

Validation data for G140

<https://www.invivogen.com/g140>

For research use only

Version 22F14-MM

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- κ B 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- κ B responses in a dose-dependent manner upon incubation with G3-YSD, a cGAS agonist. Please note no toxicity was observed with G140, even at the highest concentration tested.

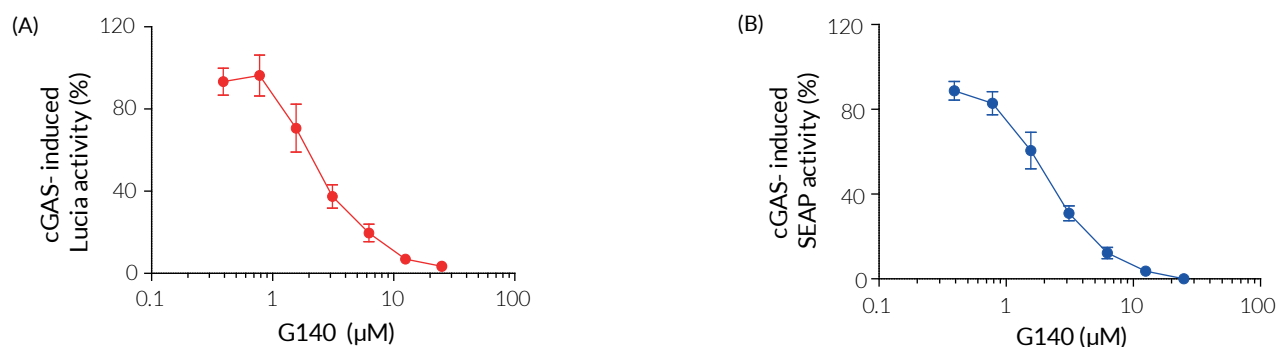


Figure 1: G140 inhibits cGAS in a dose-dependent response in THP1-Dual™ cells. The cells were incubated with increasing concentrations (0-25 μ M) of G140 for 3 hours. Following this, G3-YSD (1 μ g/ml), a specific cGAS agonist, was complexed with LyoVec™ and transfected into the cells. After an overnight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

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).

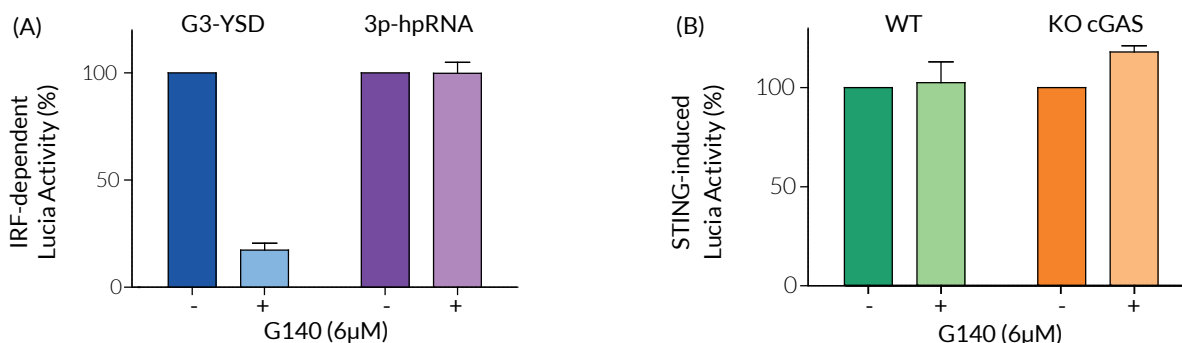


Figure 2: Specific inhibition of cGAS by G140. (A) THP1-Dual™ cells were incubated in the presence or absence of 6 μ M G140 for 3 hours. Following this, G3-YSD (1 μ g/ml), a specific cGAS agonist, or 3p-hpRNA (1 μ g/ml), a specific RLR agonist were complexed with LyoVec™ and transfected into the cells.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

TECHNICAL SUPPORT

InvivoGen USA (Toll-Free): 888-457-5873

InvivoGen USA (International): +1 (858) 457-5873

InvivoGen Europe: +33 (0) 5-62-71-69-39

InvivoGen Asia: +852 3622-3480

E-mail: info@invivogen.com