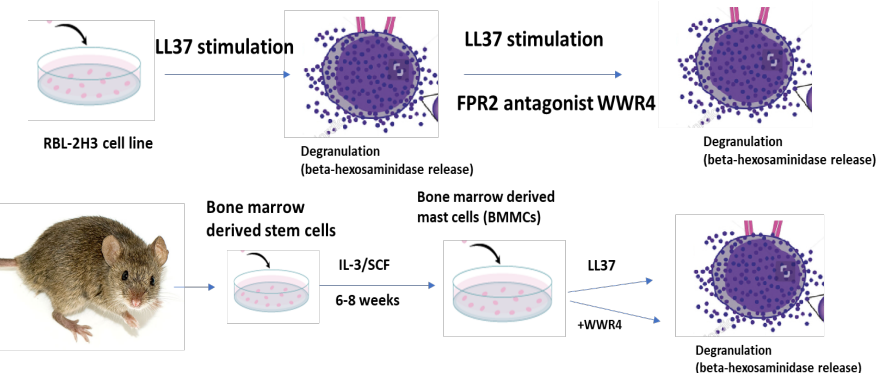


# Antimicrobial Peptide LL-37 Activates Mast Cells Independent of MrgprB2

## Background and Rationale

- Mast cells (MCs) are hematopoietic cells found in the lungs, GI, and skin
- Tightly packed granules with inflammatory mediators
- Human Mast Cell – 2 subtypes
  - MC<sub>TC</sub> contains tryptase and chymase; connective tissue (skin)
  - MC<sub>T</sub> contains chymase; mucosal (lungs, Bone Marrow Derived MC)
- Implicated in allergic reactions via IgE receptor
- IgE-independent pathway via MAS-related G-Protein Coupled Receptor X2 (MRGPRX2; mouse orthologue MrgprB2; expressed in MC<sub>TC</sub>)
- Activated by a wide range of host defense peptides and Food and Drug Administration (FDA) approved peptidergic drugs
- Evidence shows antimicrobial peptide LL-37 activates MC<sub>TC</sub> via MRGPRX2.
- However, it was recently shown that physiological concentration of LL-37 induces degranulation in human lung mast cells (MC<sub>T</sub>, does not express MRGPRX2). This suggests an alternate route of activation by LL-37.
- LL-37 activates FPR2 (N-Formyl Peptide Receptor 2) in other immune cells and there is a possibility that it also activates mast cell FPR2 which is currently unknown.

## Methods and Approach

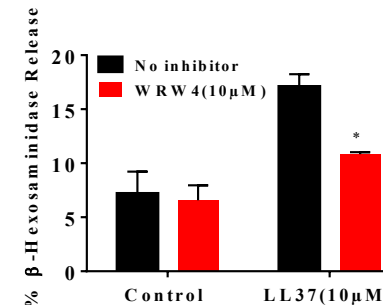
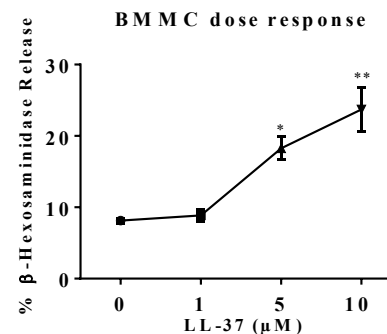
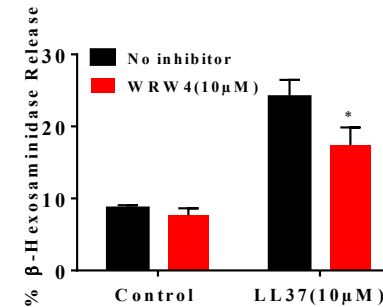
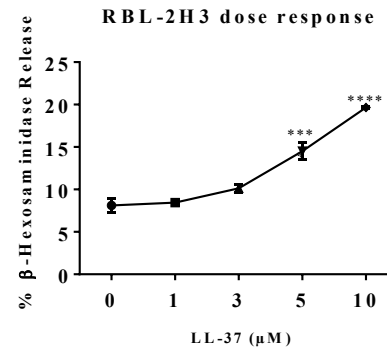


## Research Goal

- Determine if LL-37 activates murine mucosal mast cell (MC<sub>T</sub>) independent of MrgprB2.
- Identify whether LL-37 activates mucosal mast cell via FPR2 receptor

## Preliminary Results

LL-37 induces degranulation both in RBL-2H3 and BMMCs which is inhibited by WRW4.



## Summary

- LL-37 induces degranulation in RBL and BMMC devoid of MRGPRX2/MrgprB2.
- Selective antagonist of FPR2, WRW4, inhibits LL-37 induced degranulation in both RBL and BMMCs.

## Future Steps

- Data suggests LL-37 activates mast cell independent of MRGPRX2/MrgprB2 probably via mast cell FPR2 receptor
- Repeat and validate these preliminary findings
- Translate these findings to *in vivo*

## Significance

- Will help elucidate previously unknown mode of LL-37 induced mast cell activation independent of MRGPRX2

## Acknowledgements

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