

# Antibody Orientation Matters

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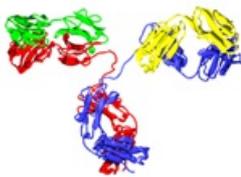


## Antibody Orientation Matters <sup>[1]</sup>

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The orientation of antibody binding to bacteria can mean life or death to the bug, according to a study published in *The Journal of Experimental Medicine* on December 10th. These findings may help explain why these bacteria cause millions of localized infections, but more serious, systemic blood infections are rare.

*Streptococcus pyogenes* -- the causative agent of strep throat -- typically invades the body's mucosal surfaces, including the throat and skin. These invasions are kept in check by Y-shaped immune proteins called antibodies, which attach to the bug via their arm (or "Fab") regions. This exposes the stalk ("Fc") portion of the antibody, which is then recognized by immune cells, allowing them to ingest and kill the bacteria. Certain bacteria, including *S. pyogenes*, fight back by expressing surface proteins that bind the Fc region of antibodies, rendering them invisible to patrolling immune cells.

The new study by Pontus Nordenfelt of Harvard University and his colleagues at Lund University in Sweden suggests that the bacteria have the upper hand in the mucosa, but the immune system wins out in the blood. The scientists found that antibodies in saliva attached to bacteria primarily via their Fc regions, but in blood the orientation was reversed, resulting in swift killing of the bug by immune cells.

The orientation of binding was dictated by the local antibody concentration -- low antibody levels (as in saliva) favored Fc-mediated binding; high antibody levels (as in blood) favored Fab-mediated binding. How this works is not entirely clear, but it's possible that the Fc binding proteins on the bacteria become saturated in the high-antibody environment of the blood, permitting free antibody to bind in the opposite orientation.

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