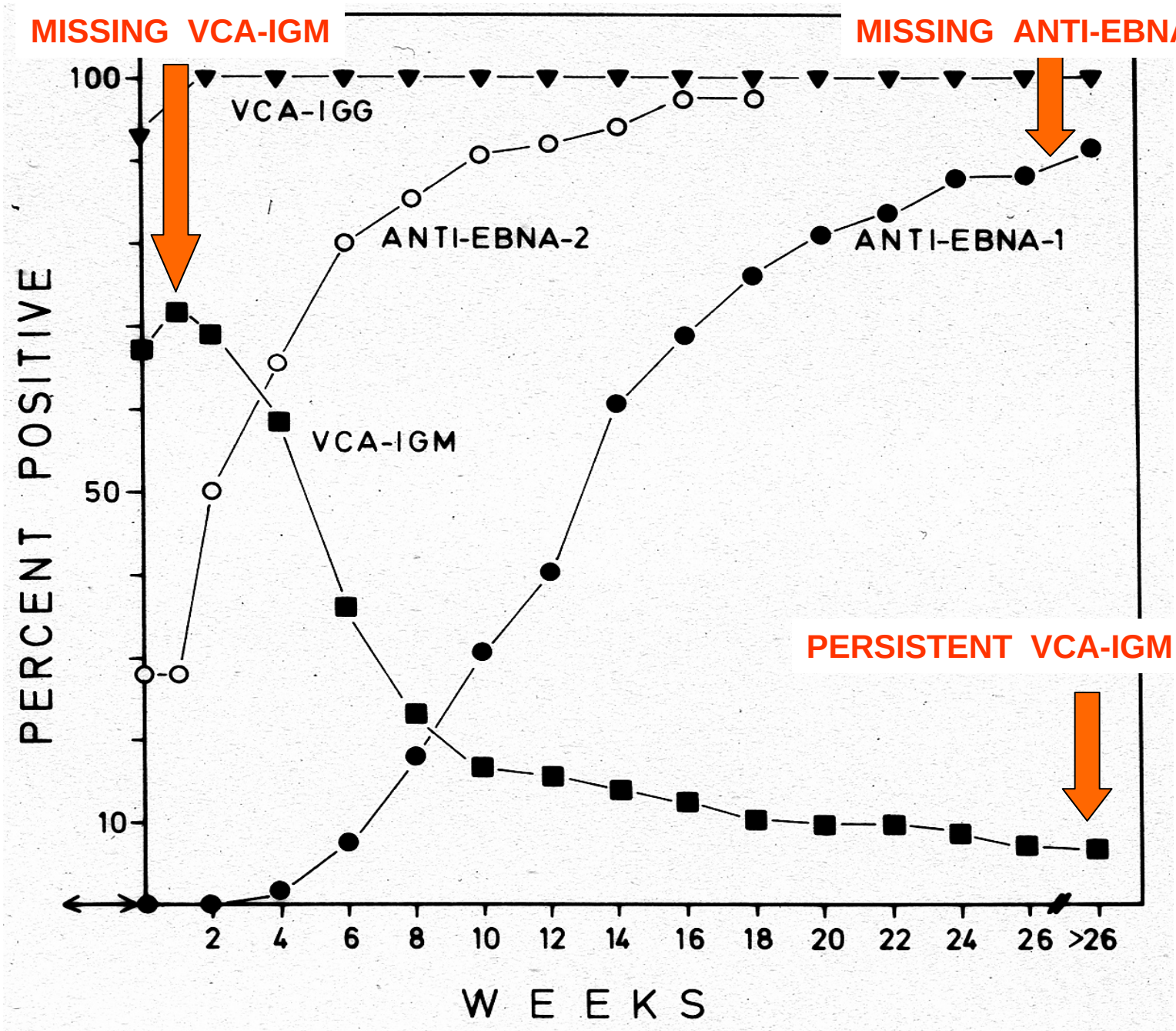
Determination of the classical markers

does not allow to draw the right conclusions

in each individual case!

The next graphs demonstrate the

problems of EBV serodiagnosis.


MISSING VCA-IGM
MISSING ANTI-EBNA-1
PERSISTENT VCA-IGM
VCA-IGG
ANTI-EBNA-2
ANTI-EBNA-1
VCA-IGM
PERCENT POSITIVE
100
50
10
2
4
6
8
10
12
14
16
18
20
22
24
26
>26
WEEKS

EBV serology using immunofluorescence in 3622 unselected cases

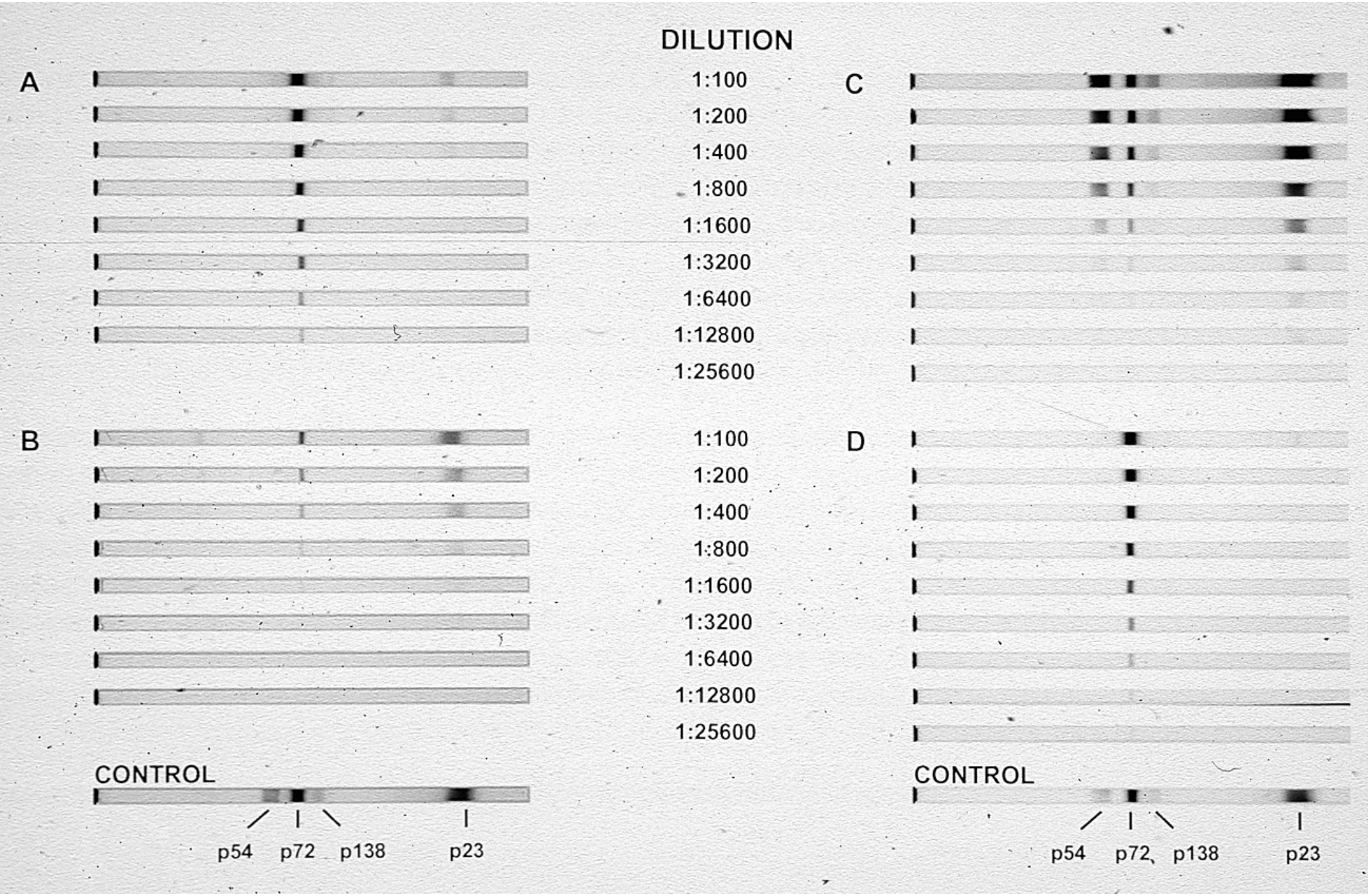
- Number of sera 3622
- Seronegative 222 (6.1 %)
- Anticellular reactivity 151 (4.1 %)

- VCA-IgG positive 3245
- Anti-EBNA-1 positive 2804 (86.4 %)
- Anti-EBNA-1 negative 441 (13.6 %)
- acute EBV infections 239
- past EBV infections with 202
- missing or lost Anti-EBNA-1

