Figure 1

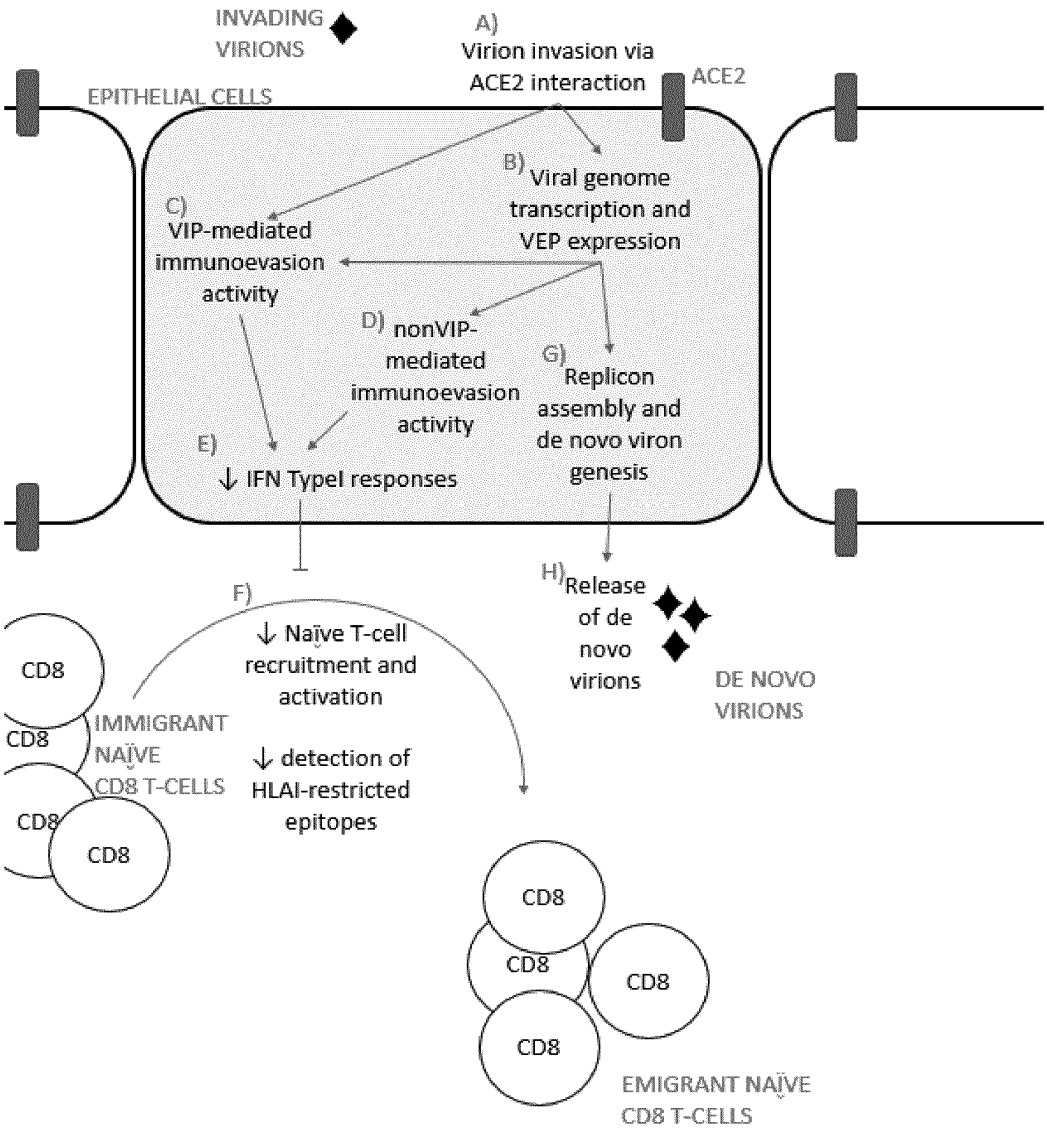

INVADING VIRIONS
A) Virion invasion via ACE2 interaction
ACE2
EPITHELIAL CELLS
B) Viral genome transcription and VEP expression
C) VIP-mediated immunoevasion activity
D) nonVIP-mediated immunoevasion activity
G) Replicon assembly and de novo viron genesis
E) ↓ IFN TypeI responses
F) ↓ Naïve T-cell recruitment and activation
↓ detection of HLAI-restricted epitopes
H) Release of de novo virions
DE NOVO VIRIONS
CD8
IMMIGRANT NAÏVE CD8 T-CELLS
EMIGRANT NAÏVE CD8 T-CELLS

