# Predictive logical modelling of TLR5 and TCR cooperation for CD4 T cell activation.

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Toll-Like Receptor 5 (TLR5) recognises the flagellin monomer, a component of the flagella of many bacteria. Flagellin is being evaluated as a vaccine adjuvant given its ability to induce pro-inflammatory signalling cascades in a variety of cell types. In T cells, flagellin directly provides a co-stimulatory signal to the T cell receptor-mediated (TCR) signals leading to proliferation and IFN-γ production. This study aim to model the cross-talk between TLR5 and TCR signalling pathways leading to CD4 T cell activation. We used the software GINsim to generate and analyse the models. First, we constructed distinct logical models for TCR and TLR5 signalling pathways based on published information and high-throughput data. Next, we validated these models using experimental data obtained in our lab. Then, we reduced these models and merged the reduced versions to obtain a model accounting for the cross-talk between the two pathways. We perform a dynamical analysis of these different models to delineate the specific effects of the cross-talk between TLR5 and TCR pathways on CD4 T cell activation. We then stimulated highly purified naïve CD4 T cells by cross-linking the CD3 molecule, in the presence or absence of flagellin, and evaluated the activation of IKKαβ, c-JUN and CREB by flow cytometry. Experimental data was used to further improve our merged model. The resulting model provides novel insights in the effects of flagellin co-stimulatory signals on CD4 T cell activation.