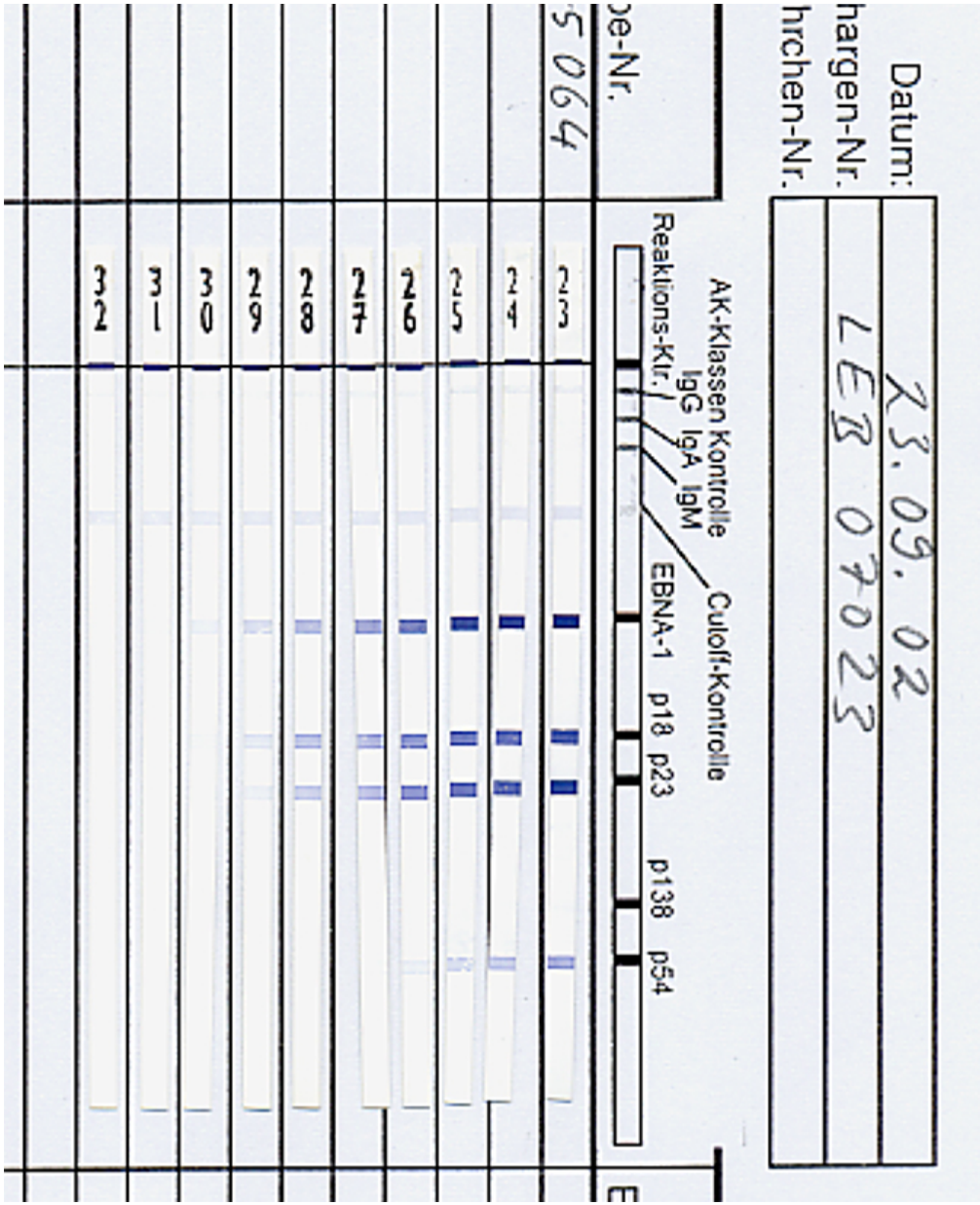
PROBLEMS OF CLASSICAL EBV-SEROLOGY

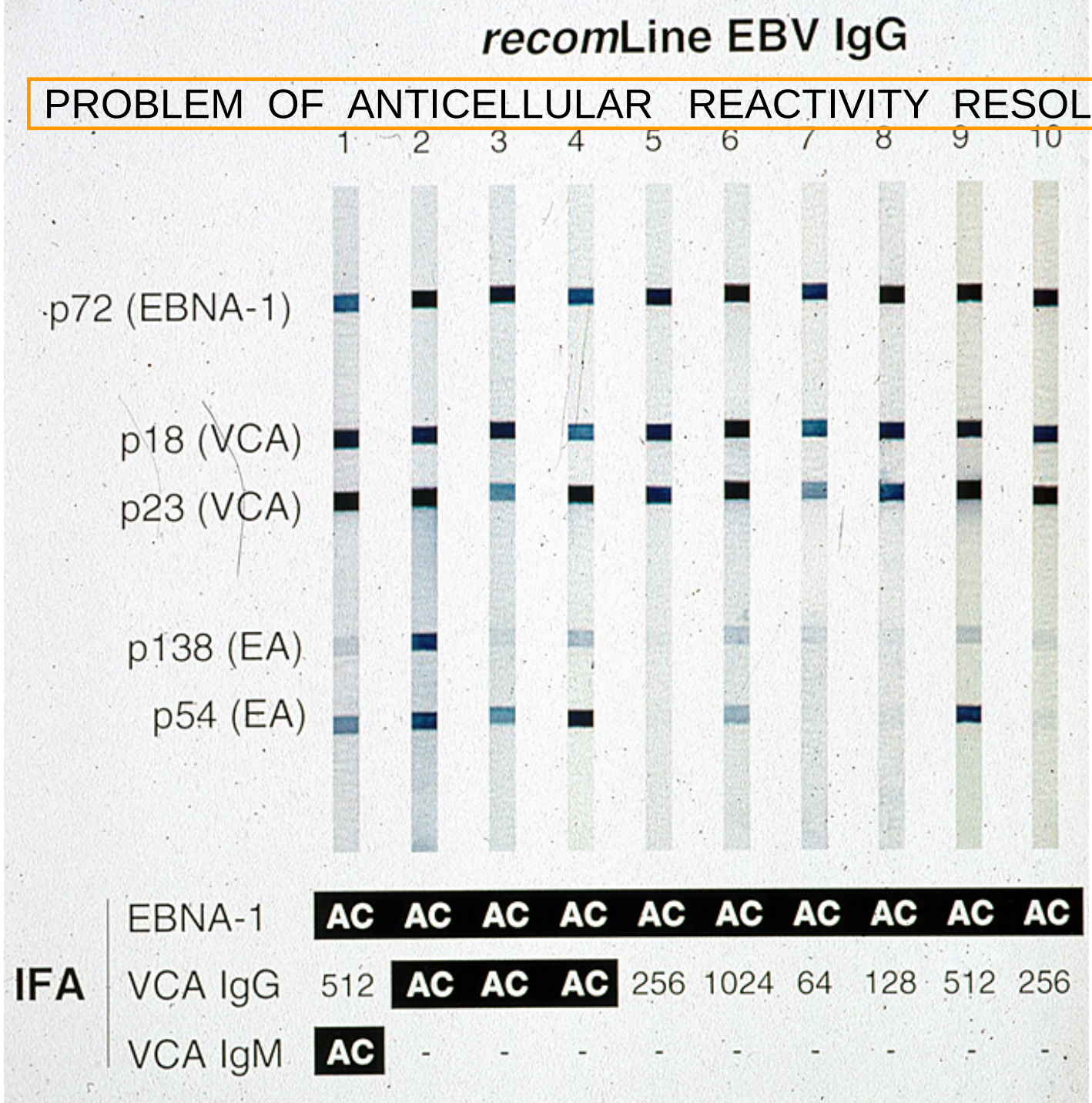
- Acute infections without detectable VCA-IgM
- Persisting VCA-IgM (false positive result)
- Lack of Anti-EBNA-1 in 6 % of persons with past EBV infection
- Secondary loss of Anti-EBNA-1 during immunosuppression
- Problem of anticellular reactivity

The immunoblot with recombinant antigens (Mikrogen) represents a quantitative system

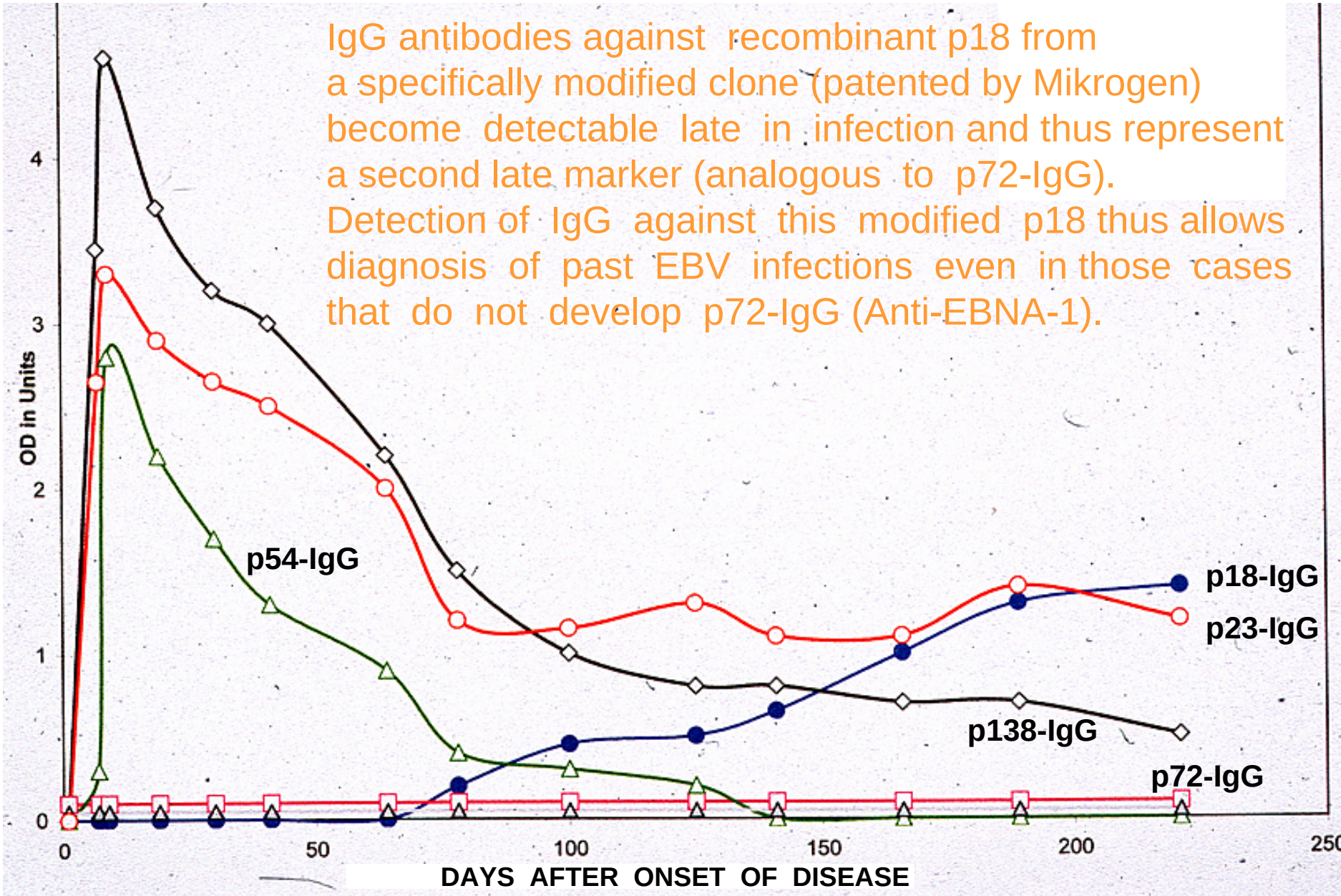


The RecomLine assay is suitable for quantitation

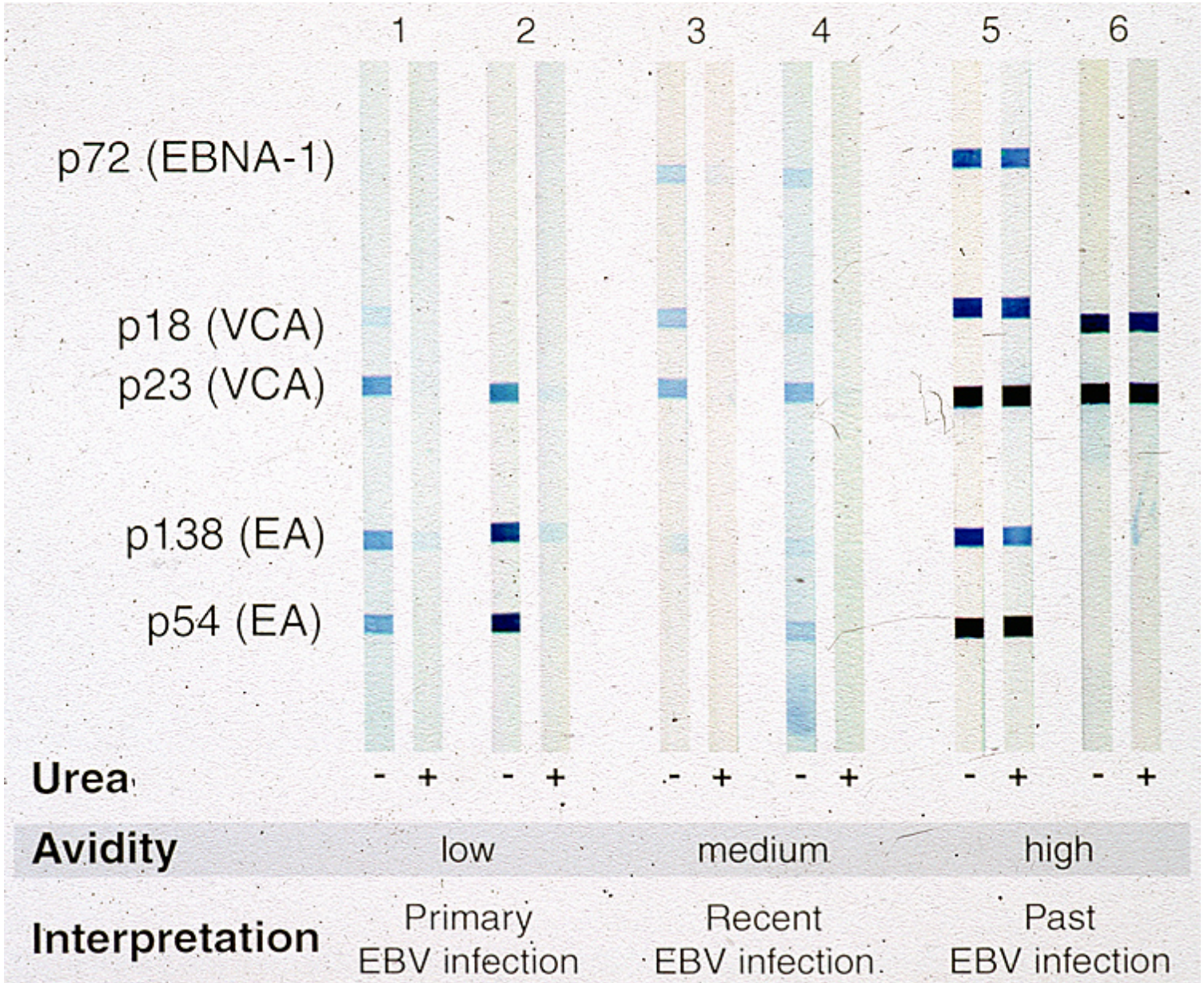



recomLine EBV IgG
PROBLEM OF ANTICELLULAR REACTIVITY RESOLVED
1 2 3 4 5 6 7 8 9 10
p72 (EBNA-1)
p18 (VCA)
p23 (VCA)
p138 (EA)
p54 (EA)
IFA
EBNA-1 AC AC AC AC AC AC AC AC AC AC
VCA IgG 512 AC AC AC 256 1024 64 128 512 256
VCA IgM AC - - - - - - - - -

