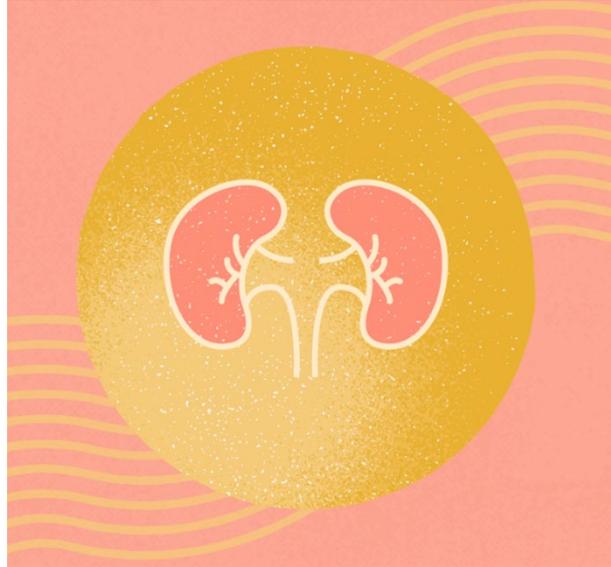
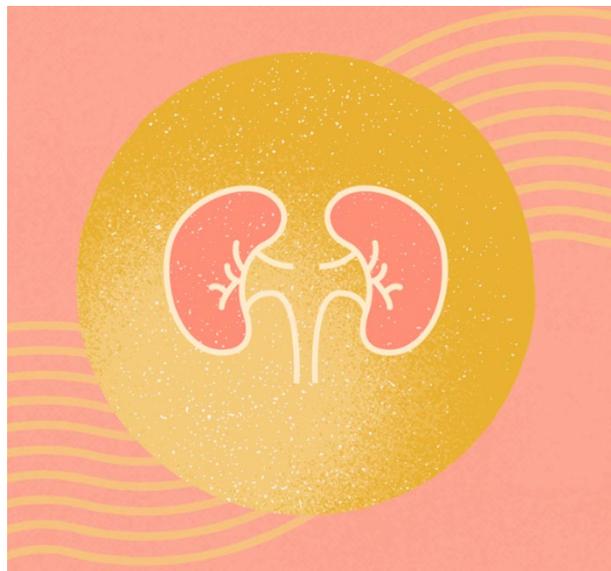


C3G and Complement



C3G and Complement



...what goes wrong???

Goals –

1. To understand what happens when complement is not properly controlled
2. To understand how we identify disease drivers
3. To understand how two recently approved AP blockers work
4. To understand how precision medicine may help you

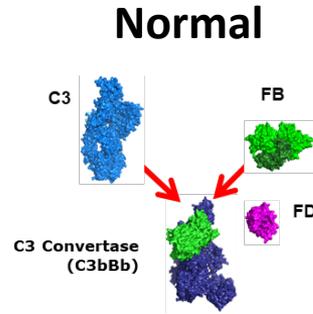
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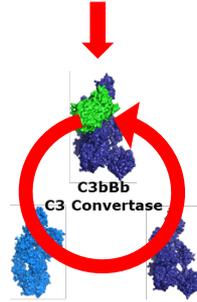
Alternative Pathway



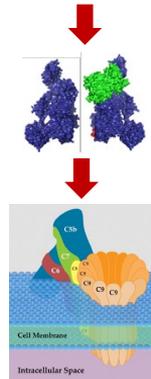
Phase 1
Initiation



Phase 2
Amplification loop



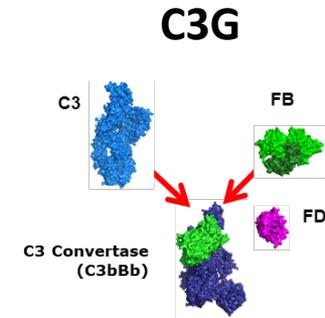
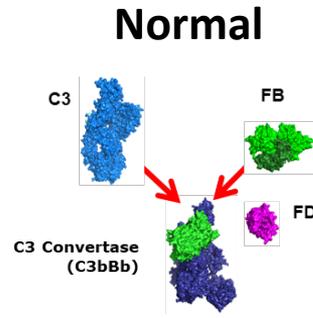
Phase 3
Terminal pathway



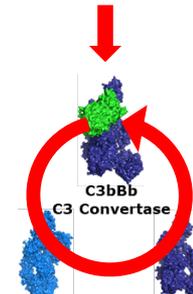
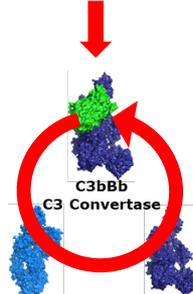
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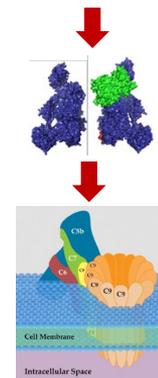
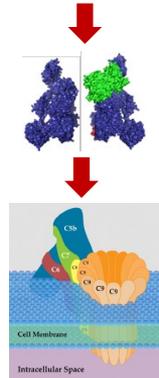
Phase 1
Initiation



