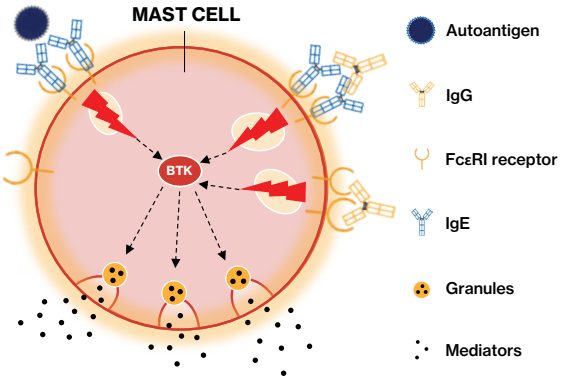
CSU Pathophysiology and the Role of BTK



Adapted with permission from Mendes-Bastos P et al.[1]

Mast cells are central to CSU pathophysiology

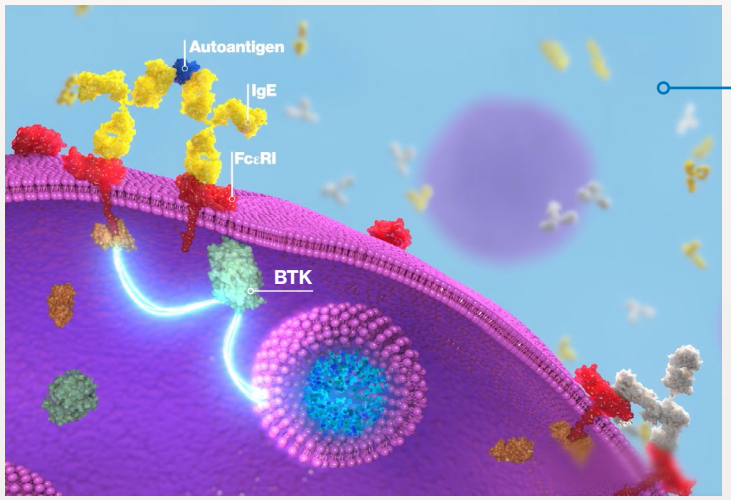
The pathogenesis of CSU involves antibody-mediated mast cell and basophil activation[1]

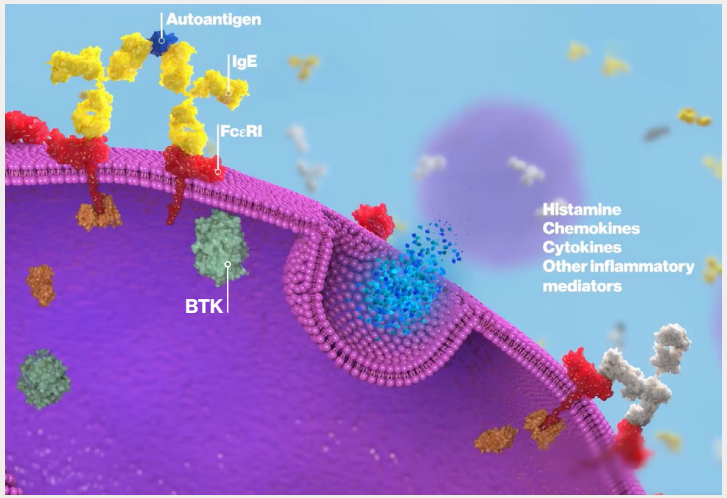
Mast cell activation occurs through[1]:

- Crosslinking of IgE by autoantigens
- Crosslinking of IgE by IgG
- Crosslinking of FcεRI by IgG

Activated mast cells release proinflammatory mediators (eg, histamines, cytokines, chemokines, proteases)[1,2]

- This leads to increased capillary permeability causing symptoms of wheals and angioedema, and stimulation of irritant receptors that causes itching[1-3]





BTK in mast cell activation

BTK[1]:

- Is activated in mast cells upon crosslinking of FcεRI
- Is the central positive regulator of FcεRI mast cell activation
- Enhances early- and late-phase reactions
- Signaling is independent of mechanism of FcεRI activation

Role of BTK in B cells and BCR signaling

BTK plays a critical role in BCR signaling[4]

BTK is expressed from pre–B cells to the mature B-cell stages[4]

B-cell activation leads to:

- Antigen presentation[5]
- B-cell differentiation and survival[5]
- Antibody and cytokine production[6]

BCR, B-cell receptor; BTK, Bruton's tyrosine kinase; CSU, chronic spontaneous urticaria; FcεRI, high-affinity IgE receptor I; Ig, immunoglobulin.

1. Mendes-Bastos P et al. *Allergy*. 2022;77(6):1719-1735. **2.** Schocket AL. *Allergy Asthma Proc*. 2006;27:90-95. **3.** Greaves M. J *Allergy Clin Immunol.* 2000;105:664-672. **4.** Maas A, Hendriks R. *Dev Immunol.* 2001;8(3-4):171-181. **5.** Hendriks RW et al. *Nat Rev Cancer.* 2014;14(4):219-232. **6.** Singh SP et al. *BMC Mol Cancer.* 2018;17:57.

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Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080

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