Mucins Enhance Neutrophil Motility

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INTRODUCTION

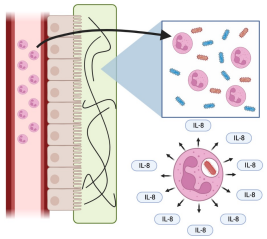
Neutrophils are the most abundant immune cell in the human body, and must exit the bloodstream to locate infection sites.

When they locate an infection, neutrophils phagocytose foreign microbes and secrete chemical signals to recruit nearby neutrophils.

The mucus barrier is a major site of neutrophil activity, acting as the body's first line of defense against foreign microbes.

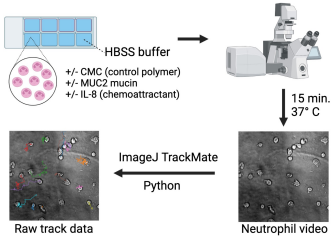
Mucins – the major hydrogel-forming glycoprotein component of mucus – may modify neutrophil motion in ways that have not yet been investigated.

We hypothesized that neutrophils would show less movement in mucin due to its viscous hydrogel-forming properties.



METHODS

We tracked neutrophil trajectories in HBSS buffer with and without the addition of hydrogel-forming CMC polymer or MUC2 mucin. The neutrophil chemoattractant interleukin-8 (IL-8) was sometimes added as well.

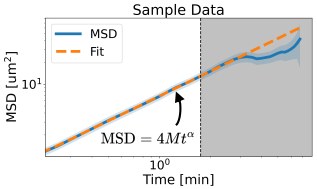


RESULTS

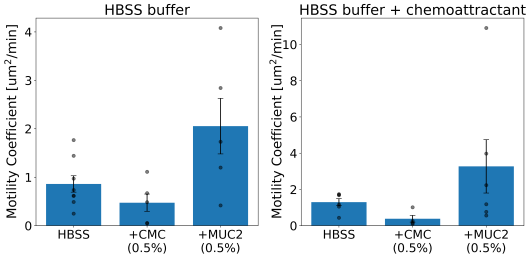
Neutrophil motility increases in mucin. We measure mean square displacement (MSD) to extract a motility coefficient. The motility coefficient measures the area covered by a cell per unit time, and therefore depends on cell speed and persistence. Our result is **characterized by both increased neutrophil speed and persistence in mucin.**

In line with previous literature[1], we assume neutrophils follow a persistent random walk (PRW) model, which describes neutrophils as random walkers with a persistence time dictating the average time that a cell moves straight before switching directions.

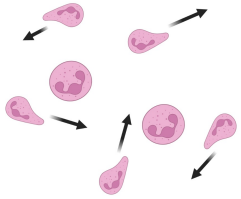
Cell motility increases in mucin but not CMC polymer:



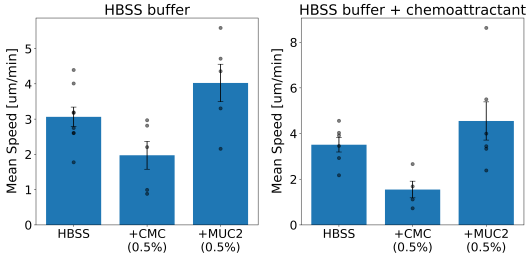
Motility is computed by fitting a line to the first 25% of the MSD curve, since MSD flattens out over time.



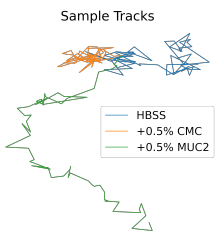
Cell speed increases in mucin but not CMC polymer:

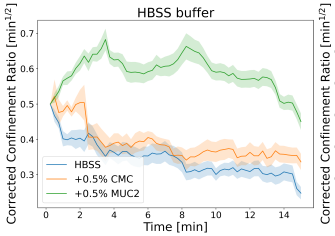


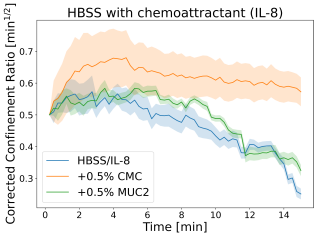
Mean cell speed is taken to be the average of all cell speeds over all consecutive frames.



Cell persistence increases in mucin with no chemoattractant:







$$\mathrm{CCR}(t) = \frac{\text{net displacement}}{\text{total path length}} \cdot \sqrt{t}$$

The confinement ratio serves as a metric for cell persistence, as a larger confinement ratio implies larger cell step sizes.

CONCLUSION

Mucin increases the motility of neutrophils in buffer, caused by an increase in speed and persistence.

The same effect is not seen in hydrogel-forming CMC polymer, indicating that this effect is caused by something other than the hydrogel-forming properties of mucin.

We find that our hypothesis that neutrophils would show less movement in mucin was false. Despite its viscosity, mucin promotes neutrophil movement.

FUTURE DIRECTIONS

Does the PRW model suffice for modeling neutrophil movement? Which other metrics could we use to validate our findings?

Does mucin affect neutrophil directed motion or ability to move towards a signal?

How do other hydrogel-forming polymers such as PEG or collagen influence neutrophil movement?

How do microbe-derived signals influence neutrophil movement?

ACKNOWLEDGEMENTS

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1. Beltman, Joost B et al. "Analysing immune cell migration." *Nature reviews. Immunology* vol. 9,11 (2009): 789-98. doi:10.1038/nri2638