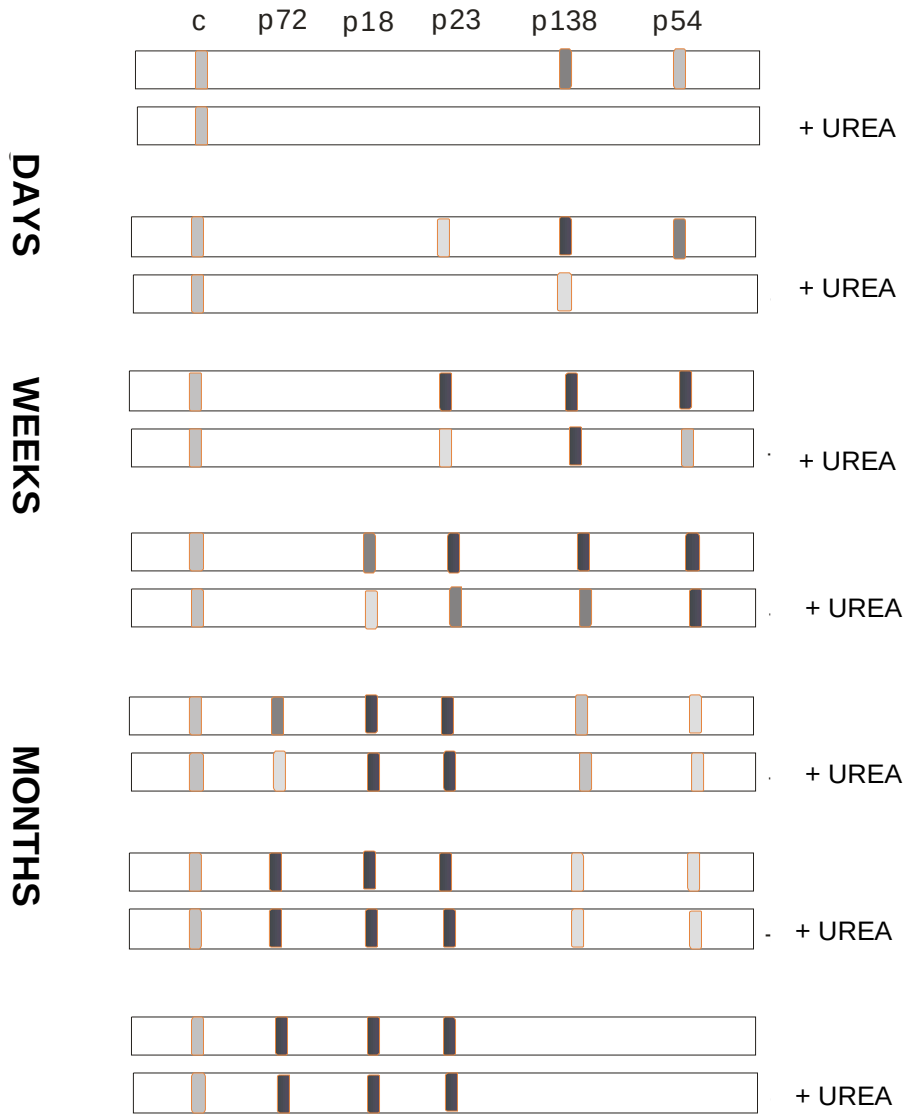
p18-IgG: A second late marker



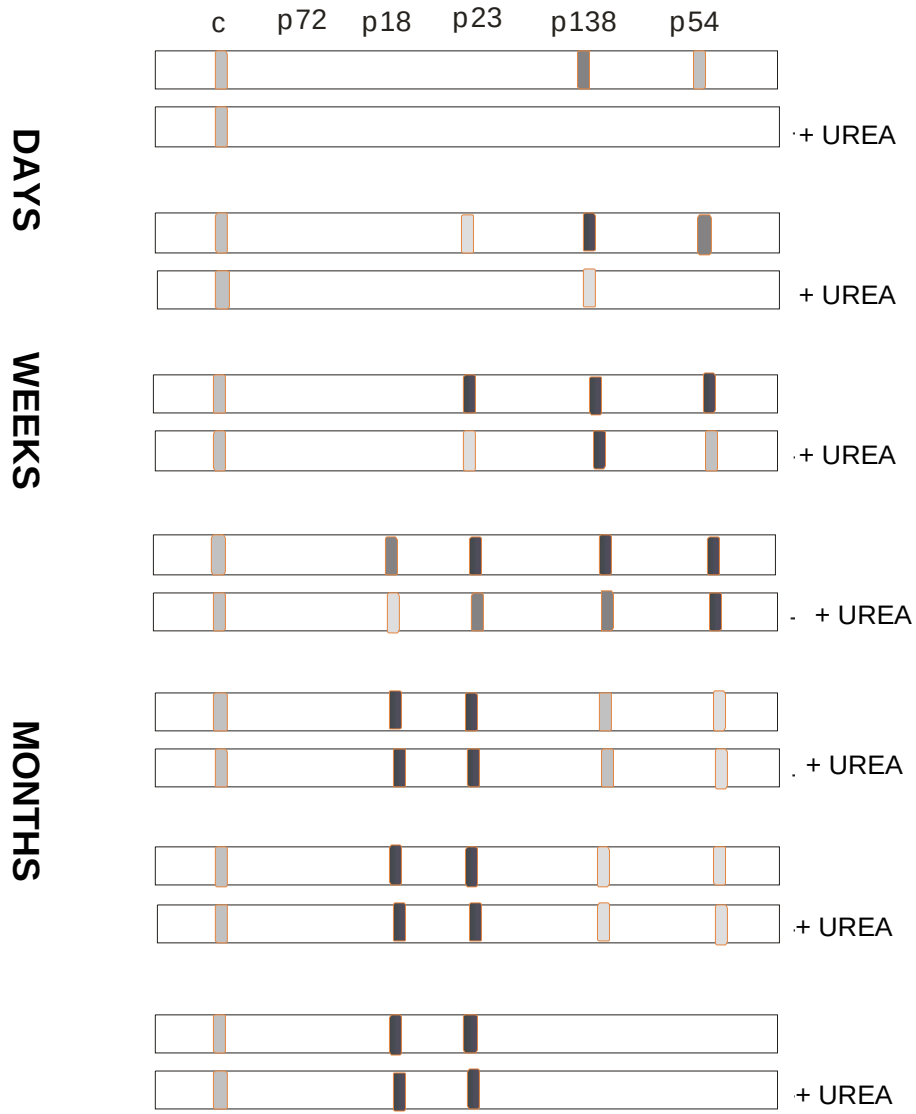
IMMUNOBLOT AND LINEASSAY ALLOW AVIDITY DETERMINATION



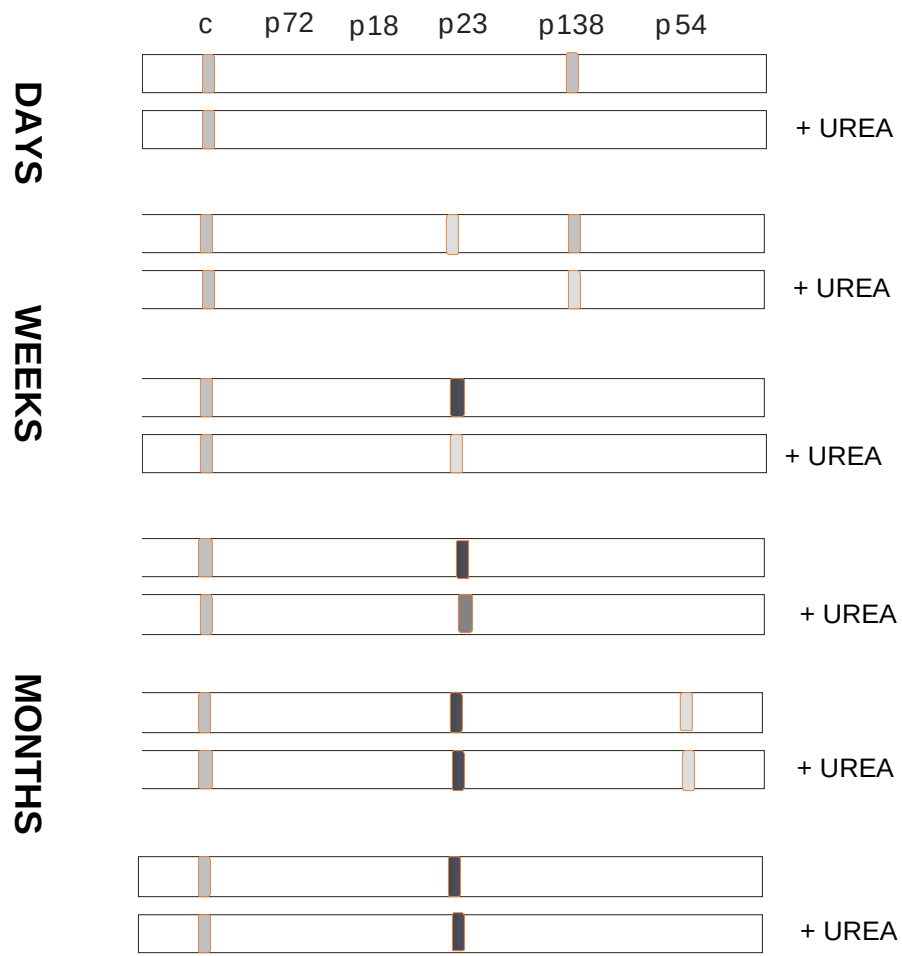
CLASSICAL SEROLOGY OF EBV INFECTIONS DETERMINED BY THE EBV RECOMLINE ASSAY (MIKROGEN)



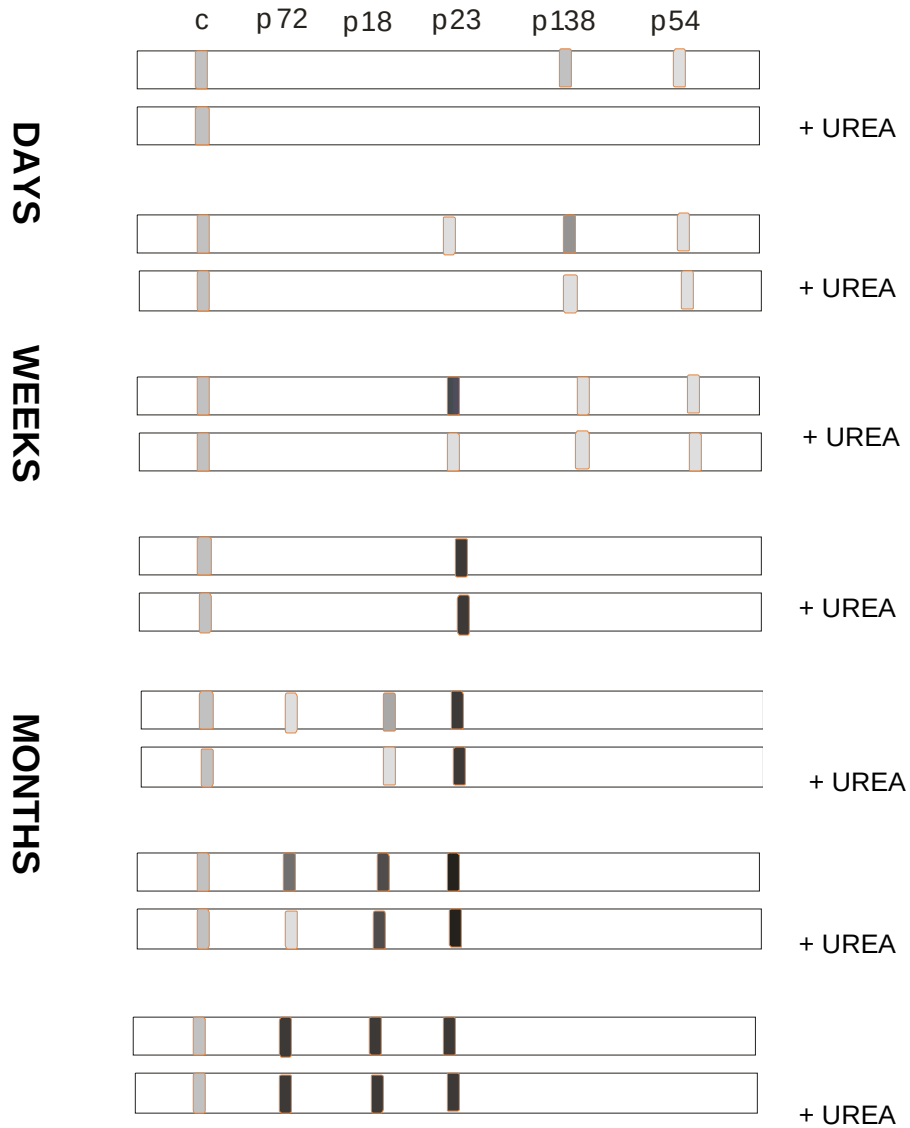
EBV INFECTION WITHOUT DEVELOPMENT OF P72-IgG: DIAGNOSIS THROUGH p18 - IgG AND AVIDITY DETERMINATION



RARE CASE OF EBV INFECTION WITHOUT BOTH LATE MARKERS



EBV INFECTION WITH DELAYED APPEARANCE OF LATE MARKERS



THANK YOU VERY MUCH!