Phase 2
Amplification loop



Phase 3
Terminal pathway



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The Four Pillars



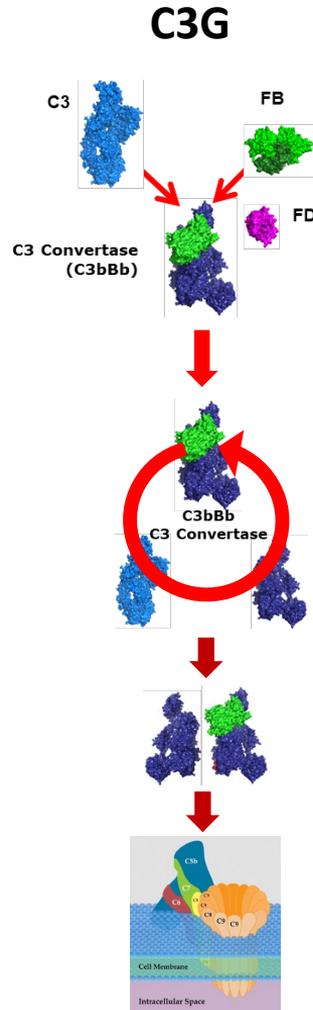
Alternative Pathway



Phase 1
Initiation

Phase 2
Amplification loop

Phase 3
Terminal pathway



Increased activity can be driven by GENETIC mutations or antibodies (which we call NEPHRITIC FACTORS). In some people, we don't know what drives disease. This is an active area of investigation.

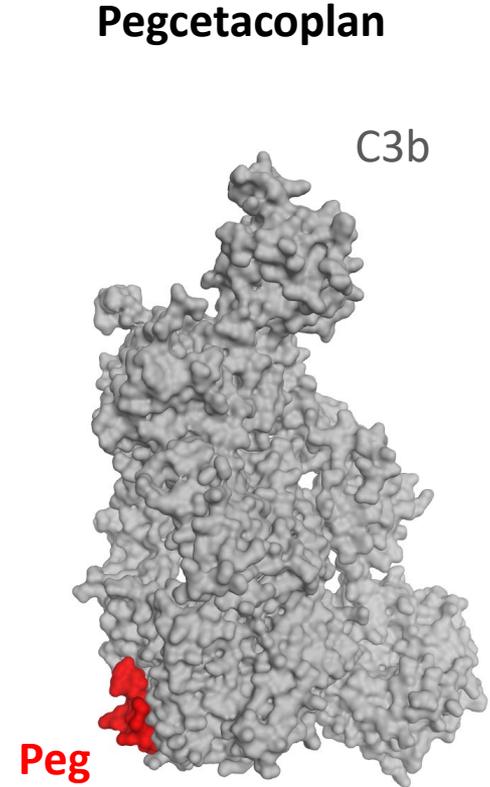
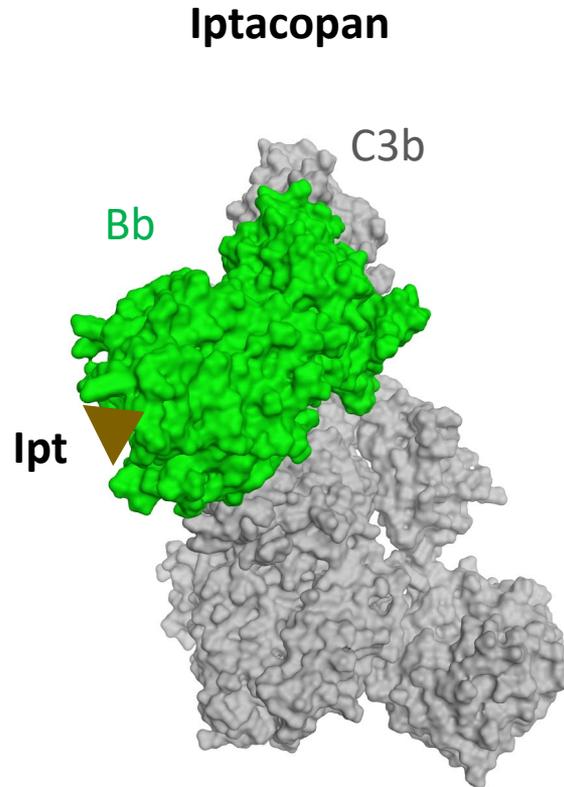
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C3G Specific Therapies



