

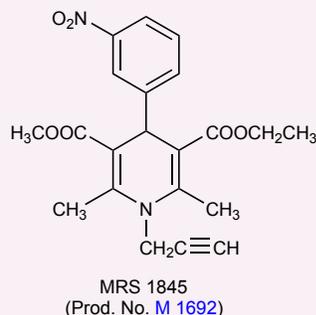
## New Product Highlights

### MRS 1845: A blocker of store-operated calcium (SOC) entry that does not activate intracellular calcium release

Cytosolic calcium acts as a ubiquitous second messenger and is involved in the regulation of a myriad of cellular processes ranging from growth and differentiation to cell death and apoptosis. Calcium signals are generated by both the release of stored calcium from the endoplasmic reticulum and the influx of extracellular calcium across the plasma membrane. While the release of stored calcium is generally mediated by **inositol 1,4,5-trisphosphate** (IP<sub>3</sub>, Prod. No. [I 7012](#)) and **cyclic ADP ribose** (cADPR, Prod. No. [C 7344](#)), influx of extracellular calcium can be directed through various mechanisms [1,2]. The entry of extracellular calcium generally results from IP<sub>3</sub>-related depletion of intracellular stores in a process referred to as capacitative calcium entry or store-operated calcium (SOC) entry. The mechanisms underlying SOC entry are poorly understood but may involve members of the transient receptor potential (TRP) family of channel proteins [3,4].

Efforts to study the phenomenon of SOC entry have been hampered by the lack of blockers that effectively abolish SOC entry without activating intracellular calcium release. Sigma-RBI has recently introduced **MRS 1845** (N-propargylnitrendipine, Prod. No. [M 1692](#)), an N-substituted dihydropyridine that possesses micromolar potency at SOC channels in HL-60 cells [5]. Unlike currently used SOC

blockers, such as **clotrimazole** (Prod. No. [C 6019](#)) and **SKF 96365** (Prod. No. [S 7809](#)), MRS 1845 does not activate intracellular calcium release at concentrations required to block SOC entry. MRS 1845 is therefore a valuable tool with which to further investigate the physiology and pharmacology of SOC entry.



#### References

1. Putney, J.W., Jr., *Proc. Natl. Acad. Sci. USA*, **96**, 14669-14671 (1999).
2. Barritt, G.J., *Biochem. J.*, **337**, 153-169 (1999).
3. Nilius, B., et al., *Endothelium*, **10**, 5-15 (2003).
4. Liu, X., et al., *J. Biol. Chem.*, **278**, 11337-11343 (2003).
5. Harper, J.L., et al., *Biochem. Pharmacol.*, **65**, 329-338 (2003).

### Interleukins 21 and 22: Two new cytokines available from Sigma-RBI

Interleukin-21 (IL-21) is a novel cytokine expressed in activated T cells that is most closely related to IL-2, IL-4 and IL-15. The receptor for IL-21 (IL-21R), also called NILR for novel interleukin receptor [1,2] forms a complex with IL-2 Ry (γc) and mediates IL-21 signaling [3,4]. Together, IL-21 and its receptor (IL-21R) appear to play important roles in the regulation of the immune system. This complex regulates the proliferation and maturation of NK (natural killer), B and T cell populations. IL-21 and its receptor activate the JAK-STAT signaling pathway.

Interleukin-22 (IL-22), also known as IL-10-related T cell-derived inducible factor (IL-TIF), was originally identified as a gene induced by IL-9 in mouse T cells and mast cells [5]. The IL-22 receptor complex consists of two receptor subunits belonging to the class II cytokine receptor family, IL-22R (formerly an orphan receptor named CRF<sub>2-9</sub>) and IL-10Rβ (formerly known as CRF<sub>2-4</sub>) [6,7]. In humans, IL-22 is produced by normal T cells upon anti-CD3 stimulation. IL-22 activates STAT1 and STAT3 in several hepatoma cell lines and upregulates the production of acute phase proteins.

Sigma-RBI is pleased to introduce both human and mouse recombinant interleukin-21 and interleukin-22 together with a series of related antibodies that will be of interest to researchers investigating the role of these important cytokines in cell signaling mechanisms.

#### Proteins

- [I 3907](#) **Interleukin 21 (IL-21)**, human, recombinant
- [I 4032](#) **Interleukin-21 (IL-21)**, mouse, recombinant
- [I 4282](#) **Interleukin-22 (IL-22)**, human, recombinant
- [I 4407](#) **Interleukin-22 (IL-22)**, mouse, recombinant
- [I 4157](#) **Interleukin-21 Receptor (IL-21R)/Fc Chimera**, mouse, recombinant

#### Antibodies

- [I 5282](#) **Anti-Interleukin-21 (IL-21), Intracellular Domain** (rabbit)
- [I 5407](#) **Anti-Interleukin-21 Receptor (IL-21R), Extracellular Domain** (rabbit)
- [I 5532](#) **Anti-Interleukin-21 Receptor (IL-21R), N-Terminal** (rabbit)
- [I 5782](#) **Anti-Interleukin-22 Receptor (IL-22R), C-Terminal** (rabbit)
- [I 5657](#) **Anti-Interleukin-22 Receptor (IL-22R), N-Terminal** (rabbit)

#### References

1. Parrish-Novak, J., et al., *Nature*, **408**, 57-63 (2000).
2. Ozaki, K., et al., *Proc. Natl. Acad. Sci. USA*, **97**, 11439-11444 (2000).
3. Asao, H., et al., *J. Immunol.*, **167**, 1-5 (2001).
4. Vosshenrich, C.A., et al., *Curr. Biol.*, **11**, R175-R177 (2001).
5. Dumoutier, L., et al., *J. Immunol.*, **164**, 1814-1819 (2000).
6. Xie, M.H., et al., *J. Biol. Chem.*, **275**, 31335-31344 (2000).
7. Kotenko, et al., *J. Biol. Chem.*, **276**, 2725-2732 (2001).