NOW IT IS YOUR TURN!

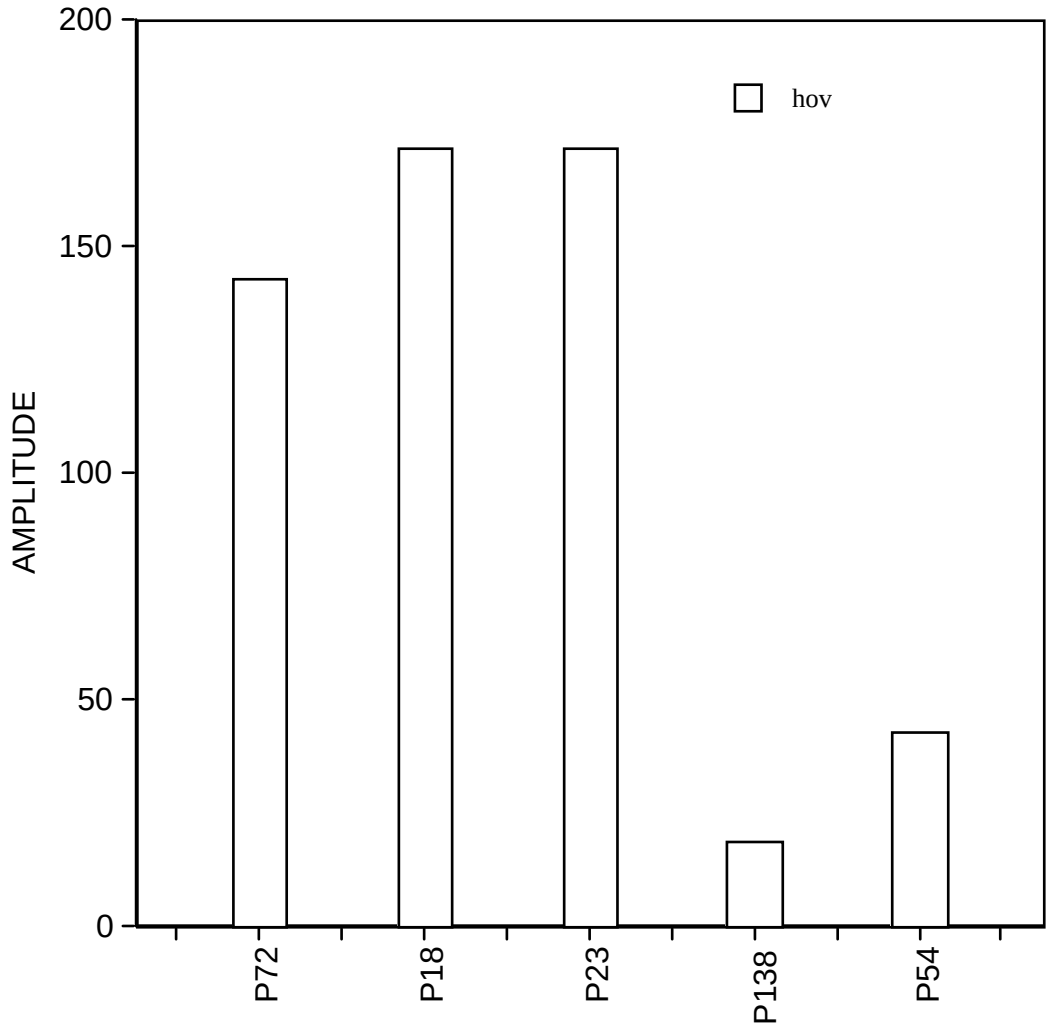
You will now see the optical density reading of several diagnostically interesting cases tested in the EBV RecomLine Assay (IgG).

Please make your judgement.

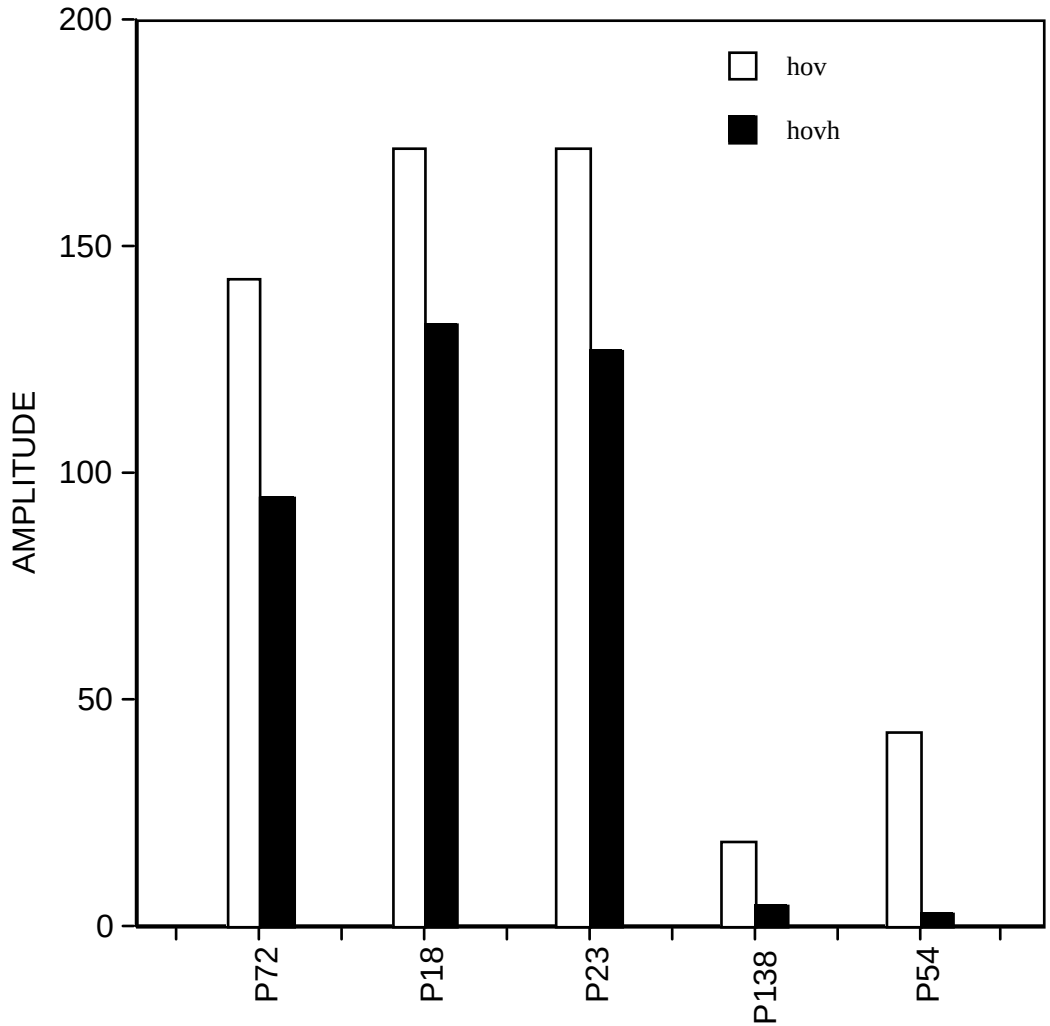
We then present the data of the avidity determination (urea treatment, columns marked in black) and the final serological diagnosis.

High avidity: less than 50 % of p23- IgG and less than 40 % of p18-IgG, p72-IgG removed by urea. High avidity is typical for past infection, low avidity is indicative for acute infection.

ACUTE OR PAST?



PAST INFECTION! BOTH LATE MARKERS PRESENT, HIGH AVIDITY OF p72-, p18- AND p23-IgG



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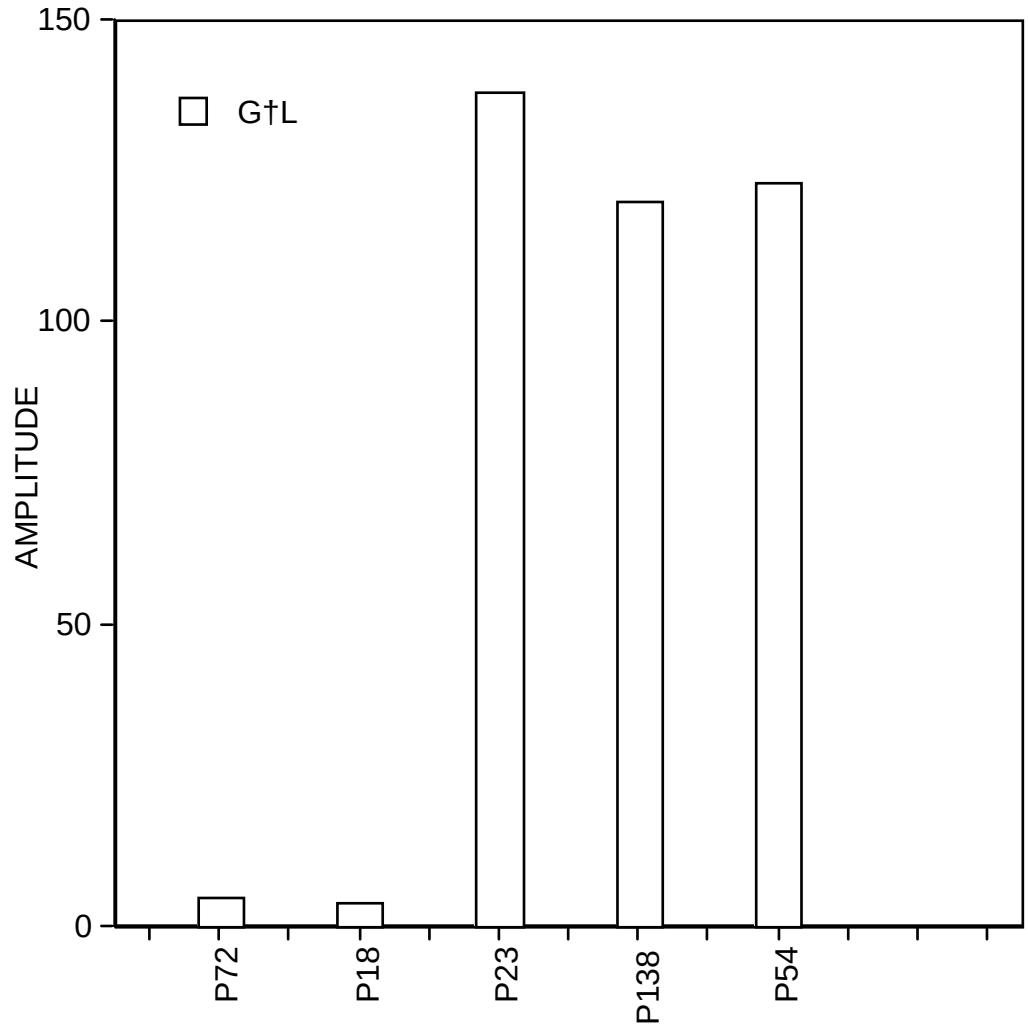
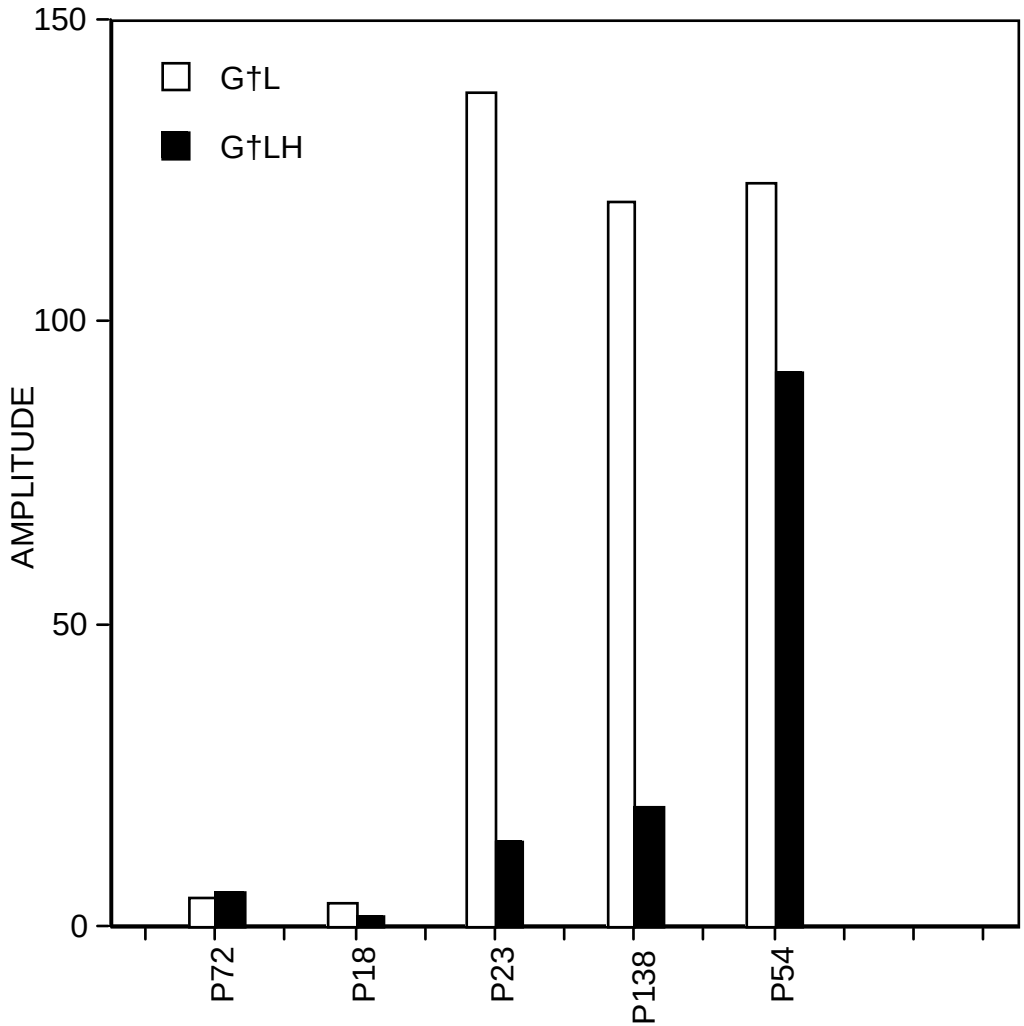

