

# (B-B3IMMB09) Immunobiologie - 26 juni 2018

Opleiding: BETA BIO Bachelor Biologie

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**Tijdsduur:** 2 uur  
**Aantal vragen:** 18  
**Gegenereerd op:** 25 jun. 2018

## **Inhoud:**

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- C. Antwoordformulier ..... **6**
- D. Correctiemodel ..... **5**

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Leg uw collegekaart en identiteitsbewijs (met foto) op tafel.

Enkele regels van orde:

- De eerste 30 minuten mag u de zaal niet verlaten.
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- Toiletbezoek dient gemeld te worden. Er zal een surveillant met u meelopen.
- Steek uw hand op bij vragen, onduidelijkheden, extra papier etc.
- Bij bijzondere omstandigheden kan de examinator van bovenstaande regels afwijken.

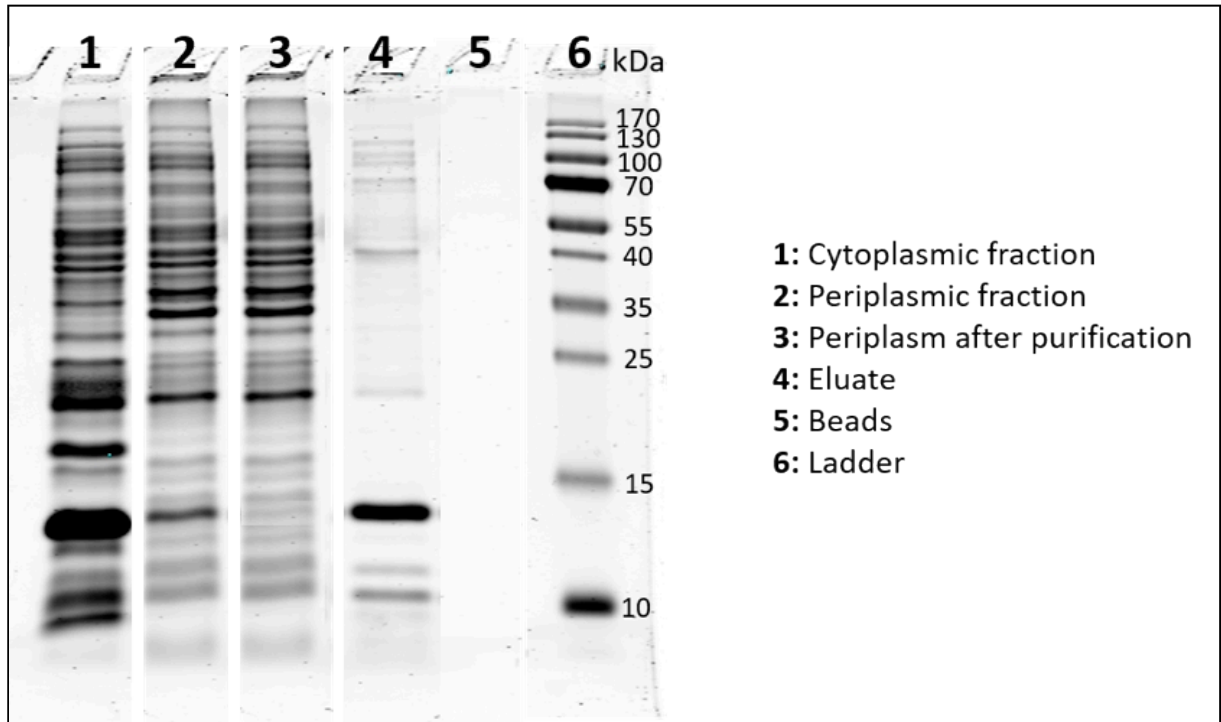
Veel succes!

