Validation data for G140

https://www.invivogen.com/g140

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Version 20G09-ED

G140 is a small molecule inhibitor of the cytosolic double-stranded DNA (dsDNA) sensor cyclic GMP-AMP synthase (cGAS). G140 has been shown to have a dose-dependent inhibitory activity on both cGAS-induced IRF and NF-κB signaling pathways **(Figure 1)**. Additionally, G140 is highly specific for cGAS with no noted off-target effects on other cytosolic sensors (i.e. RLRs and STING) **(Figure 2)**.

Dose-dependent inhibition of cGAS by G140

Treatment of THP1-Dual™ cells with G140 results in the inhibition of the cGAS-inducible **(A)** IRF and **(B)** NF-κB responses in a dose-dependent manner upon incubation with G3-YSD, a cGAS agonist. Please note no toxicity was oberseved with G140, even at the highest concentration tested.

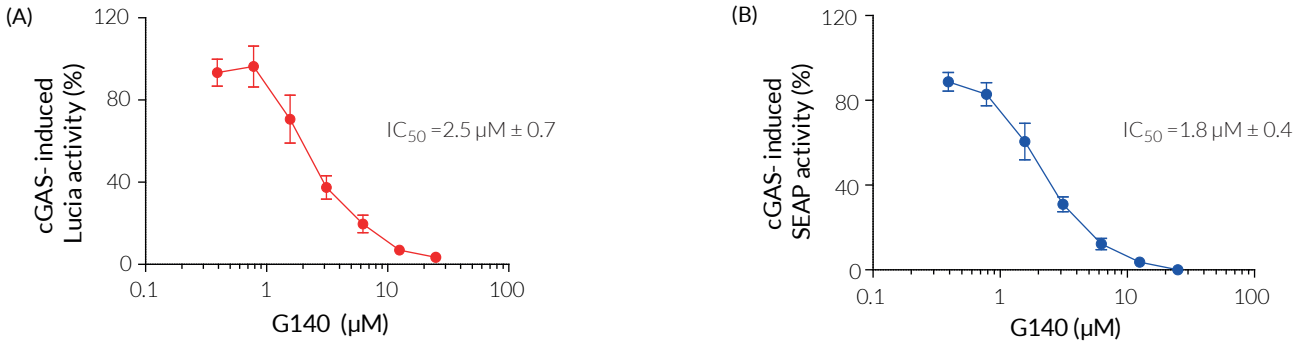

Figure 1: G140 inhibits cGAS in a dose-dependent response in THP1-Dual™ cells. The cells were incubated with increasing concentrations (0 - 25 µM) of G140 for 3 hours. Following this, G3-YSD (1 µg/ml), a specific cGAS agonist, was complexed with LyoVec™ and transfected into the cells . After an overnight incubation, activation of cGAS was assessed by measuring **(A)** IRF-dependent Lucia activity and **(B)** NF-κB -dependent SEAP activity, using QUANTI-Luc™ and QUANTI-Blue™ Solution, respectively. Data are shown as percentage (%) of cGAS activity and IC_{50} ± std error.

Specificity of G140

Treatment of THP1-Dual™ cells and THP1-Dual™ KO-cGAS with G140 results in the specific inhibition of the cGAS-inducible IRF response, with no notable effect on the induction of cytosolic **(A)** RLR sensors (with 3p-hpRNA) and **(B)** STING (with 2'3' cGAMP).

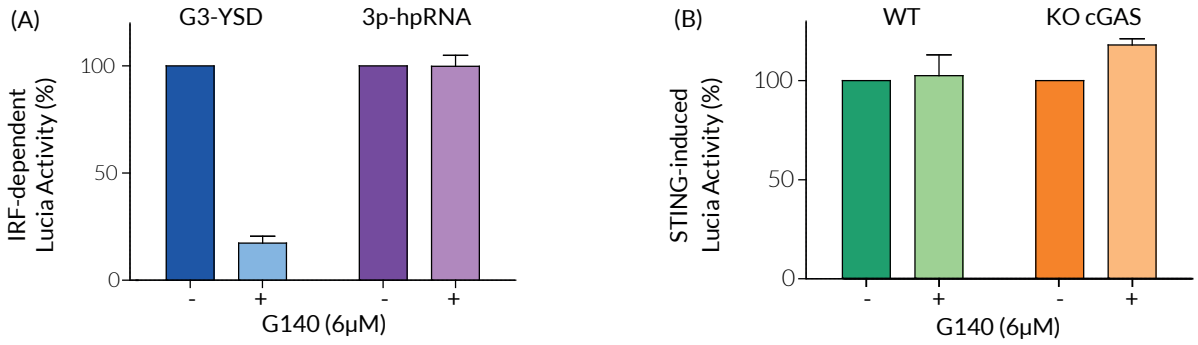

Figure 2: Specific inhibition of cGAS by G140. (A) THP1-Dual™ cells were incubated in the presence or absence of 6µM G140 for 3 hours. Following this, G3-YSD (1 µg/ml), a specific cGAS agonist, or 3p-hpRNA (1 µg/ml), a specific RLR agonist were complexed with LyoVec™ and transfected into the cells. **(B)** THP1-Dual™ cells (WT) and THP-Dual™ KO-cGAS (KO-cGAS) cells were incubated in the presence or absence of 6µM G140 for 3 hours. Following this, 2'3'-cGAMP (10 µg/ml), a STING agonist was added to the cells. After overnight incubation, the IRF response was assessed using QUANTI-Luc™. Data are shown as percentage (%) of (A) general IRF- or (B) STING-induced Lucia luciferase activity.

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