150
100
50
0
AMPLITUDE
G†L
P72
P18
P23
P138
P54

ACUTE EBV INFECTION! LATE MARKERS ARE MISSING AND p23-IgG SHOWS LOW AVIDITY



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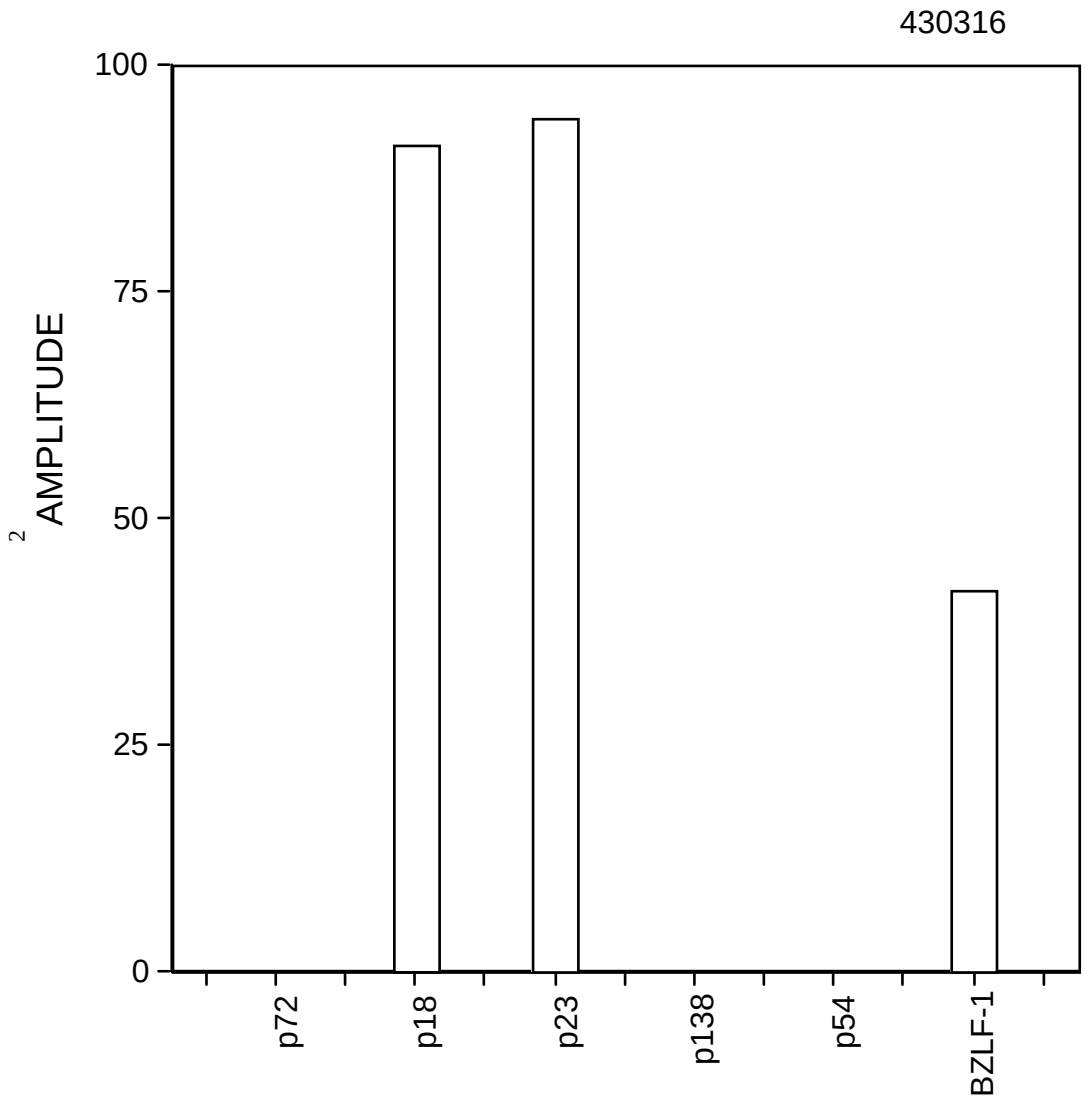
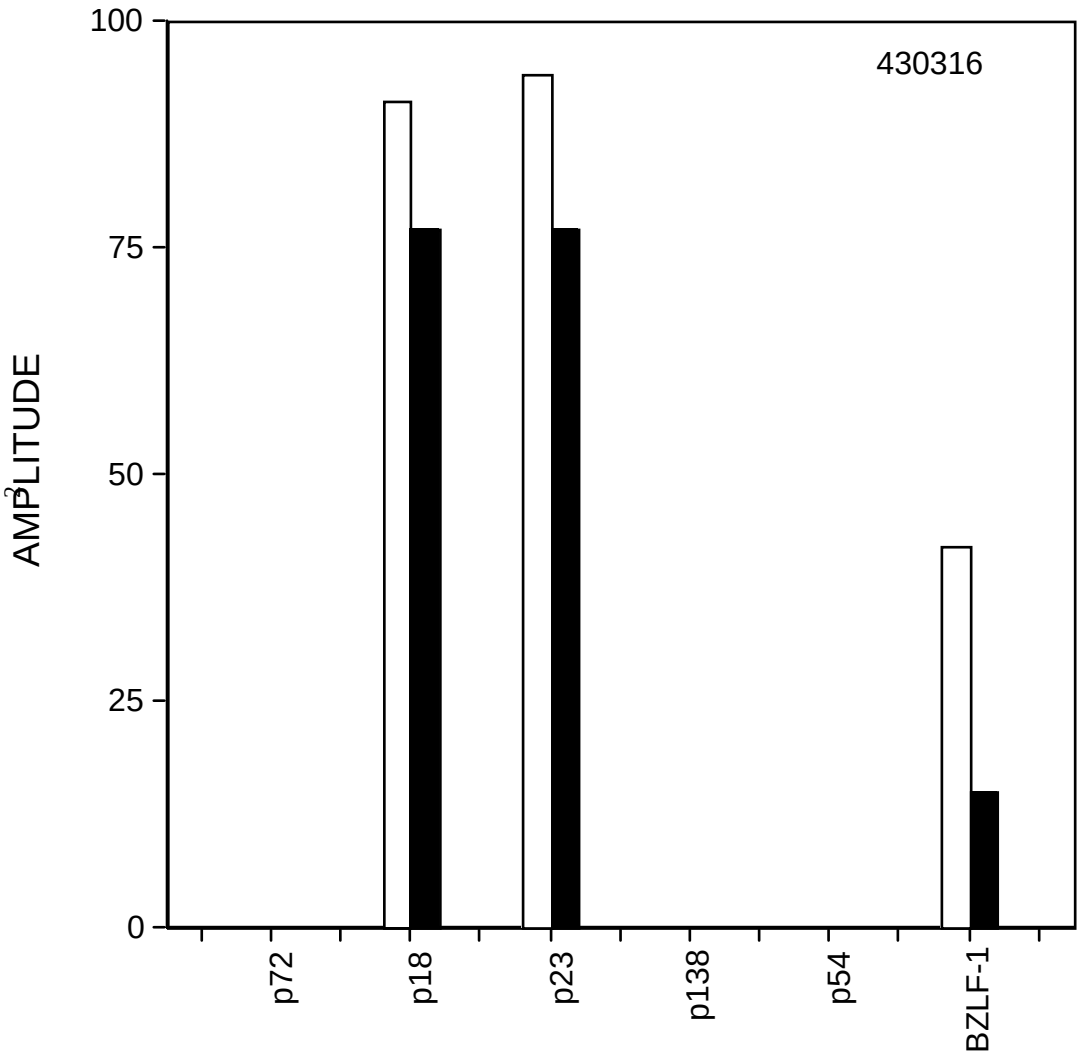

430316
100
75
50
25
0
AMPLITUDE
2
p72
p18
p23
p138
p54
BZLF-1

PAST EBV INFECTION WITHOUT p72-IgG.
p18-IgG INDICATES PAST INFECTION.
CONFIRMATION BY HIGH AVIDITY OF p18- and p23-IgG.



