
**Chapter 14:** Biochemical Events in Basophil/Mast Cell Activation and Mediator Release (Pages 235-256)

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1. Which of the following is secreted first upon Mast Cell activation?
   A. Leukotriene C4
   B. Prostaglandin D2
   C. Histamine
   D. IL-5

2. How many IgE antibodies can bind to each α subunit of the IgE receptor?
   A. 1
   B. 2
   C. 3
   D. 4

3. Which of the following serves the role of receptor kinase for the IgE receptor on Mast Cells and Basophils?
   A. Lyn
   B. Syk kinase
   C. fyn
   D. Btk

4. Which of the following Class 1A PI3K kinase subunits are expressed on human basophils?
   A. p110α
   B. p110β
   C. p110δ
   D. p86

5. Which of the following Phospholipase C enzymes are critical for IgE stimulation of mast cells and basophils?
   A. PLC-β
   B. PLC-δ
   C. PLC-ε
   D. PLC-γ

6. Which IgE receptor subunit is considered optional in humans, not generally expressed on non-mast cells and basophils?
   A. α
   B. β
C. δ
D. ε

7. Which kinase is considered a key component in the early stages of FcεRI-mediated signaling?
A. Src-family kinase, Lyn
B. Src-family kinase, ZAP70
C. ITAM
D. SH2

8. In mast cells, the primary generation of diacylglycerols results from the activity of what?
A. Phospholipase C
B. Phospholipase E
C. Leukotriene C4
D. Phospholipase D

9. In mast cells, SHP-1 appears to regulate the generation of cytokines and signaling to what protein?
A. JNK
B. Grb2
C. MAFA
D. Dok-1

10. Activation of the various NFAT (nuclear factor of activated T cells) family members is dependent on which of the following?
A. Casein kinase I
B. Glycogen synthase
C. Calcineurin
D. Quanine nucleotide

Answers
1. C, page 235-236
It is possible to classify three types of secretion: (1) rapid from pre-formed pools, (2) rapid but newly synthesized, and (3) slow but newly synthesized. Granule contents such as histamine represent the first group while arachidonic acid metabolites such as leukotriene C4 or prostaglandin D2 represent the second group. Cytokines, chemokines, and growth factors represent the third group.

2. A, page 237
The α subunit has a large two-domain chain that binds IgE antibody monomerically, a transmembrane segment, and short cytoplasmic tail. Although IgE is composed of two heavy chains, two IgE antibodies cannot bind to the α subunit due to unique use of both IgE heavy chains in the binding pocket of FcεRIα.
3. B, page 240
Src-family kinases like Lyn and fyn are the initiators of receptor phosphorylation, but it is Syk kinase that serves the role of receptor kinase.

4. A, page 240
Class 1A members of this large family are the PI3 kinases composed of an 85kDa regulatory subunit and a 110kDa catalytic subunit. The class 1A enzymes typically interact and mediate signaling from receptor tyrosine kinases or immunoreceptors. The catalytic subunit (p110) has three forms, α, β, δ. Human basophils have been found to express only p110δ,\cite{57} and a specific inhibitor of p110δ completely inhibits secretion.

5. D, page 241
During IgE-mediated stimulation of mast cells and basophils, it is PLC-γ1 and PLC-γ2 activity that appears to be critical.

IgE Receptor Structure

7. A, page 237
Brief Overview of the Early Stages of FcRI-Mediated Signaling

8. D, page 245
Focus on Specific Steps – Phospholipase D and phospholipase A2

9. A, page 248
Self Regulation or Signal Termination

10. C, page 253
Latter Signaling Events – Cytokine generation


Chapter 19: Biology of Mast Cells and Their Mediators (Pages 311-328)

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Chapter 19 – Biology of Mast Cells and Their Mediators – Pages 311-328
Dr. Madhu Narra & Dr. Christopher Martin

1. Which of the following is a preformed mediator of mast cells?
A. PGD₂
B. IL-4
C. TNF-α
D. LTC₄

2. Which of the following is a feature of MC₉ type of human mast cells?
A. Granules contain chymase
B. Found in the submucosa
C. “Scroll-poor” granules
D. T-cell dependency