Can Kesmir

**Aantal vragen:** 18

**In totaal zijn 35 punten voor deze toets te behalen, 17,5 punten zijn nodig om voor de toets te slagen.**

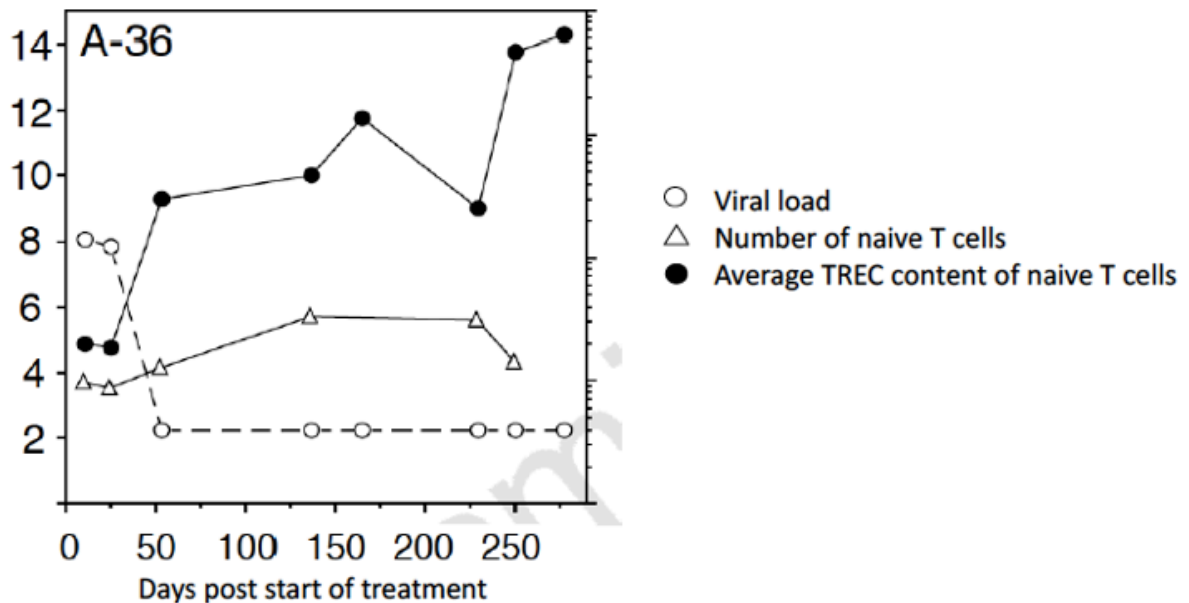
- 1 A His-tagged protein of ~14 kDa with a signal sequence for periplasmic localization was produced in *E. coli*. The periplasmic fraction was separated from the rest of the cell (cytoplasmic fraction) and was incubated with Nickel beads. Elution was performed with 300mM imidazole and the eluate was dialyzed to PBS buffer. Different steps of the experiment were evaluated on an SDS-PAGE gel, shown in the image below.



- 2 pt. a. a) What conclusions would you draw from this gel?
- 2 pt. b. b) How would you proceed with this experiment?

- 2 An HIV-infected individual starts anti-viral therapy. In the figure below you can see how the amount of virus, the number of naive T cells and the average T cell receptor excision circle (TREC) content of the naive T cells in the blood of the patient change over time post-start of treatment.

The number of naive T cells at the start of the therapy is much lower than in age-matched healthy controls and increases slowly over time. The average TREC-content of the naive T cells is also lower than normal at start of therapy but normalizes quite rapidly during therapy.



- 1 pt. a. a) What is the most likely explanation for the low TREC-content of naive T cells before the start of treatment?
- 1 pt. b. b) What is the most likely explanation for the increase in the average TREC-content of naive T cells during anti-viral therapy?
- 2 pt. c. In the article in which these data were published (Douek et al. 1998), the following conclusion was drawn from these data: "Our results indicate that thymic function in adults may be suppressed in HIV-infected individuals and can be improved by the reduction of viral load."  
To what extent do these data support or dis-support these two statements? Give an explanation in max. 3 sentences

3 At birth, the size of the repertoire of  $\gamma:\delta$  T-cell receptors is \_\_\_\_\_ its size at adolescence.

- 1 pt. a. larger than  
b. about the same as  
c. smaller than

**4** Ebola infection is modeled often by the following equations:

$$dT/dt = \lambda - d_T T - \beta VT$$

$$dI/dt = \beta VT - \gamma I,$$

$$dV/dt = pI - cV,$$

where  $V$  stands for free viral particles,  $T$  for target cells and  $I$  for infected cells.