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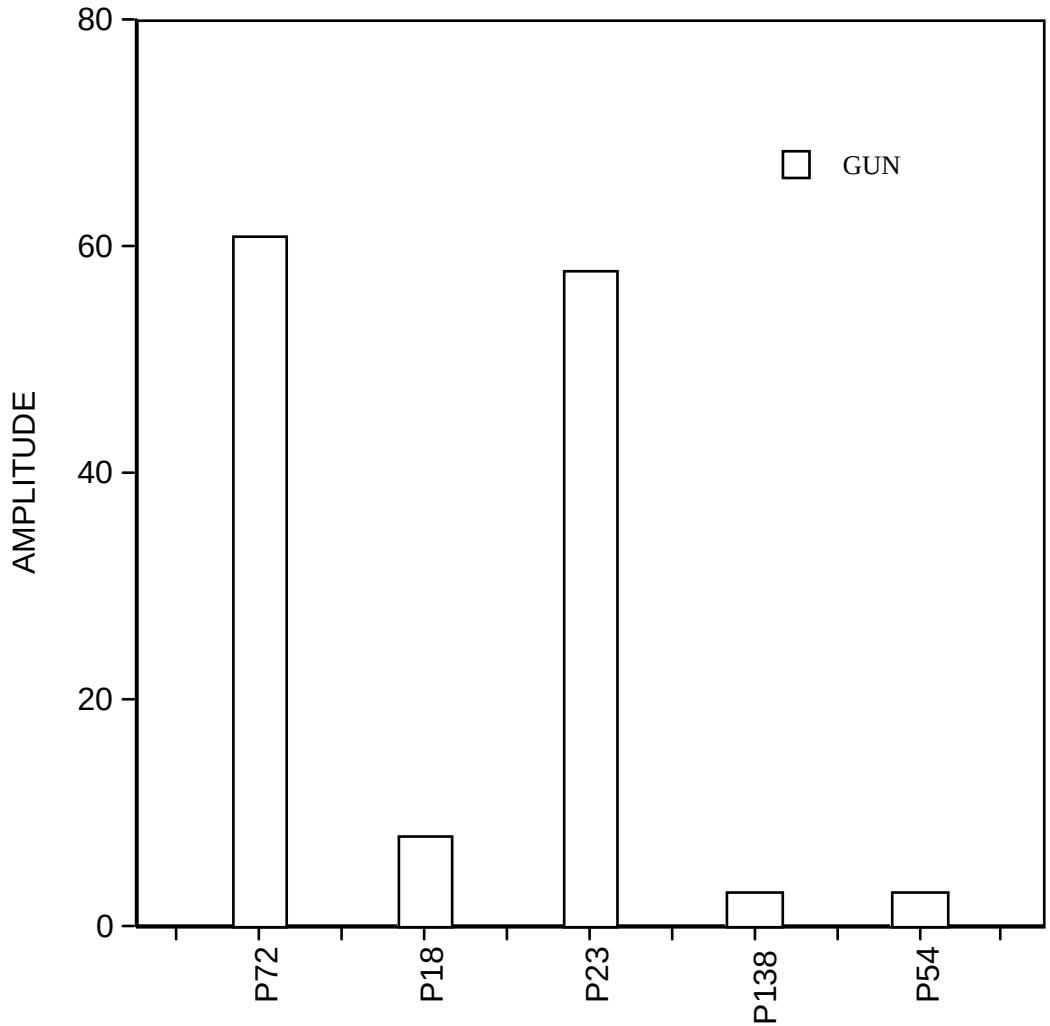
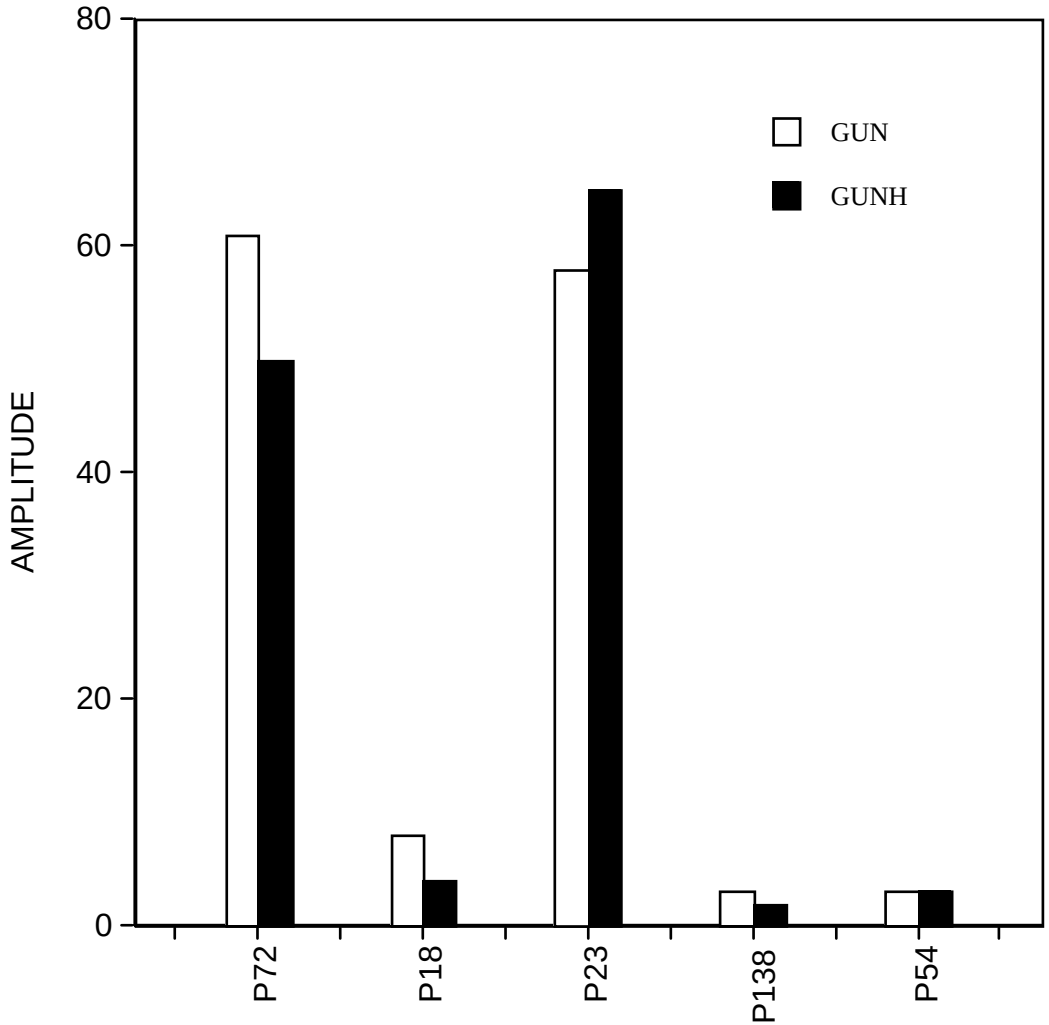

80
60
40
20
0
AMPLITUDE
GUN
P72
P18
P23
P138
P54

PAST EBV INFECTION WITHOUT p18-IgG.
p72-IgG INDICATES PAST INFECTION.
CONFIRMATION BY HIGH AVIDITY OF p72- and p23-IgG.



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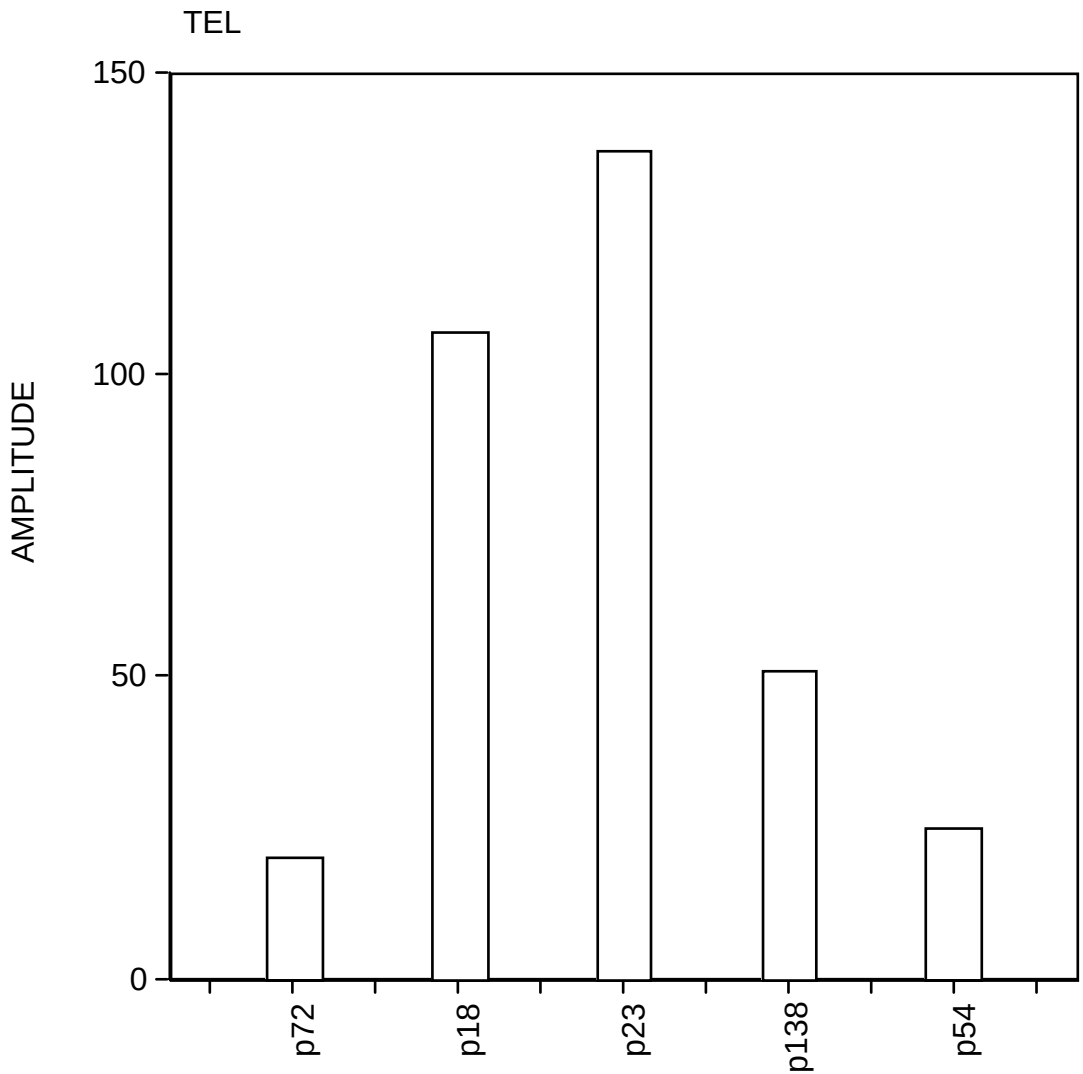
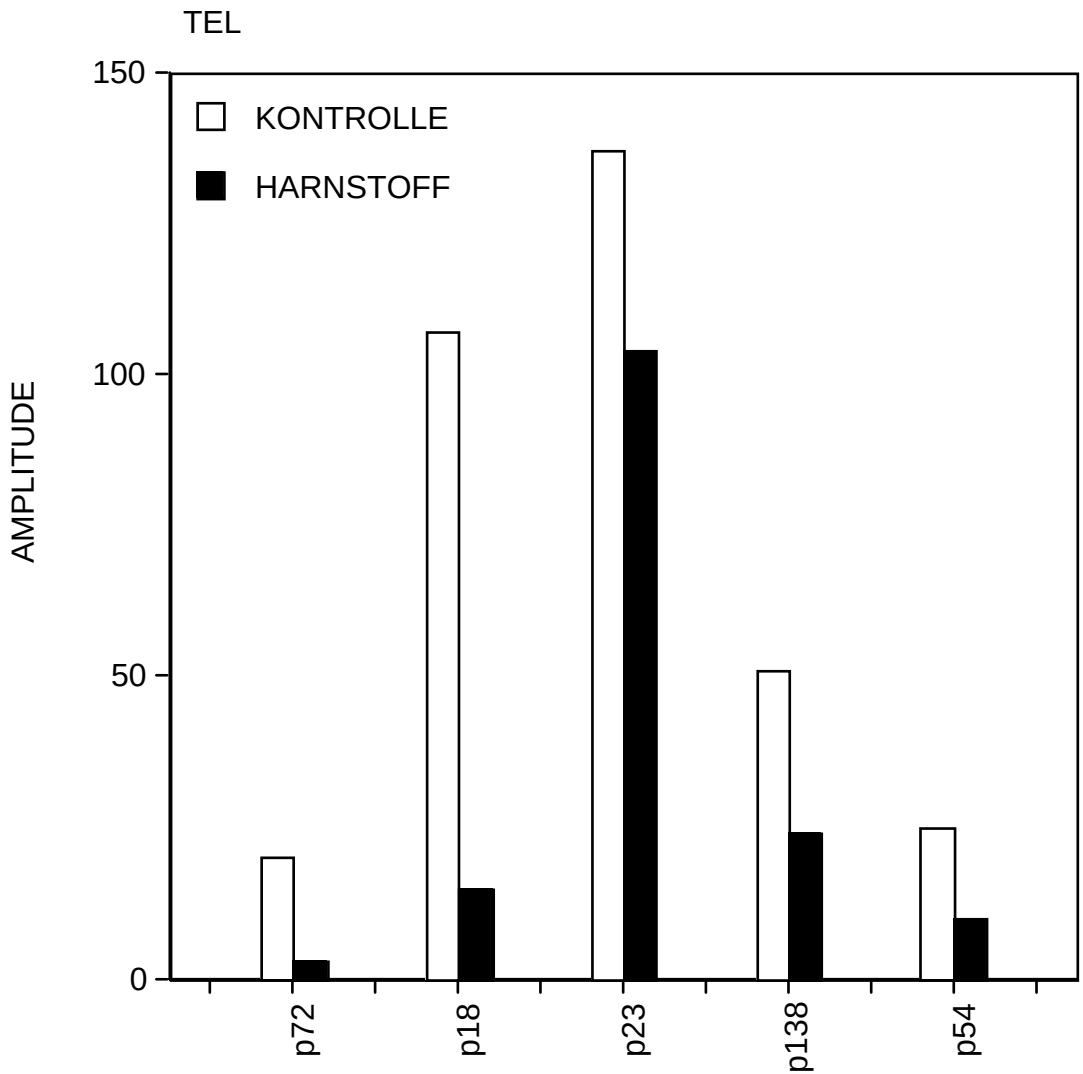

