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研究課題名	Analysis of the mechanisms of co-infection with Mycobacterium and HIV in human macrophage linage cells	
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(Form 2-2)

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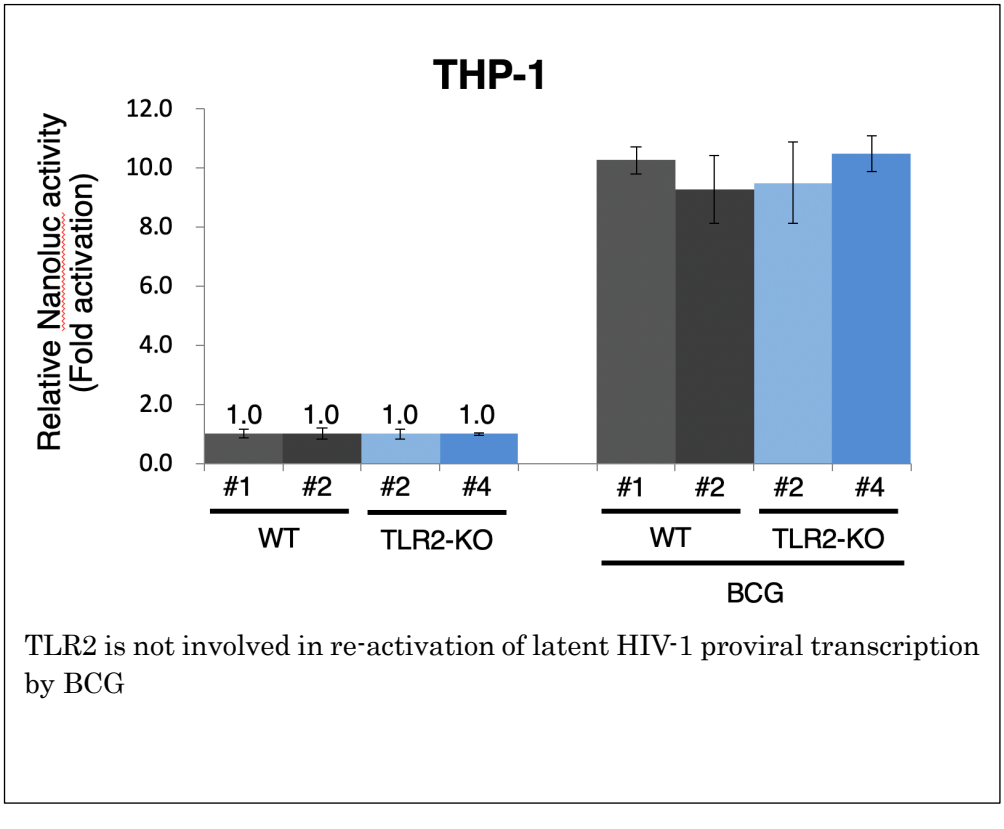
Report

We previously found that infection with the BCG strain of Mycobacterium tuberculosis (Mtb) upregulates transcription of HIV-1 latent provirus in HIV-1 latently infected model cells derived from human monocyte cells, THP-1 cells, indicating that latent HIV-1 can be re-activated by Mtb infection. Furthermore, we tried to elucidate signaling transduction pathways involved in re-activation of latent HIV-1 by Mtb infection. It is known that toll-like receptors (TLRs) recognize structure of Mtb-derived pathogens and induce innate immune responses in response to Mtb infection. MyD88 is an adaptor protein essential for the signal transduction through almost all TLRs. Therefore, we established MyD88-defficient HIV-1 latent model THP-1 cells using a CRISPR/Cas9 system. In conclusion, we found that Mtb infection induces re-activation of latent HIV-1 in both TLR-dependent and independent manners.

This year, we focused on a TLR-dependent pathway leading to re-activation of latent HIV-1 provirus by Mtb and tried to identify TLRs that re-activate latent HIV-1 provirus. The cellular components of Mtb are mainly recognized by TLR2. Furthermore, it has been reported that stimulation with a TLR2 ligand strongly induces HIV-1 proviral transcription. Therefore, we established TLR2-dificient HIV-1 latent model THP-1 cells using a CRISPR/Cas9 system to elucidate whether TLR2 is involved in re-activation of latent HIV-1 provirus by Mtb infection. Two clones of wild-type cells or TLR2-deficient cells were incubated with BCG. There was no difference in a NanoLuc reporter activity between wild-type and TLR2-deficient cell clones. Interestingly, this result strongly indicates that TLR2 is not involved in re-activation of latent HIV-1 provirus by Mtb. We are currently trying to identify other TLRs than TLR2 that are involved in re-activation of latent HIV-1 provirus by Mtb.



TLR2 is not involved in re-activation of latent HIV-1 proviral transcription by BCG