

Validation data for CP-690550

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Version 19K16-MM

CP-690550 (Tofacitinib) specifically inhibits Janus kinase 3 (JAK3), which has a pivotal role in cytokine receptor-mediated signal transduction, including interferon (IFN) signaling. Indeed, extracellular signals from IFNs are transduced by JAK and signal transducer and activator of transcription (STAT) signaling pathway, ultimately leading to the transcription of IFN stimulated genes (ISGs). The ability of CP-690550 to inhibit IFN signaling pathway was tested in HEK-Blue™ IFN- α/β cells, which respond to type I and type III IFNs. Results obtained with this cell line show that CP-690550 can effectively block the IFN- λ (IL-29) and the IFN- α/β signaling pathway (figure 1).

Evaluation of inhibitory activity of CP-690550

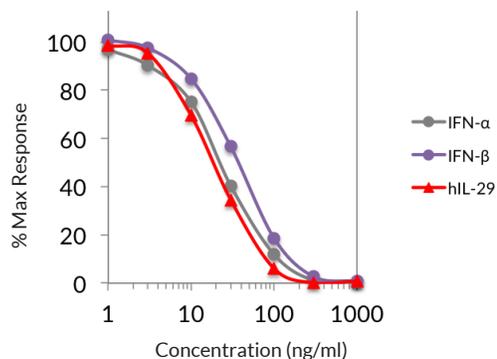


Figure 1. Effect of CP-690550 on HEK-Blue™ IFN- α/β cell response to type I and type III IFNs: HEK-Blue™ IFN- α/β cells were incubated with 3 U/ml hIFN- α 2b (grey), 1 U/ml hIFN- β 1 (purple) or 10 ng/ml hIL-29 (hIFN- λ 1) (red) and increasing concentrations of CP-690550. After 24h incubation, IFN-induced ISG activation was assessed by measuring SEAP levels in the supernatant using QUANTI-Blue™. Percentages of maximal response (no inhibitor) for each cytokine are shown.

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 Hong Kong: +852 3622-3480
E-mail: info@invivogen.com