1. Cytokine production is tightly regulated at different molecular level.

* We will construct the mathematical model in each module.
* We will also test different regulation mechanisms by the model.
* We will link all the modules together.
* We will link all the modules with TLR4 model (but seems not match *trif ko* late phase for the NFkB activity, why?).

1. TNF feedback is critical in determining stimulus specificity in the TLR signaling.

* Linking TLR4 model + TNF production model + TNF receptor model can capture all the data, suggesting the TNF feedback is more important in MyD88 mediated signaling.
* Testing this idea, by studying CpG and PIC, which are mediated by MyD88 and TRIF respectively.
  + We see big difference in CpG responses but not PIC (readouts: TNF mRNA and Elisa). Adding CpG and PIC module into the big model confirms the difference.
  + The big model also suggested upstream NFkB should also see the same result
  + We tested in NFkB activity
* Lastly, functional study (image and RNAseq)