- 3 pt. **a.** a) Explain the biological processes this model describes using your own words. What do the different parameters stand for?
- 2 pt. **b.** It is known that innate immunity is important to control Ebola infection, especially macrophages. Given what you know about macrophages, write one differential equation that describes the macrophage dynamics.
- 2 pt. **c.** How can you add the effect of macrophages to the original model above? Assume that the cytokines produced by the macrophages increase the clearance of the viral particles.

**5** If, during development, none of the KIRs expressed by a NK cell are able to interact with self-MHC class I molecules, then the NK cell retains expression of \_\_\_\_\_.

1 pt.

- a.** KIR2DL1
- b.** CD94:NKG2A
- c.** LILRB1
- d.** KIR2DL2/3

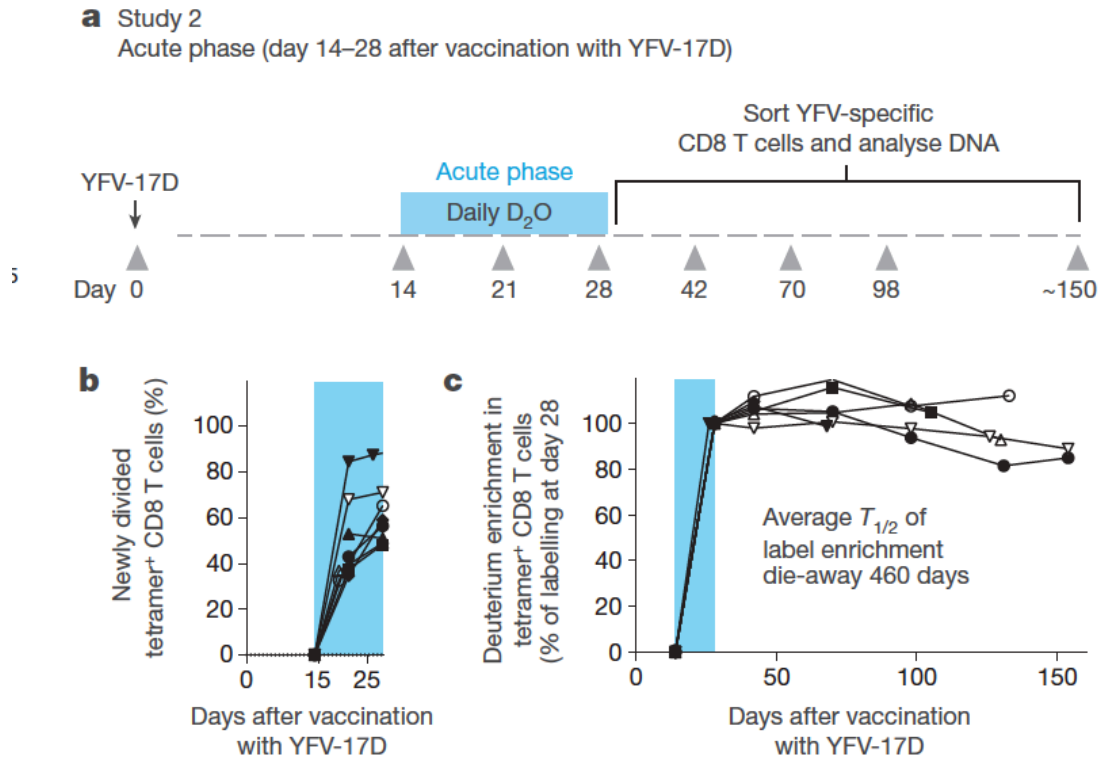
**6** Chimpanzees seem to have experienced an ancient selective sweep which was most likely caused by a pathogen. The genetic footprint of this sweep is still visible in the genome of the contemporary living animals. Which pathogen was the most likely cause of this sweep AND which genetic region was targeted/affected in an ancestral chimpanzee population?

1 pt.

