# *Influence of lipid composition on membrane activity of antimicrobial polymers*

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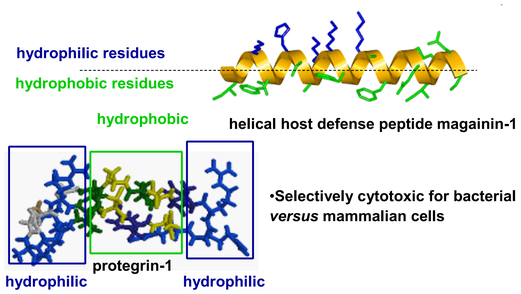
## Introduction

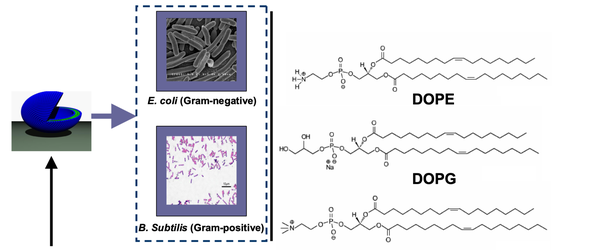
•Natural amphiphilic cationic peptides exhibit antimicrobial activity




•Selectively cytotoxic for bacterial *versus* mammalian cells

Phospholipid membrane composition believed to be critical

## Lipid Story




**•Bacterial Membrane**

•Charge is uniform on the inner and outer surface (leaflet) of the membrane

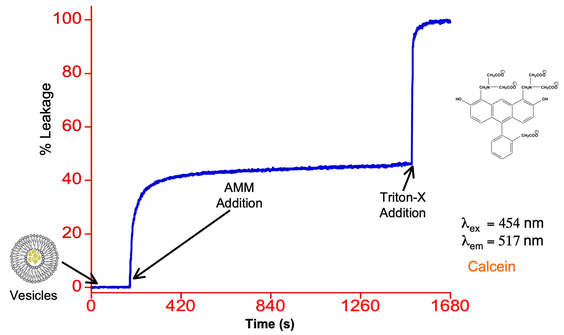
•Contain PE and PG lipids

**Mammalian Membrane**

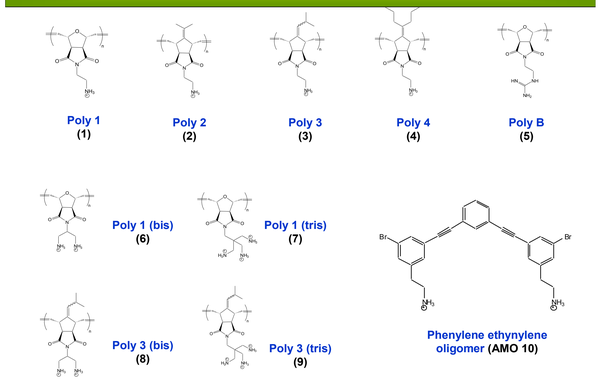
•Asymmetric, outer surface neutral and the inner surface negatively charged

•Rich with PC on the outer surface.