Figure 2

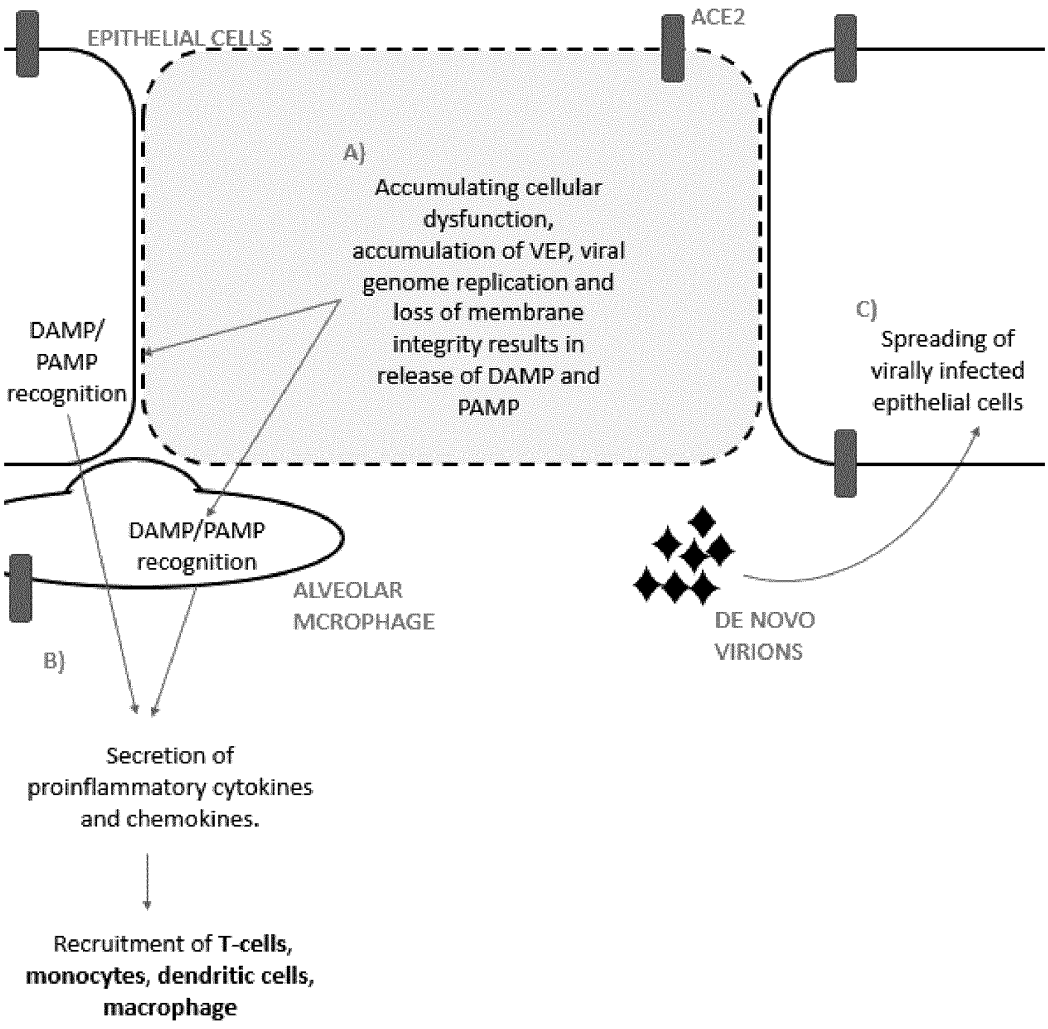

EPITHELIAL CELLS
ACE2
A)
Accumulating cellular dysfunction, accumulation of VEP, viral genome replication and loss of membrane integrity results in release of DAMP and PAMP
DAMP/ PAMP recognition
C)
Spreading of virally infected epithelial cells
DAMP/PAMP recognition
ALVEOLAR MCROPHAGE
DE NOVO VIRIONS
B)
Secretion of proinflammatory cytokines and chemokines.
Recruitment of T-cells, monocytes, dendritic cells, macrophage

