Validation data for CYT387

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CYT387, also known as Momelotinib, is a potent ATP-competitive inhibitor of Janus kinases JAK1 and JAK2, thereby interrupting signaling via the JAK-STAT (signal transducers and activators of transcription) pathway. As a result, CYT387 prevents JAK-STAT activation which plays a pivotal role in cytokine receptor-mediated signal transduction, including interferon (IFN) signaling. Indeed, extracellular signals from IFNs are transduced by JAK-STAT signaling pathway, ultimately leading to the transcription of IFN stimulated genes (ISGs). The ability of CYT387 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 CYT387 can effectively block the IFN-λ (IL-29) and the IFN-α/β signaling pathway (figure 1).

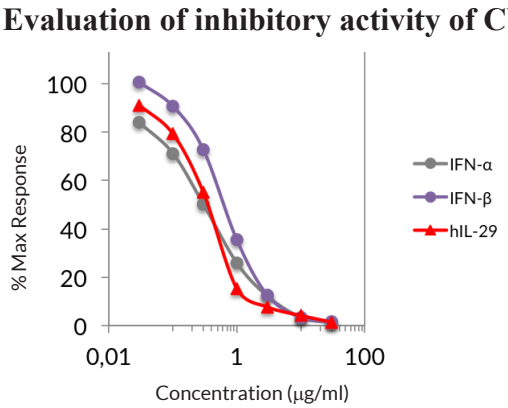

Figure 1. Effect of CYT387 on HEK-Blue™ IFN-α/β cell response to type I and type III IFNs: HEK-Blue™ IFN-α/β cells were incubated with 3 U/ml hIFN-α2b (grey), 1 U/ml hIFN-β1 (purple) or 10 ng/ml hIL-29 (hIFN-λ1) (red) and increasing concentrations of CYT387. After 24h incubation, IFN-induced ISG activation was assessed by measuring SEAP levels in the supernatant using QUANTI-Blue™. Percentages of maximal response (no inhibitor) for each cytokine are shown.

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