- a.** SIV and MHC class I region
- b.** HIV and MHC class II region
- c.** HCV and T cell repertoire
- d.** Malaria and MHC class I region

7 Below figure is taken from Akondy et al 2017. In this study healthy individuals were vaccinated yellow fever virus (YFV). The figure legends reads as:

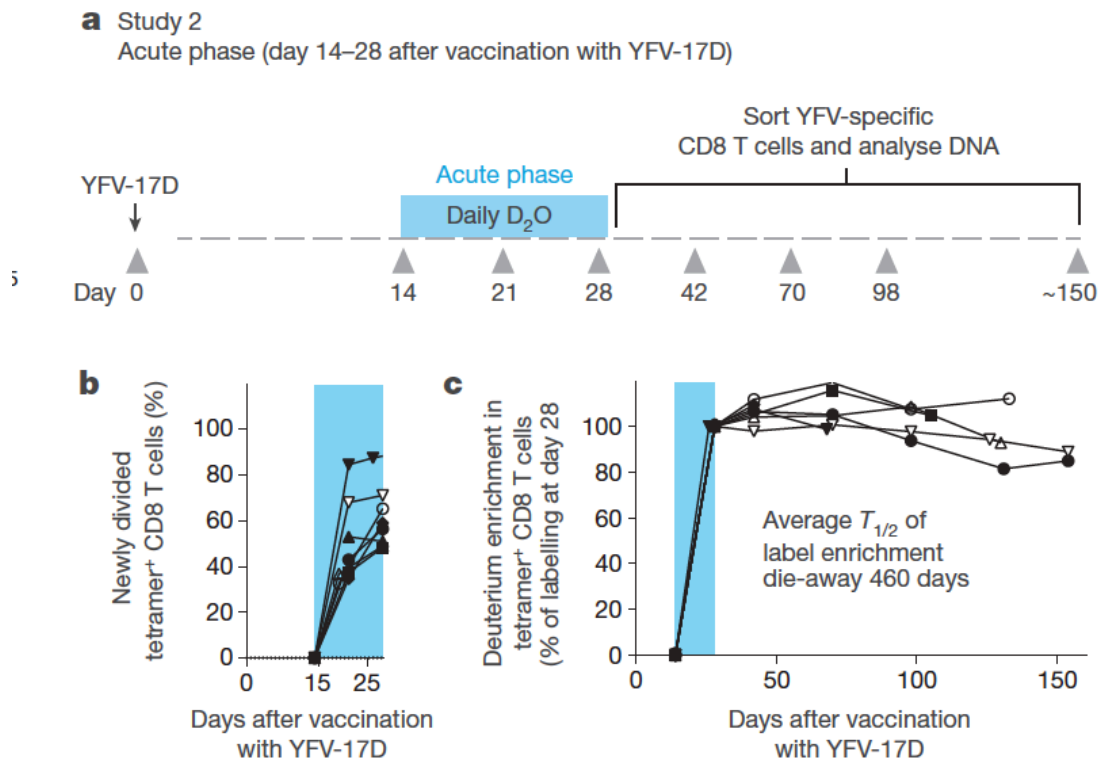
"Heavy water labelling during different stages of the immune response to investigate the in vivo kinetics of YFV-specific CD8 T cells. **a**, Design for study. **b**, The percentage of YFV-tetramer+ cells that incorporated deuterium during the D<sub>2</sub>O intake period (shaded blue area). **c**, Die-away curves of deuterium enrichment after label washout. Data are normalized to maximum label incorporation, seen at day 28 (n=7)."



Mention one surprising (not expected) result in this graph. Why is it not expected?

8 Below figure is taken from Akondy et al 2017. In this study healthy individuals were vaccinated yellow fever virus (YFV). The figure legends reads as:

"Heavy water labelling during different stages of the immune response to investigate the in vivo kinetics of YFV-specific CD8 T cells. **a**, Design for study. **b**, The percentage of YFV-tetramer+ cells that incorporated deuterium during the D2O intake period (shaded blue area). **c**, Die-away curves of deuterium enrichment after label washout. Data are normalized to maximum label incorporation, seen at day 28 (n=7)."