Figure 3

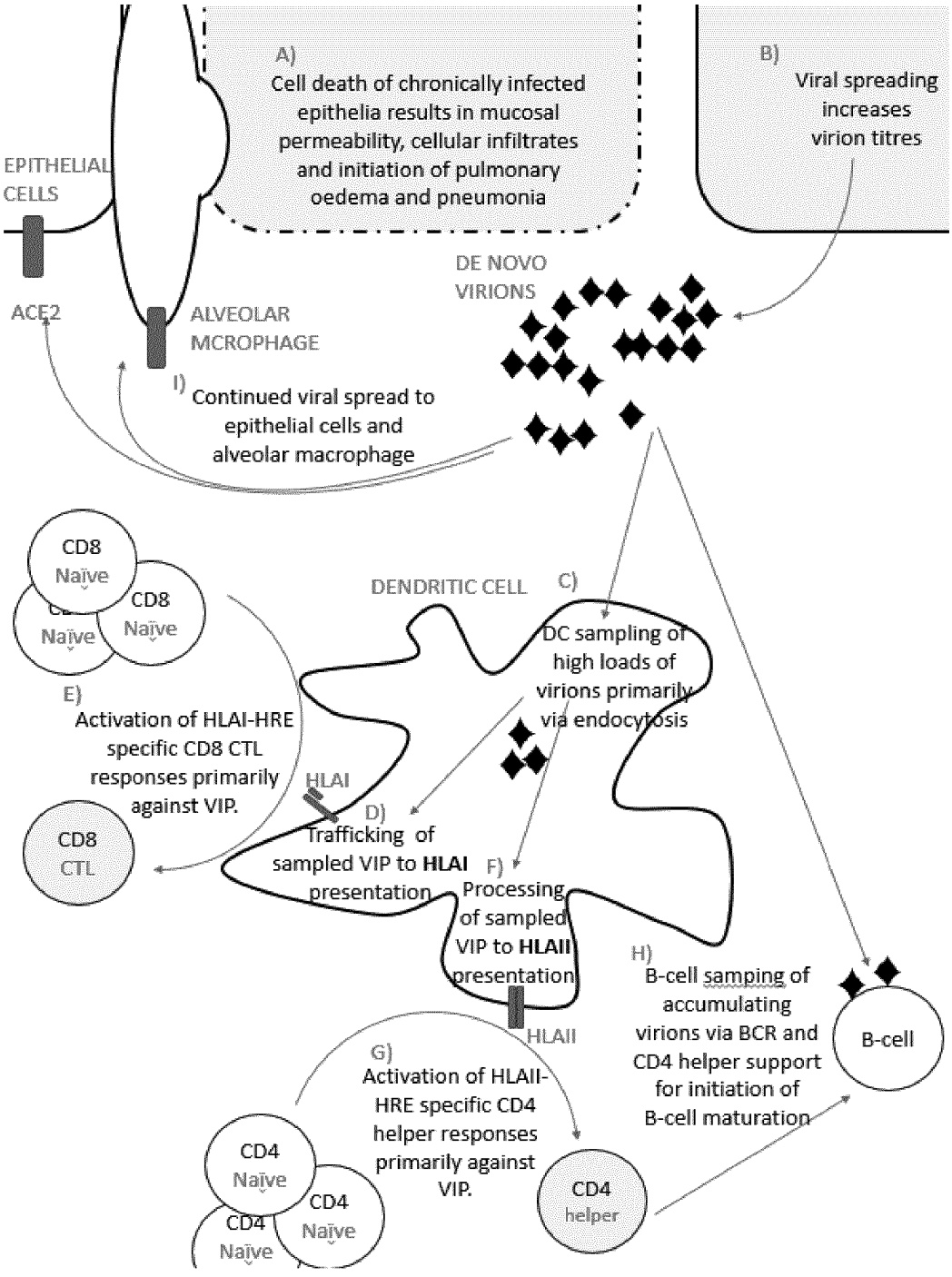

A)
Cell death of chronically infected epithelia results in mucosal permeability, cellular infiltrates and initiation of pulmonary oedema and pneumonia
B)
Viral spreading increases virion titres
EPITHELIAL CELLS
ACE2
ALVEOLAR MCROPHAGE
DE NOVO VIRIONS
I)
Continued viral spread to epithelial cells and alveolar macrophage
CD8 Naïve
CD8 Naïve
CD8 Naïve
E)
Activation of HLAI-HRE specific CD8 CTL responses primarily against VIP.
CD8 CTL
DENDRITIC CELL
C)
DC sampling of high loads of virions primarily via endocytosis
HLAI
D)
Trafficking of sampled VIP to HLAI presentation
F)
Processing of sampled VIP to HLAII presentation
HLAII
H)
B-cell samping of accumulating virions via BCR and CD4 helper support for initiation of B-cell maturation
B-cell
G)
Activation of HLAII-HRE specific CD4 helper responses primarily against VIP.
CD4 Naïve
CD4 Naïve
CD4 Naïve
CD4 helper