3. Mast cell progenitors express
A. Kit
B. SCF
C. FcεR1
D. Tryptase

4. Increased circulating IgE levels
A. Increase mast cell FcεR1 expression by increasing mRNA encoding FcεR1α
B. Increase mast cell FcεR1 expression due to stabilization of receptors at the cell membrane
C. Decrease mast cell FcεR1 expression by decreasing mRNA encoding FcεR1α
D. Decrease mast cell FcεR1 expression due to destabilization of receptors at the cell membrane

5. Which of the following is a marker for mast cell activation in the body?
A. α-trypase
B. Pro-β tryptase
C. Mature β-tryptase
D. Pro-pepsin

6. Which is representative of a pre-formed mast cell proteoglycan?
A. Tryptase
B. Chymase
C. Carboxypeptidase
D. Heparin

7. Which is true regarding apoptosis of mast cells?
A. IL-15 activates mast cell apoptosis via Bcl-x₁
B. Mastocytosis results in mast cell dependence on high levels of SCF for development, proliferation, and survival
C. SCF regulates the expression of antiapoptotic molecules Bcl-2 and Bcl-x₁ in human mast cell cultures
D. A loss-of-function mutation in the IL-4 receptor portends a better prognosis in human Mastocytosis
8. The primary pathway of histamine metabolism is catalyzed by which enzyme?
A. Diamine oxidase
B. Histaminase
C. Histamine N-methyltransferase
D. Histamine peroxidase

9. Which is true of H3 receptors?
A. Enhances antigen presentation by dendritic cells
B. Suppression of TNF-α and IL-12
C. Highly expressed on peripheral leukocytes
D. Found at presynaptic receptors in the central and peripheral nervous system

10. During bee-sting anaphylaxis, which is representative of circulation patterns?
A. β-Tryptase peaks 1-2 hours after sting, histamine peaks 1-2 hours after sting
B. β-Tryptase peaks 15-30 minutes after sting, histamine peaks 5-10 minutes after sting
C. β-Tryptase peaks 1-2 hours after sting, histamine peaks 5-10 minutes after sting
D. β-Tryptase peaks 1-2 hours after sting, histamine peaks 45-60 minutes after sting

Answers
1. C, pages 312 (table 19.1), 322
TNF-α is a preformed cytokine that is synthesized and stored by human mast cells. PGD₂ and LTC₄ are arachidonic acid metabolites that are newly generated mediators. IL-4 is produced de novo after mast cell activation.

2. D, page (table 19.2)
MC₇ cells are dependent on T-cells for their development, unlike MC₇ cells which are T-cell independent. MC₇ granules contain tryptase alone without chymase and the granules are “scroll-rich” in their ultrastructure. These cells are found in the mucosal surfaces.

3. A, pages 315, 316
Mast cell progenitors express the receptor protein-tyrosine kinase “Kit”, which is encoded by the proto-oncogene c-kit. SCF (stem cell factor) is the ligand for Kit that is produced by the cells in the surrounding tissues. FcεR1 and tryptase are produced by differentiated mast cells, not the progenitors.

4. B, page 319
Increased circulating IgE levels increase FcεR1 expression due to stabilization of receptors at the cell membrane. IL-4, not IgE, has been shown to upregulate FcεR1 expression by increasing mRNA encoding FcεR1α.

5. C, page 321
α-tryptase and pro-β tryptase are released constitutively are a marker for total body mast cell burden. Mature β-tryptase is released from secretory granules on activation and is a marker for mast cell activation.
6. D, page 312
A, B, and C are all neutral proteases.

7. C, page 318

8. C, page 320
The primary pathway of histamine degradation is via methylation. A secondary pathway, catabolized by diamine oxidase (histaminases), involves oxidation.

9. D, page 320
A is true of H1 receptors, as is B. C is true of H4 receptors.

10. C, page 323
Tryptase, given its longer half-life can be checked up to a few hours after an event to help confirm diagnosis of anaphylaxis.