1 pt. **a.** In the first 14 days no CD8 T cells are made by these individuals.

**a.** TRUE

**b.** FALSE

1 pt. **b.** During days 14-28, all YFV specific CD8 T cells are deleted.

**a.** TRUE

**b.** FALSE

**9** DNA viruses associated with cancer development include \_\_\_\_\_. (Select all that apply.)  
1 pt.

- a.** human herpesvirus 8 (HHV8)
- b.** human papillomavirus (HPV)
- c.** human immunodeficiency virus (HIV-1)
- d.** Epstein–Barr virus (EBV)



## Casus 1

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Zie bijlage: Li et al, Cancer cell 2005

Zie bijlage: Milinski et al Proc. Roy. Soc. 2013

Zie bijlage: Joswick et al Nat. Comm. 2015

Zie bijlage: Hirano et al Nature 2013

Zie bijlage: Allen et al J. Virol. 2004

Zie bijlage: Single et al, Nat. Gen. 2007

Zie bijlage: Sun et al Nature 2009

Zie bijlage: Van Allen et al, Science 2015

**10**

1 pt.

### Gebruik bij deze vraag casus 1 op pagina 8

The majority of the specific T cells during an RSV infection is found at:

- a. in the local lymph nodes
- b. in spleen
- c. in blood
- d. in bone marrow

**11**

1 pt.

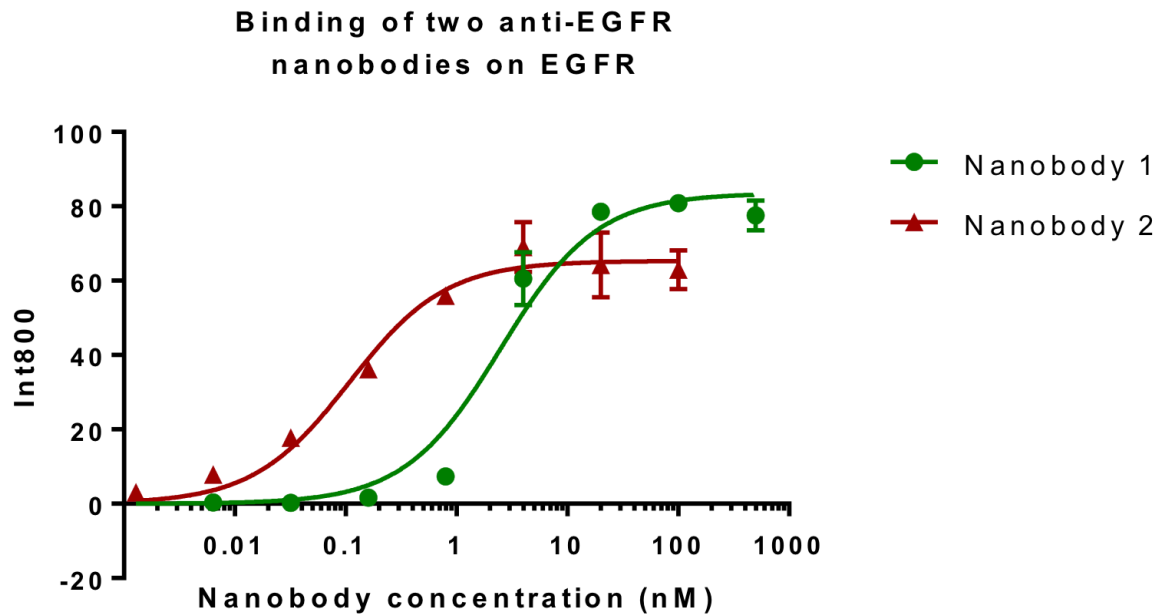
### Gebruik bij deze vraag casus 1 op pagina 8

One of the side effects of treating tumor patients with anti-CTLA4 monoclonal antibodies is \_\_\_\_\_ .

- a. the development of autoimmune disease
- b. increased levels of mutation in tumor cells
- c. upregulation of CT antigens
- d. lymphoproliferative disorder

- 12 The binding of two anti-EGFR nanobodies (coupled to an 800CW fluorophore) was evaluated with a binding assay on purified EGFR. The results are shown in the graph below.  
1 pt.