Figure 4

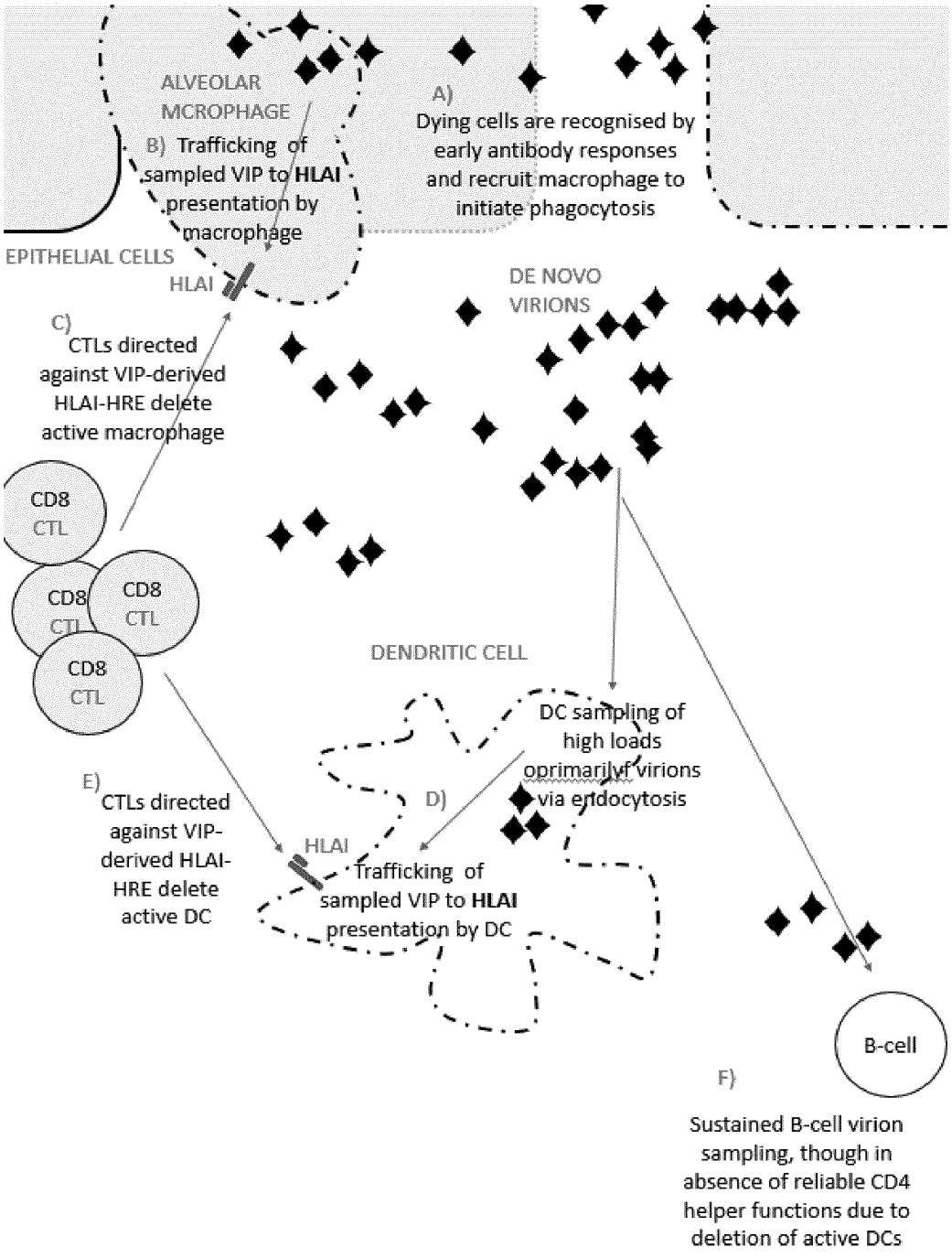

ALVEOLAR MCROPHAGE
A)
Dying cells are recognised by early antibody responses and recruit macrophage to initiate phagocytosis
B) Trafficking of sampled VIP to HLAI presentation by macrophage
EPITHELIAL CELLS
HLAI
DE NOVO VIRIONS
C)
CTLs directed against VIP-derived HLAI-HRE delete active macrophage
CD8 CTL
CD8 CTL
CD8 CTL
CD8 CTL
DENDRITIC CELL
DC sampling of high loads oprimarily virions via endocytosis
D)
E)
CTLs directed against VIP-derived HLAI-HRE delete active DC
HLAI
Trafficking of sampled VIP to HLAI presentation by DC
B-cell
F)
Sustained B-cell virion sampling, though in absence of reliable CD4 helper functions due to deletion of active DCs

Figure 5

A)

HLA-A	HLA-B	HLA-C
A*01:01	B*07:02	C*03:04
A*02:01	B*08:01	C*04:01
A*03:01	B*15:01	C*06:02
A*11:01	B*35:01	C*07:01
A*23:01	B*44:03	C*07:02
A*24:01		

B-C)

