

Product Information

3-Mpr-Phe-Cha-Cha-Arg-Lys-Pro-Asn-Asp-Lys-amide

Product Number **M 2192**
Storage Temperature $-20\text{ }^{\circ}\text{C}$

Synonyms: 3-mercapto-propionyl-Phe-Cha-Cha-Arg-Lys-Pro-Asn-Asp-Lys-amide, 3-Mpr-F-Cha-Cha-RKPNDK-NH₂, Mpr-NH₂

Product Description

Molecular formula: C₆₁H₁₀₀N₁₆O₁₃S
Molecular Weight: 1297.6

3-Mpr-Phe-Cha-Cha-Arg-Lys-Pro-Asn-Asp-Lys-amide is a PAR (protease-activated receptor) modifying peptide that is a PAR-2 agonist and a PAR-1 antagonist. It is a synthetic short peptide modeled after the amino acid sequence of the proteolytically exposed tethered ligands that activate PARs in the absence of proteases. These are sometimes called TRAPs (Thrombin Receptor-Activating Polypeptides). The group of PAR modifying peptides includes: 3-Mpr-F-Cha-Cha-RKPNDK-NH₂, SLIGRL-NH₂, SLIGKV-NH₂, AYPGKF-NH₂, and tcY-NH₂. Table 1 summarizes the properties of this group of PAR modifying peptides.

PARs have important physiological roles in vessel wall biology, thrombosis, and the cardiovascular system. The consequences of PAR activation in vascular injury, inflammation, tissue injury, and tumor micro-environment make them targets of pharmacological studies and drug discovery. PARs belong to a superfamily of G protein-coupled seven transmembrane receptors, but possess a distinctive activation mechanism. PARs are activated by proteolytic cleavage of the N-terminal peptide leading to exposure of the cryptic receptor-activating sequence, which acts as a ligand still tethered to the receptor molecule and binds and activates the same receptor molecule.

There are four receptor subtypes referred to as PAR-1, PAR-2, PAR-3, and PAR-4. Other subtypes are suspected. PAR-1, PAR-3, and PAR-4 receptors are activated by thrombin (also known as thrombin receptor), while the PAR-2 receptor is activated by trypsin, mast cell tryptase, and coagulation factors VIIa and Xa. The full complement of activating proteases may not have been fully elucidated.

PAR-1, PAR-3, and PAR-4 receptors are expressed in platelets and are considered to act mainly in platelet activation. All three have been cloned and characterized as receptors for thrombin, the major serine effector protease of coagulation, vascular injury, and inflammation. The PAR-1 receptor is known to be coupled to G proteins, G_q and G_i. PAR-1 activation results in the activation of phospholipase C (PLC), leading to the formation of inositol triphosphate (IP₃), and diacylglycerol (DAG) followed by calcium mobilization and activation of protein kinase C (PKC). Other evidence indicates that PAR-1 is involved in the activation of the cascade of tyrosine kinase (Src family), PI3 kinase (PI3K), protein kinase B (Akt), and mitogen-activated protein kinase (MAPK).

The PAR-2 receptor is expressed at high levels in colon, pancreas, small intestine, and kidney as well as endothelial, epithelial, and smooth muscle cells. It is involved in digestive exocrine functions, triggering amylase secretion and pancreatic duct epithelial cell ion channel activation. The PAR-2 receptor is coupled to G_q and G_i, and its activation leads also to IP₃/DAG accumulation and cAMP modulation.

Given what is known of the physiological roles of these receptors, PAR selective agonists and antagonists are potential therapeutic agents in the management of human diseases. In addition, their receptor isoform-selectivity holds promise in making them ideal tools for elucidating the intracellular signaling mechanisms of these structurally related receptors.

Precautions and Disclaimer

This product is for R&D use only, not for drug, household, or other uses. Please consult the Material Safety Data Sheet for information regarding hazards and safe handling practices.

References

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2. Bernatowicz, M.S., et al., Development of potent thrombin receptor antagonist peptides. *J. Med. Chem.*, **39**, 4879-4887 (1996).
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KAA/RP/MAM 8/04

Table 1.
Properties of PAR modifying peptides

Compound	EC ₅₀ in μM	IC ₅₀ in μM	Activity/Selectivity	References
SLIGRL-NH₂ (Product No. S 9317)	5		PAR-2 agonist; for rat/mouse receptors, activates keratinocyte inositolphospholipid hydrolysis and calcium mobilization.	3, 4, 5
SLIGKV-NH₂ (Product No. S 9192)			PAR-2 agonist; most potent for all species tested.	5
AYPGKF-NH₂ (Product No. A3227)	25 – 50		PAR-4 agonist; 10x more potent than natural ligands for mouse (GYPHKF) or human (GYPGQV).	6
tcY-NH₂ (Product No. C 7363)			PAR-4 antagonist; inhibits endostatin release and platelet aggregation mediated by thrombin.	7, 8
Mpr-F-Cha-Cha-RKPNDK-NH₂ (Product No. M 2192)	20 μM calcium signaling	17 μM for PAR-1 mediated calcium signaling; 6.4 μM for thrombin-induced platelet aggregation	PAR-2 agonist/PAR-1 antagonist.	9

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