Which of these statements is correct?



- a. Nanobody 1 has a lower B<sub>max</sub> and a higher K<sub>D</sub> than Nanobody 2.
- b. Nanobody 1 has a higher B<sub>max</sub> and a lower K<sub>D</sub> than Nanobody 2.
- c. Nanobody 1 has a higher B<sub>max</sub> than Nanobody 2 and they both have the same K<sub>D</sub>.
- d. None of the above is correct.
- 13 Which of the following does NOT describe a mechanism that ensures that only infected cells are attacked by NK cells?  
1 pt.
- a. NK cells go through an education process where the receptor profile is adjusted according to the MHC of the host.
- b. NK cells require direct contact with target cells.
- c. NK cells require many combinations of receptor–ligand interactions to kill a target cell.
- d. KIRs recognize polymorphic ligands, that are different in every individual.

**14** Many different viruses encode proteins that function to down-regulate MHC class I expression on host cells following infection with the virus. This immune evasion mechanism allows the virus to hide from CD8 T lymphocytes that normally detect virus-infected cells by using their T cell antigen receptor to recognize viral peptides bound to MHC class I proteins on the surface of the infected cell. To counteract this immune evasion strategy, NK cells have:

1 pt.

- a. Activating receptors that recognize MHC class I proteins
- b. Activating receptors that recognize viral capsid proteins
- c. A mechanism to secrete antiviral peptides
- d. Inhibitory receptors that recognize MHC class I proteins

**15** Which of the following statements is correct?

1 pt.

- a. VLR genes made of Leucine-rich repeats, as demonstrated to be lamprey T and B cell receptors, are also present in mammals, because NKT cell receptors are generated this way.
- b. The complement system is often activated via antibodies, and therefore is as old as the adaptive immune systems.
- c. Toll-like receptors generate a specific form of host defense that is found only in insects.
- d. Polymorphic KIR molecules are only found in mammals.

- 16** More than 4 million women and men in the United States and 150 million people worldwide are estimated to be hepatitis C virus (HCV) seropositive. Most of these individuals are chronically infected with the virus and are at high risk of cirrhosis, hepatocellular carcinoma, and liver-related death. Only a minority of the people who are infected with HCV is able to clear the virus. HCV is a small, enveloped, single-stranded, positive-sense RNA virus. It codes 10 different proteins.

4 pt.

The table below is taken from Kunniholm et al 2010, who studied the associations between HCV infection and HLA molecules.