TEL
AMPLITUDE
150
100
50
0
p72
p18
p23
p138
p54

RECENT EBV INFECTION! HIGH AVIDITY OF p23-IgG, PRESENCE OF p18-IgG WITH LOW AVIDITY



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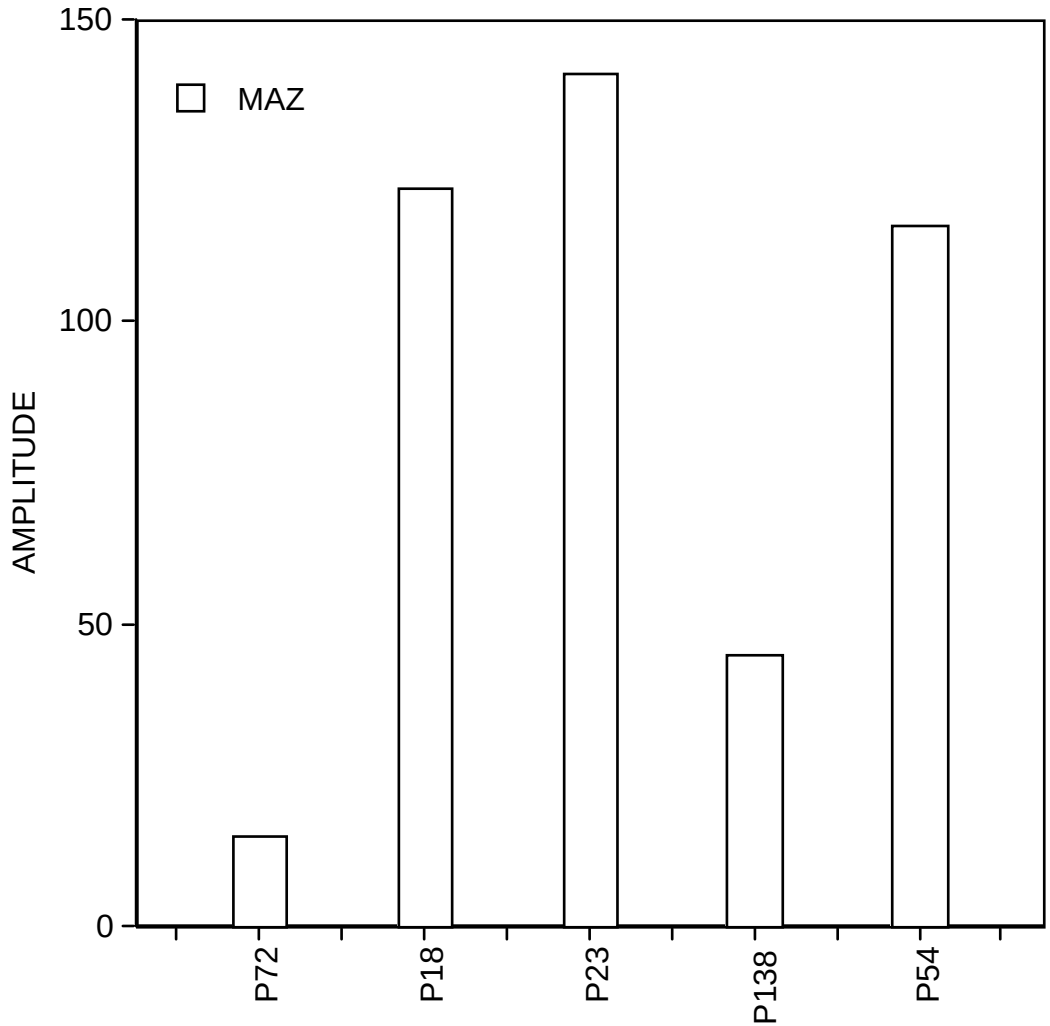
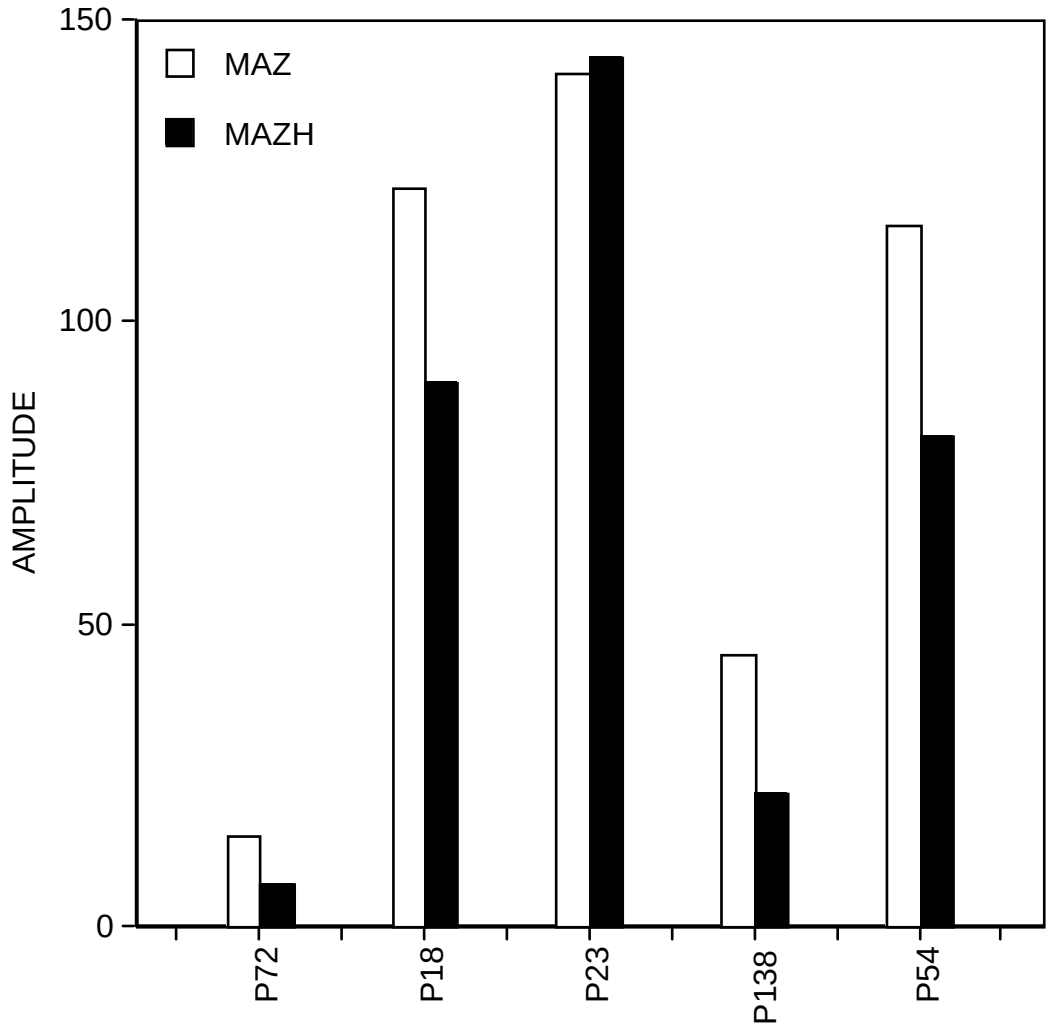

150
100
50
0
AMPLITUDE
MAZ
P72
P18
P23
P138
P54

PAST INFECTION WITHOUT p72-IgG



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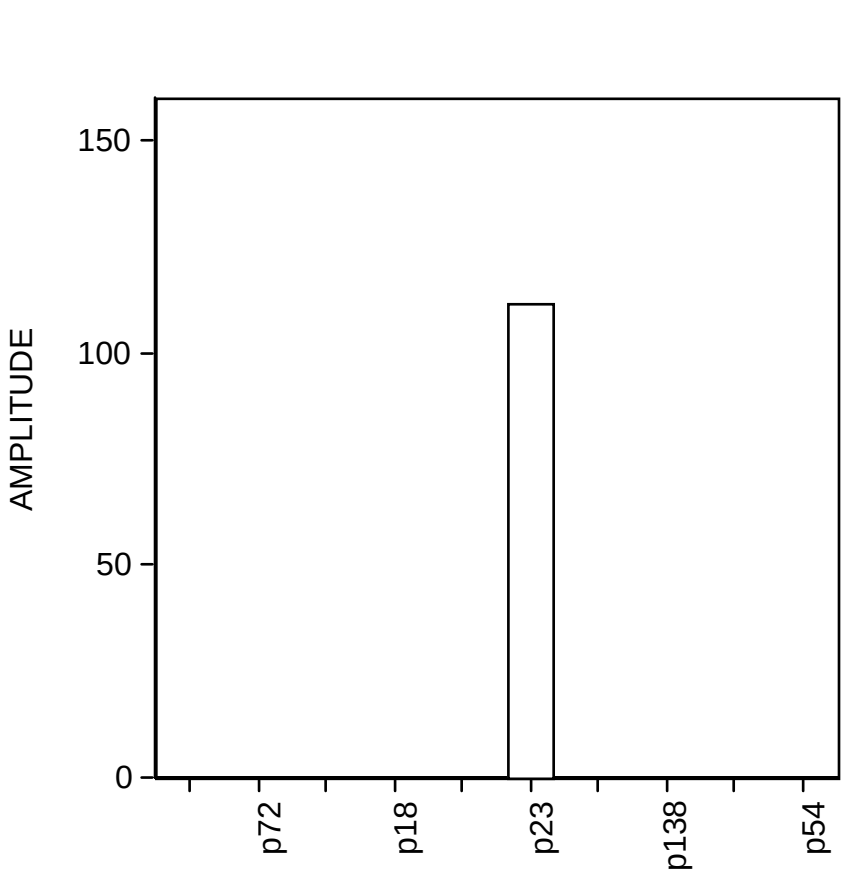
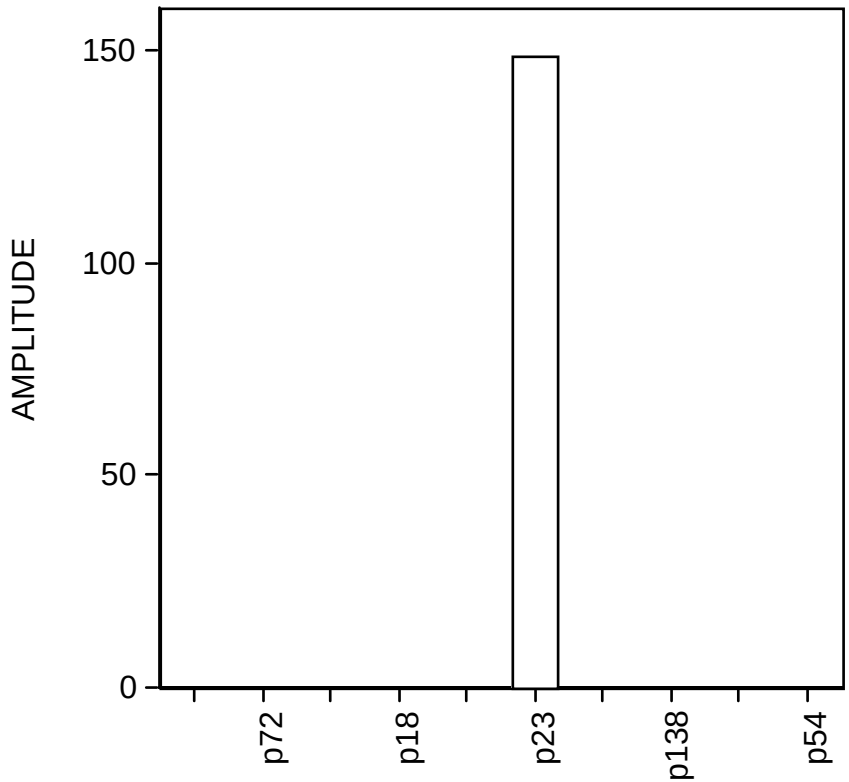
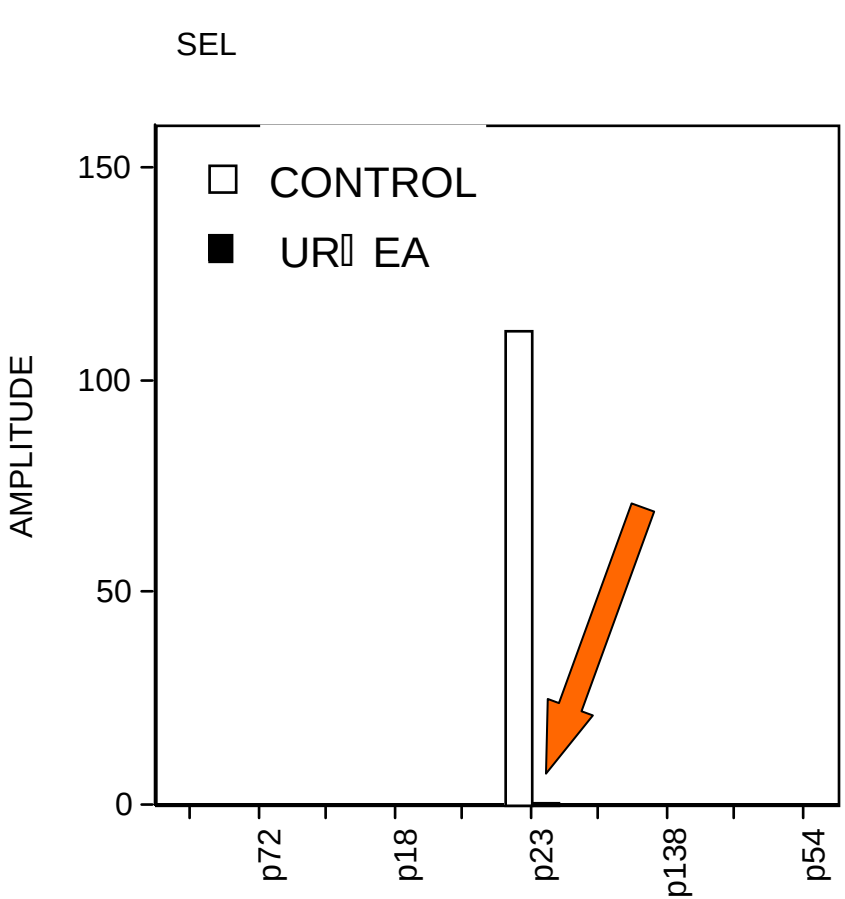
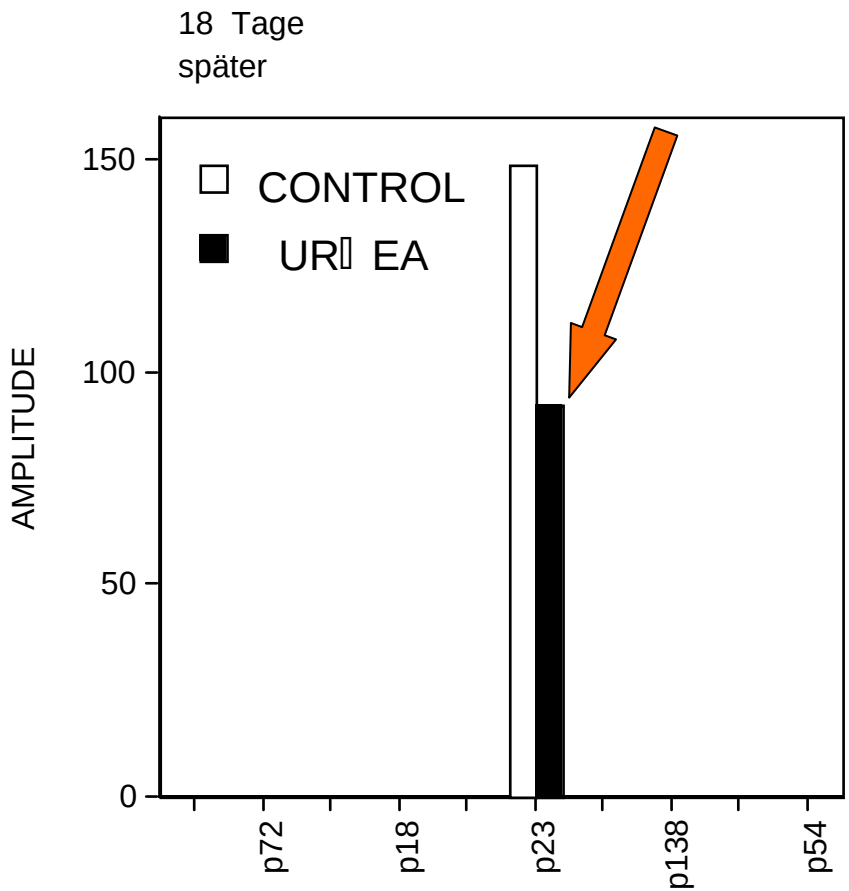