- **Iptacopan (Anti-FB)**
 - Oral FB inhibitor
 - Blocks C3 convertase activity
 - FDA-approved for C3G: March 2025
- **Pegcetacoplan (Anti-C3)**
 - Subcutaneous infusion
 - Binds C3/C3b, prevents C3 cleavage
 - FDA-approved for C3G: July 2025



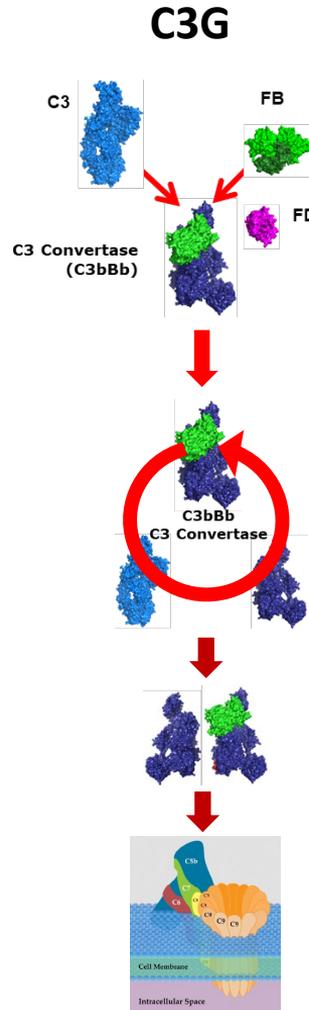
Alternative Pathway



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Initiation

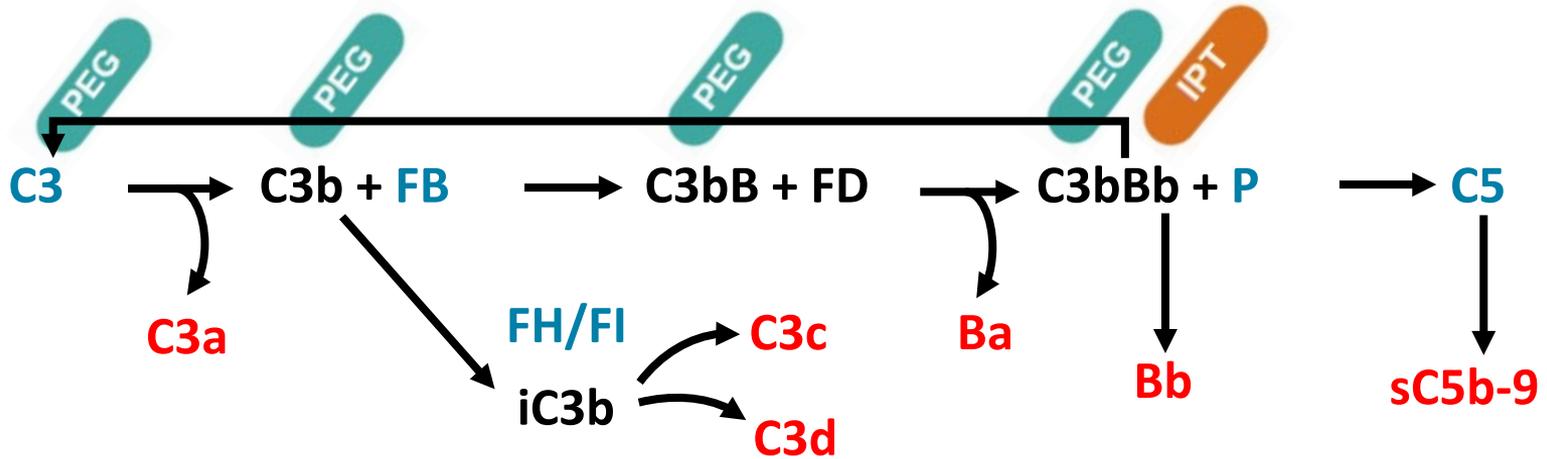
Phase 2
Amplification loop

Phase 3
Terminal pathway



ALL AP activity is STOPPED
with Iptacoplan and
Pegcetacoplan.

Iptacopan and Pegcetacoplan



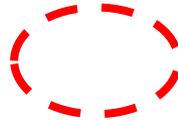
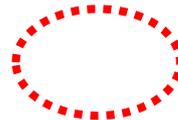
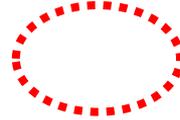
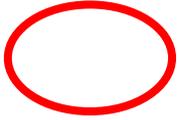
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Unique Signatures



Unique Signatures



Different effects on C3 and properdin may help identify patient subtypes and guide personalized therapy



The MORL Renal Group provides unrivaled expertise in complement diagnostics for patients with C3G and the TMAs.

Thank you to the persons with C3G who trust us with their care, providers who reach out to us for guidance, and the NIH for supporting our research.