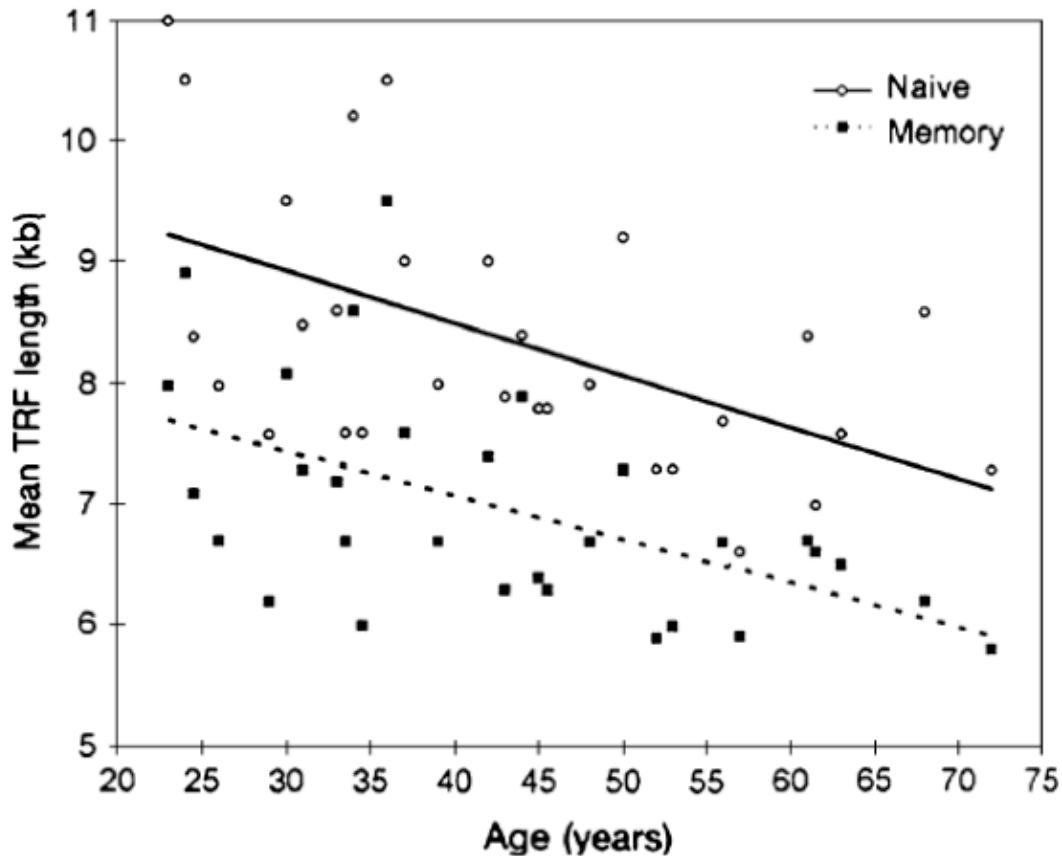
Design a computational analysis using the methods you learned in this course to research why some HLA molecules are associated with clearance while others associate with chronic infections.

**Table 1. HLA Alleles and Allele Groups with a High Prior Probability of Association with HCV Viremia\***

<b>Associations with HCV Viremia in HCV-Seropositive Individuals</b>		
<b>Allele</b>	<b>HCV RNA Status</b>	<b>References</b>
DQB1*0301	Clearance	28,51-56
DRB1*0101	Clearance	14,28,57,58
DRB1*0301	Persistence	14,28
DRB1*0401	Clearance	14,52
DRB1*1101	Clearance	51,54-56
DRB1*1501	Clearance	14,59
B*18	Persistence	14
B*27	Clearance	14
B*57	Clearance	12,13
Cw*01	Clearance	12,14
Cw*04	Persistence	12,15

\*HLA alleles associated with HCV viremia in two or more prior studies, or strongly associated with HCV viremia in a single study (see Materials and Methods).

- 17 1 pt. In a large population of healthy individuals, the average telomere length of naive and memory T cells was measured. The results are plotted in the below figure. What would happen with the average telomere length of memory T cells if the chance that a naive T cell gets activated into the memory T-cell pool is increased?



**Fig. 1. Comparison of the mean TRF length of naive and memory T cells.** Thirty donors were studied, ranging in age from 24 to 72 years. Open circles denote the mean TRF length of each individual's naive T cells; the solid line represents the regression analysis of the TRF lengths of naive cells as a function of age; solid squares denote the mean TRF length of each individual's memory T cells; the dotted line represents the regression analysis of the TRF lengths of memory cells as a function of age. Reprinted with permission from Weng *et al.*(22). Copyright 1995, The National Academy of Sciences. TRF, telomere restriction fragment.

- a. It will stay the same
- b. It will decrease
- c. It will increase

**18** When a subpopulation of unvaccinated individuals are protected against a pathogen because the vast majority of individuals in the overall population are vaccinated, this is called \_\_\_\_\_.  
1 pt.

- a. partial immunization
- b. combined immunity
- c. subunit vaccination
- d. herd immunity

Naam:

Handtekening:

Datum:

 -  - 

Geboortedatum:

 -  - 

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Veel succes!

Can Kesmir

**1**

4 pt.

**a.**

Antwoord:

2

4

6

8

**b.**

Antwoord:

2

4

6

8

**2**

4 pt.

**a.**

Antwoord:

2

4

6

8

**b.**

Antwoord:

2

4

6

8



**c.**

Antwoord:

2

4

6

8

**3**  
1 pt.

A

B

C

**4**  
7 pt.

**a.**

Antwoord:

2

4

6

8

**b.**

Antwoord:

2

4

6

8

**c.**

Antwoord:

2

4

6

8

**5**

1 pt.