## Dye Leakage Assay



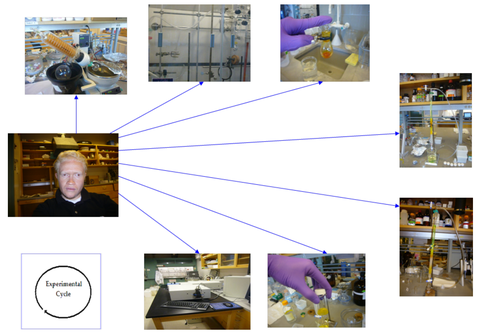

## Antimicrobial Macromolecules



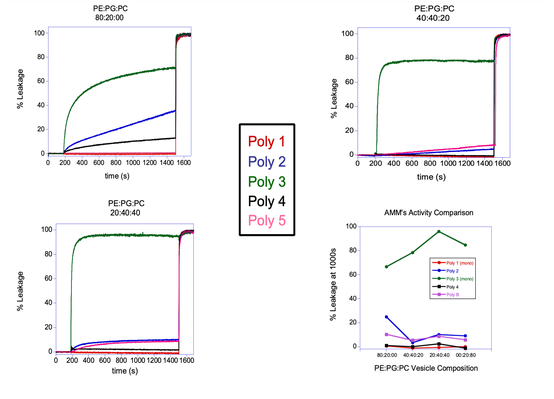

## Bioactivity of Antimicrobial Macromolecules

| Compound | $MIC_{E.\ coli}$ (μg/mL) | $HC_{50}$ (μg/mL) | Selectivity ($HC_{50}/MIC_{(E.\ coli)}$) |
|---|---|---|---|
| AMO (**10**) | 0.1 | 88 | 880 |
| Poly 1 (**1**) | 400 | 2150 | 5.4 |
| Poly 1 (bis) (**6**) | 200 | 2000 | 10 |
| Poly 1 (tris) (**7**) | 150 | 1000 | 6.7 |
| Poly 2 (**2**) | 200 | >4000 | >20 |
| Poly 3 (**3**) | 25.0 | <1 | <0.04 |
| Poly 3 (bis) (**8**) | 15 | 350 | 23.3 |
| Poly 3 (tris) (**9**) | 88 | 450 | 5.1 |
| Poly 4 (**4**) | 200 | <0.005 | <2.5 x $10^{-5}$ |
| Poly B (**5**) | 10 | 538 | 53.8 |

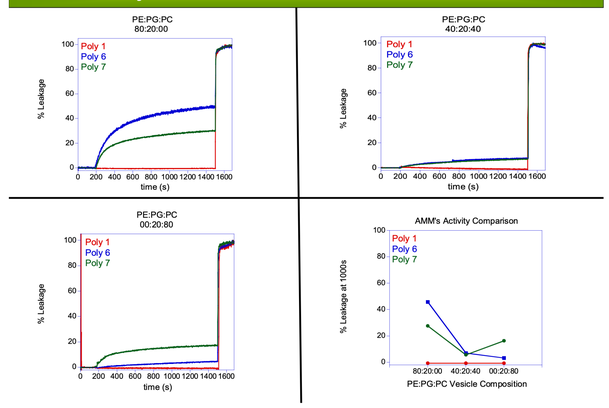
## Experimental Procedures



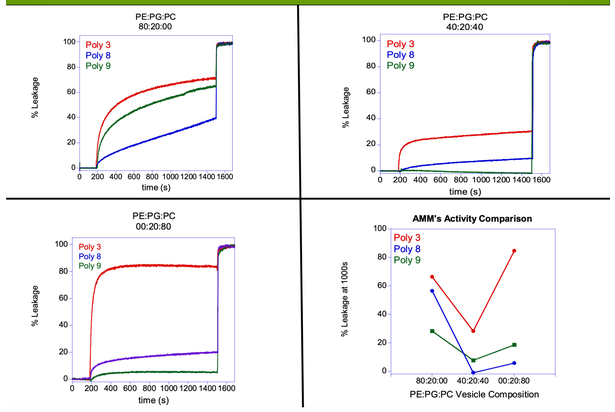

## AMMs with Different Vesicles



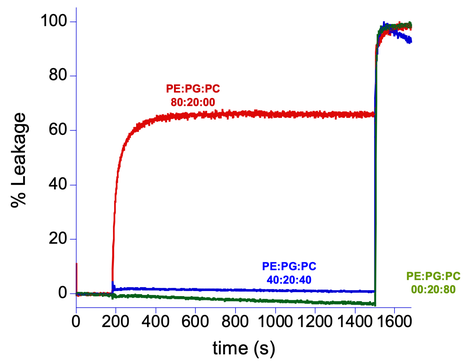

## Poly 1, 6 & 7 with Different Vesicles




## Poly 3, 8 & 9 with Different Vesicles




## AMO 10 with Different Vesicles




## Summary

- **Poly 1, Poly 4** & **Poly 5** remained inactive against all the vesicles studied here.
- **Poly 3** remained equally active against all the vesicles.
- **Poly 1 – 9** and **AMO 10** correlated their biological activity (MIC, $HC_{50}$) with the membrane activity against PE/PG/PC vesicles.
- Certain percentage of **PE** lipids are extremely necessary for the membrane activity of oligomer **10** and some polymers.

## Conclusion

**Lipid type and structure are critically more important than lipid head group charges for selective membrane interactions.**

### Acknowledgment

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