Validation data for MRT67307

https://www.invivogen.com/mrt67307

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Version 19E07-NJ

MRT67307 is a potent, reversible kinase inhibitor specifically blocking the function of TBK1 (TANK binding kinase 1) and IKKε (I-kappa-B kinase (IKK) epsilon or IKBKE), thereby preventing the phosphorylation of IRF3 (interferon regulatory factor 3) and subsequent expression of interferon stimulated genes (ISGs). Unlike BX795 from which it is derived, MRT67307 has no noted effect on the canonical IKKs, IKKα or IKKβ, that are involved in the activation of NF-κB. Co-incubation of THP1-Dual™ cells with increasing concentrations of MRT67307 and the 3p-hpRNA RIG-I agonist, or the 2'3'-cGAMP STING agonist, results in a dose-response inhibition of IRF signaling, evidenced by a decreased ISG-induced expression of the Lucia luciferase reporter (**Figure 1**). Co-incubation of THP1-Dual™ cells with either MRT67307 or BX795 inhibitors, and the 3p-hpRNA RIG-I agonist, results in a significant inhibition (2% to 30%) of IRF signaling. MRT67307 has no effect on the NF-κB signaling, while BX795 induces a significant inhibition (OD_{630nm}: 0.3) of NF-κB-induced expression of the secreted embryonic alkaline phosphatase (SEAP) reporter (**Figure 2**).

Dose-dependent inhibition of IRF signaling

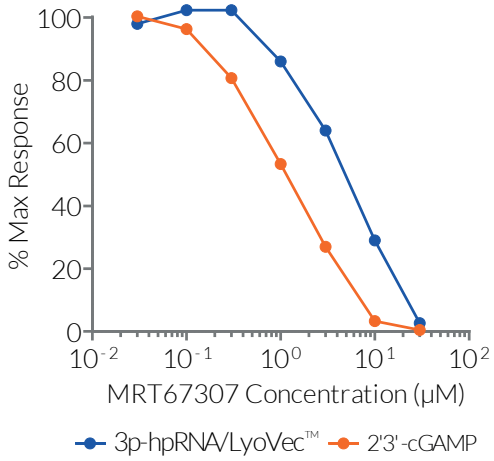

Figure 1: Inhibition of 3p-hpRNA and 2'3-cGAMP-induced responses in THP1-Dual™ Cells: 2x10^5 THP1-Dual™ cells were transfected with 1 µg/ml 3p-hpRNA/Lyovec™ or incubated with 30 µg/ml 2'3'-cGAMP in the presence of absence of increasing concentrations of MRT67307. After overnight incubation, activation of IRF was assessed by measuring Lucia luciferase activity in the supernatant, using QUANTI-Luc™ detection reagent. Percentages of the maximal response for the ligand with no inhibitor are shown.

MRT67307 inhibition of TBK1/IKKε

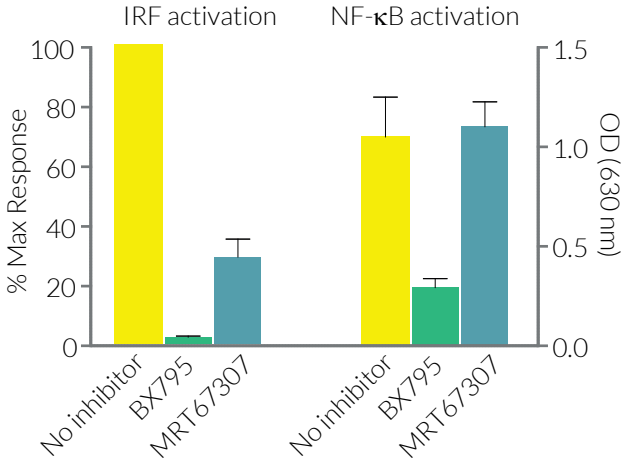

Figure 2: Inhibition of 3p-hpRNA-induced responses in THP1-Dual™ Cells: 2x10^5 THP1-Dual™ cells were transfected with 1 µg/ml 3p-hpRNA/Lyovec™ with or without 1 µg/ml BX795 or 3 µg/ml MRT67307. After overnight incubation, activation of IRF was assessed by measuring Lucia luciferase activity in the supernatant using QUANTI-Luc™ detection reagent. Percentages of the maximal response for the ligand with no inhibitor are shown on the left axis. The activation NF-κB was assessed by measuring SEAP activity in the supernatant using QUANTI-Blue™ Solution detection reagent. OD at 630 nm are shown on the right axis.

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