A

B

C

D

**6**

1 pt.

A

B

C

D

**7**

2 pt.

Antwoord:

2

4

6

8

**8**

2 pt.

a.  A  B

b.  A  B

**9**

1 pt.

A  B  C  D

Er zijn meerdere antwoorden mogelijk

**10**

1 pt.

A  B  C  D

**11**

1 pt.

A  B  C  D

**12**

1 pt.

A  B  C  D

**13**

1 pt.

A  B  C  D

**14**

1 pt.

A  B  C  D

**15**

1 pt.

A  B  C  D

**16**

4 pt.

Antwoord:

2

4

6

8

**17**

1 pt.

A B C

**18**

1 pt.

A B C D

## Correctiemodel

1.

4 pt.

Correction criterion	Points
Criterion 1	2 points
<i>Total points:</i>	<i>2 points</i>

b.

Correction criterion	Points
Kwaliteit van het antwoord	2 points
<i>Total points:</i>	<i>2 points</i>

2.

4 pt.

Correction criterion	Points
Increased T-cell division: HIV increases the division rate of naive T cells which leads to dilution of TRECs and hence a decrease in their average TREC-content.	1 point
<i>Total points:</i>	<i>1 point</i>

b.

Correction criterion	Points
Normalization of T-cell division, because treatment leads to reduction of viral load and the virus causes the increase in the T-cell division rate in untreated HIV infection.	1 point
<i>Total points:</i>	<i>1 point</i>

c.

Correction criterion	Points
. Although these data do not exclude the possibility that thymic output is affected in HIV-infected individuals, they provide evidence neither for decreased thymic output in HIV, nor for improvement of thymic output during therapy. The data can perfectly be explained by changes in T-cell division rates only	2 points
<i>Total points:</i>	<i>2 points</i>

3.

A

1 pt.

4.  
7 pt.

Correction criterion	Points
Criterium 1	3 points
<i>Total points:</i>	<i>3 points</i>

Correction criterion	Points
$dm/dt = \mu - \delta * m$ $\mu$ is the production from the bone marrow and $\delta$ is the death rate.	2 points
<i>Total points:</i>	<i>2 points</i>

Correction criterion	Points
$dv/dt = pI - cV - c_2MV$	2 points
<i>Total points:</i>	<i>2 points</i>

5. B  
1 pt.

6. A  
1 pt.

7.  
2 pt.

Correction criterion	Points
More T cells are labeled after labeling has stopped.	2 points
<i>Total points:</i>	<i>2 points</i>

8.  
2 pt.

- a. B  
b. B

9.  
1 pt.

B  
D

10.  
1 pt.

A

11.  
1 pt.

A

12. D  
1 pt.

13. D  
1 pt.

14. D  
1 pt.

15. D  
1 pt.

**16.**  
4 pt.

Correction criterion	Points
Kwaliteit van het antwoord	4 points
<i>Total points:</i>	<i>4 points</i>

---

**17.** C  
1 pt.

**18.** D  
1 pt.

## Cesuur

Behaalde punten	Cijfer
35	10
34	9,74
33	9,49
32	9,23
31	8,97
30	8,71
29	8,46
28	8,20
27	7,94
26	7,69
25	7,43
24	7,17
23	6,91
22	6,66
21	6,40
20	6,14
19	5,89
18	5,63
17	5,37
16	5,11
15	4,86
14	4,60
13	4,34
12	4,09
11	3,83
10	3,57
9	3,31
8	3,06
7	2,80
6	2,54

5	2,29
4	2,03
3	1,77
2	1,51
1	1,26
0	1,00



## Vraag-identificatiecodes

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Deze identifiers kunnen worden gebruikt om de precieze vraag in de vragenbanken te identificeren. Gebruik deze code in combinatie met de documentcode wanneer u feedback doorgeeft, zodat precies duidelijk is op welke vraag en -versie uw feedback van toepassing is.

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