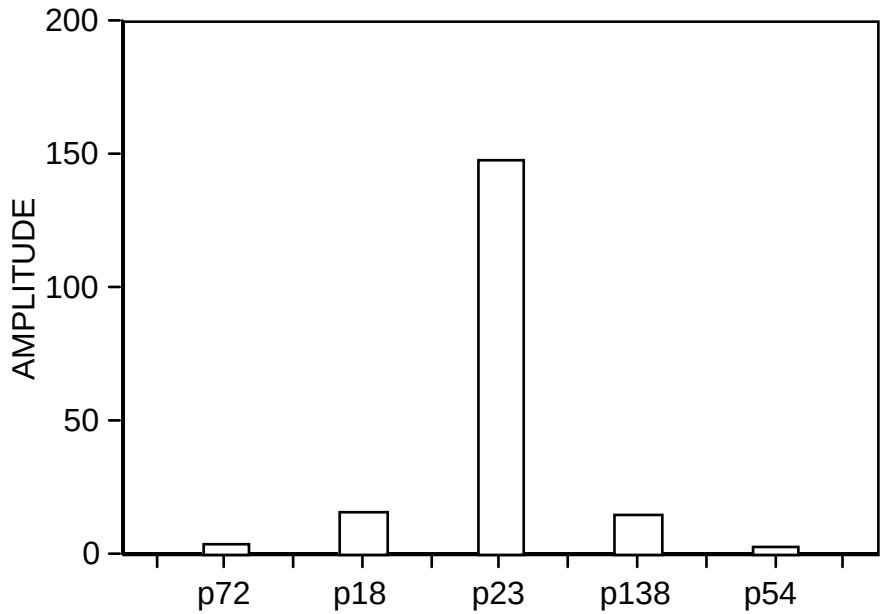
18 days later



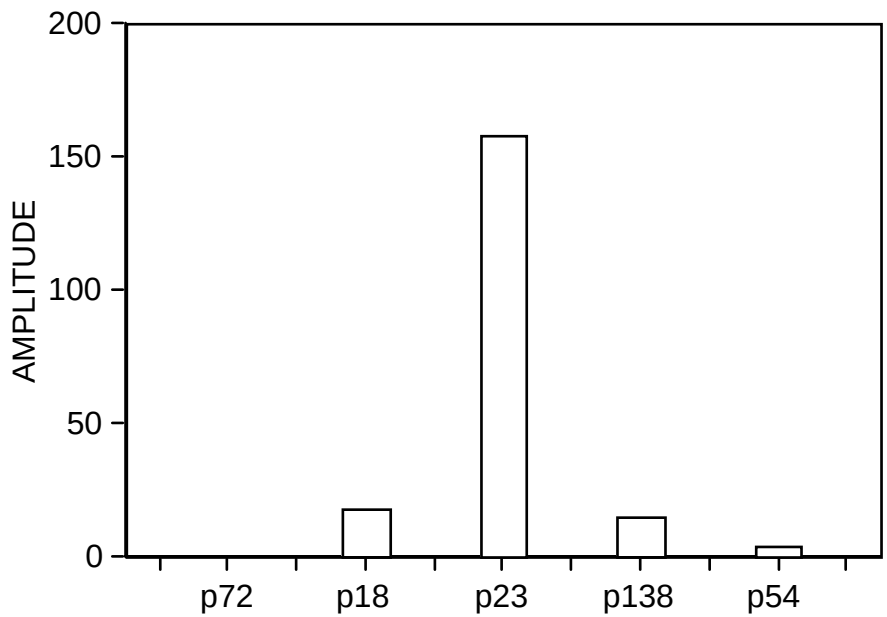
ACUTE EBV INFECTION WITH DELAYED OR MISSING LATE MARKERS



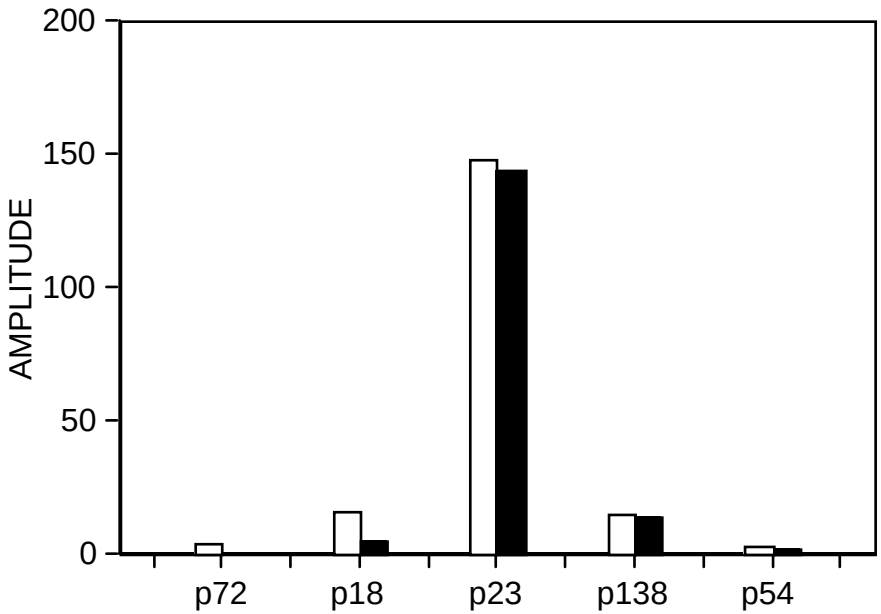


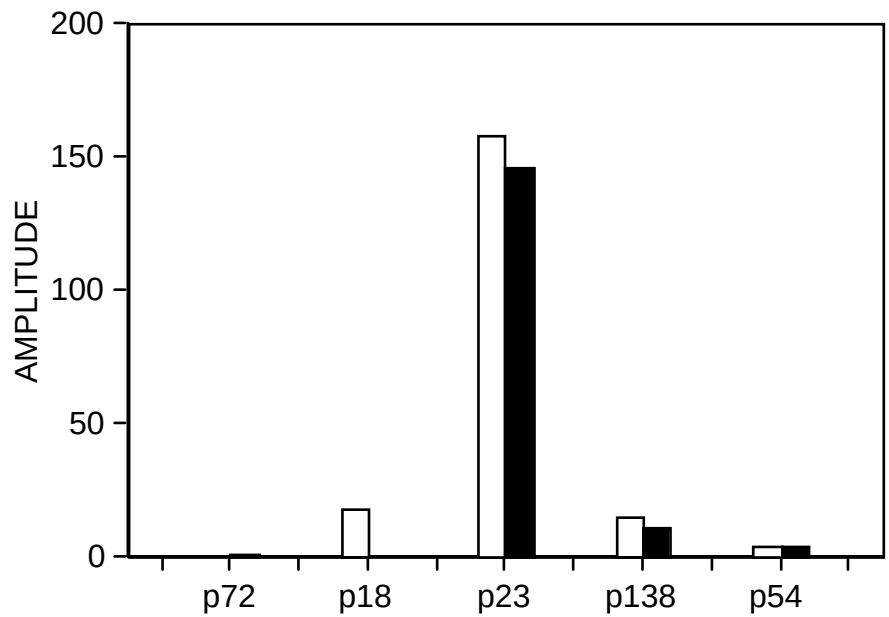


8 months later



PAST EBV INFECTION WITHOUT BOTH LATE MARKERS.
FREQUENCY: 1 / 2000





SUMMARY

- Immunoblot and Lineassay (using recombinant, purified antigens) :
  - resolve the problems of anticellular reactivity
  - represent quantitative tests, allowing avidity determination.

- Antibody profiles in acute, recent and past EBV infections:
  - Basic pattern, complicated by stochastics.
  - 20 % of past infections show aberrant serological profiles.

- The use of a second late marker (p18-IgG, Mikrogen EBV RecomLine) resolves the problem of missing or lost Anti-EBNA-1.

- The use of the late markers p72- and p18-IgG, together with
- p23-, p54- and p138-IgG leads to clear serological results even in cases of aberrant serological response.
- Some cases require avidity determination for final determination.