Validation data for cAIMP and its analogs

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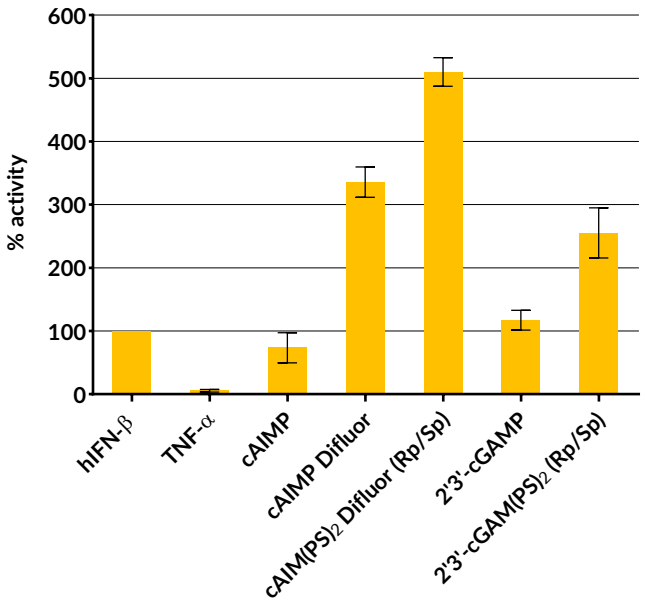
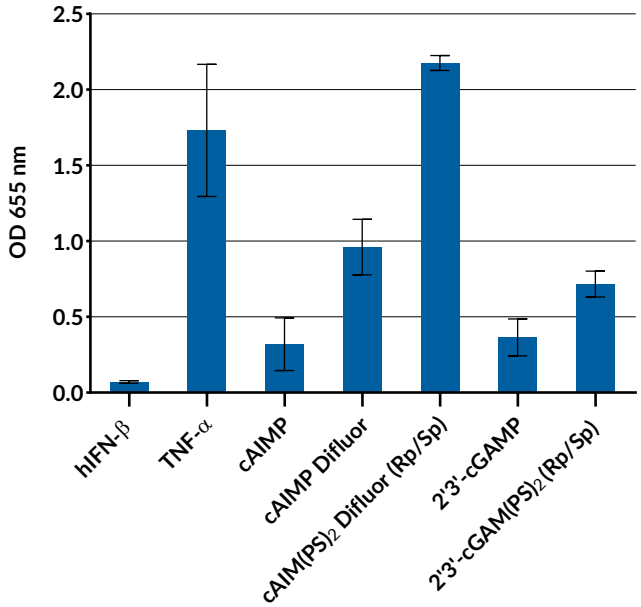
cAIMP and its analogs are novel STING-activating cyclic dinucleotides (CDNs) that induce NF-κB and interferon (IFN) signaling. The activity of these CDNs has been compared to the reference agonist for human STING, 2'3'-cGAMP (see figures 1 & 2) using the THP1-Dual™ cells, a cell line derived from the human THP-1 monocyte cell line by stable integration of two inducible reporter constructs. As a result, these cells allow the simultaneous study of the IFN regulatory factor (IRF) pathway, by assessing the activity of a secreted Lucia luciferase, and the NF-κB pathway, by monitoring the activity of SEAP. Interestingly, cAIMP exhibits similar potency to 2'3'-cGAMP, while the difluorinated (cAIMP Difluor) and bisphosphorothioate Difluor (cAIM(PS)$_2$ Difluor (Rp/Sp)) analogs are more potent than cAIMP and 2'3'-cGAMP.

IRF INDUCTION (Lucia luciferase reporter)



NF-κB INDUCTION (SEAP reporter)



THP1-Dual™ cells were stimulated for 24 hours with human IFN-β (1 x 10^4 U/ml), TNF-α (300 pg/ml), cAIMP, cAIMP Difluor, cAIM(PS)$_2$ Difluor (Rp/Sp), 2'3'-cGAMP and 2'3'-cGAM(PS)2 (Rp/Sp). All CDNs were used at 10 µg/ml.

Figure 1: IRF induction was determined by measuring the relative light units (RLUs) in a luminometer using QUANTI-Luc™, a Lucia luciferase detection reagent. The IRF induction of each ligand is expressed relative to that of hIFN-β at 1 x 10^4 U/ml (taken as 100%).

Figure 2: NF-κB induction was determined using QUANTI-Blue™, a SEAP detection reagent, and by reading the optical density (OD) at 655 nm. TNF-α has been included as a positive control to activate the NF-κB signaling pathway.

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