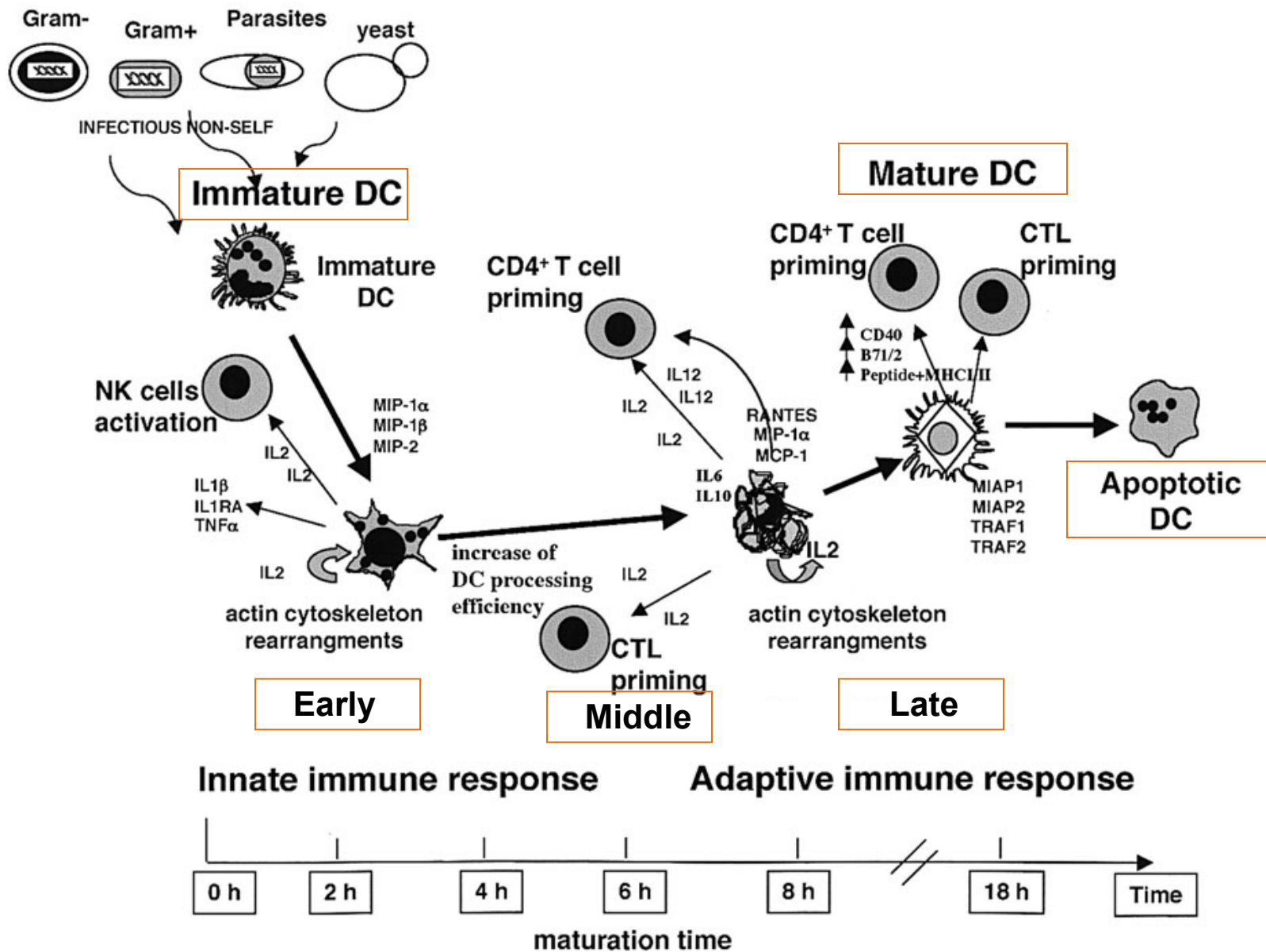


DC Maturation Process



Adapted from Granucci et al. EMBO J. 2003. 22: 2546-51

CytoActive : Biological questions we want to ask

1. Diagnostic point of view: When DC cells are infected by a pathogen, various factors are secreted at different times, and other cells of the immune system are activated. They in turn secrete factors that influence DC maturation and its subsequent response.

If factors x, y, z, ... are detected:

Can we predict which pathogen initially infected the DC?

(plan therapy)

Can we predict which other cells of the immune system were activated and which were not?

(detect immunodeficiencies and counteract them by supplementing the missing factors)

Can we predict the stage of maturation of DCs?

(predict how long ago infection occurred)

2. From an experimental point of view, the model would allow to analyze and compare the different DC response, depending on whether the various parameters (especially other cells of the immune response: B, T, NK, ...) are present or absent.

What happens to the response when we “remove” or “add” such or such parameter?

(help design and interpret bench experiments)

What will be the DC and immune response in case of co-infection by several pathogens?

Also in case a second infection occurs subsequently to a first one (since DCs become refractory to later signals), what will be the outcome?

3. From a pharmaceutical point of view, the model will allow to predict the effect of a particular drug on DCs and other cells of the immune system. Would also allow minimizing the side effects associated with a drug.

Can we predict at which stage of infection a particular drug should be administered, so that it specifically target DCs (or other cells), and at the right time?

Fictive example (based on CytoActive database): anti-IL12 (drug). IL-12 is produced by DCs upon infection by Gram- bacteria (E.Coli), starting at the middle stage (8-18h). It stimulates IFN γ production by DC and activates TH1 cells. Anti-IL12 would be efficient to suppress TH1 activation when administered ~8hrs following E.Coli infection.