NMO Breakout Session

2024 RNDS SRNA

DEAN WINGERCHUK, MD

PETER SGUIGNA, MD

TAMMY SMITH, MD PHD

Disclaimer

We cannot provide personal medical advice, but as Neurologists who treat patients with NMO and other immune-mediated neurologic diseases, we are ready to discuss in partnership with YOU so we can all learn from each other.

Overview

- Clinical criteria, diagnosis
- Diagnostic testing
- FDA-approved treatments and off-label treatments
- Future immunotherapies
- Symptom management
- Important things to talk to your doc about
- Building a multidisciplinary care team

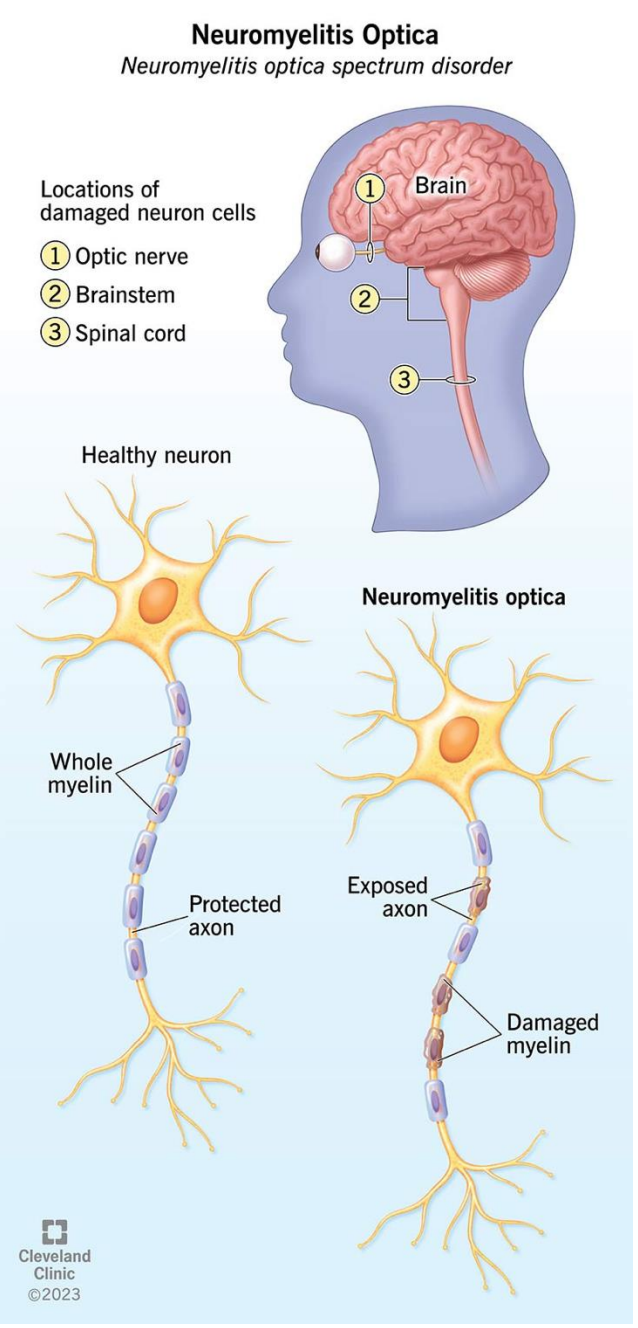
Overview- This Time is for YOU

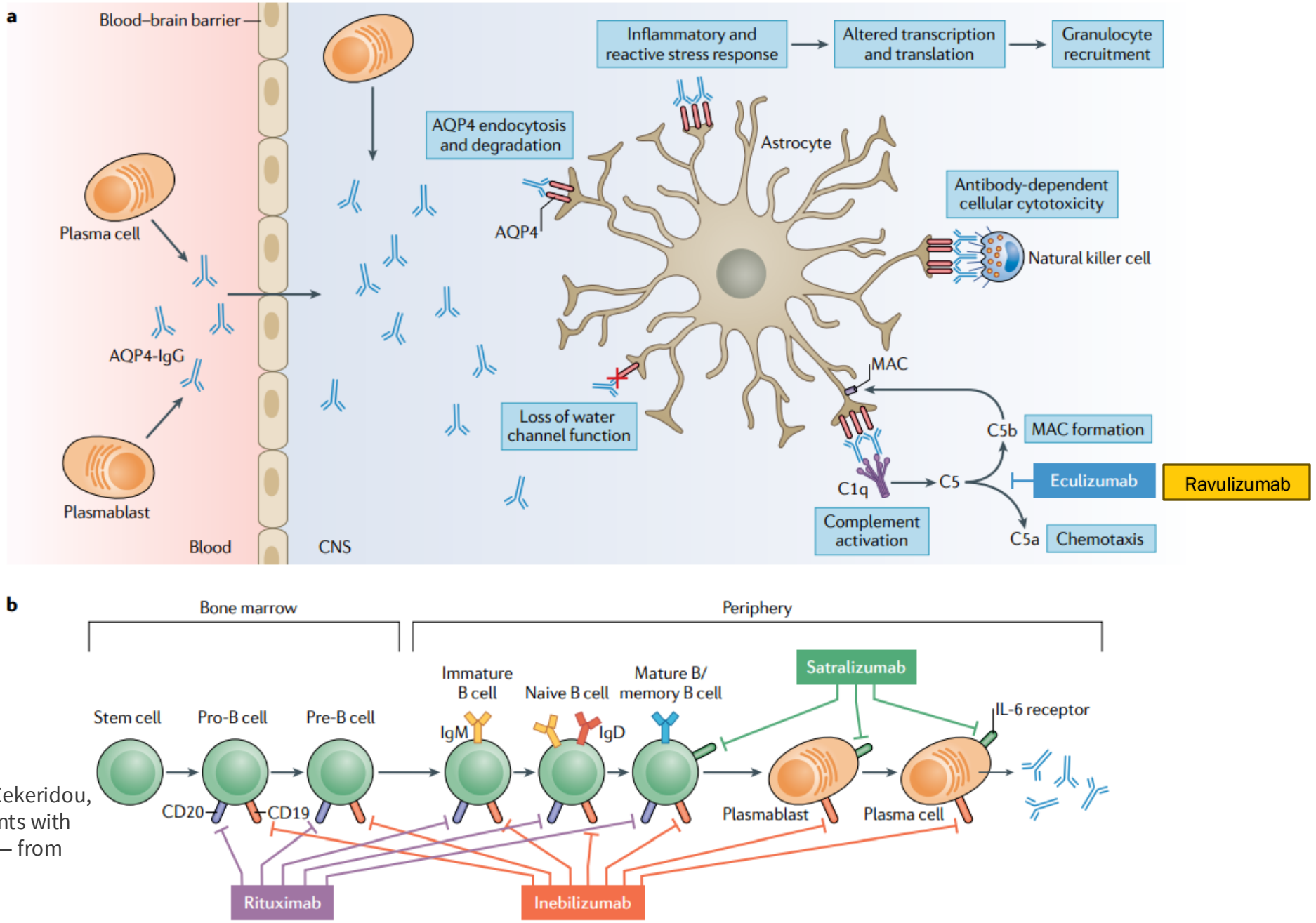
- Clinical criteria, diagnosis
- Diagnostic testing
- FDA-approved treatments and off-label treatments
- Future immunotherapies
- Symptom management
- Important things to talk to your doc about
- Building a multidisciplinary care team

Tell us what you want to cover!

Clinical Criteria, Diagnosis

- Optic neuritis
- Acute myelitis
- Area postrema syndrome
- Acute brainstem syndrome
- Symptomatic narcolepsy or acute diencephalic syndrome w/typical MRI
- Symptomatic cerebral syndrome w/ typical MRI





Adapted from: Pittock, Sean J., Anastasia Zekeridou, and Brian G. Weinshenker. “Hope for Patients with Neuromyelitis Optica Spectrum Disorders — from Mechanisms to Trials.” *Nature reviews. Neurology* 17.12 (2021): 759–773.

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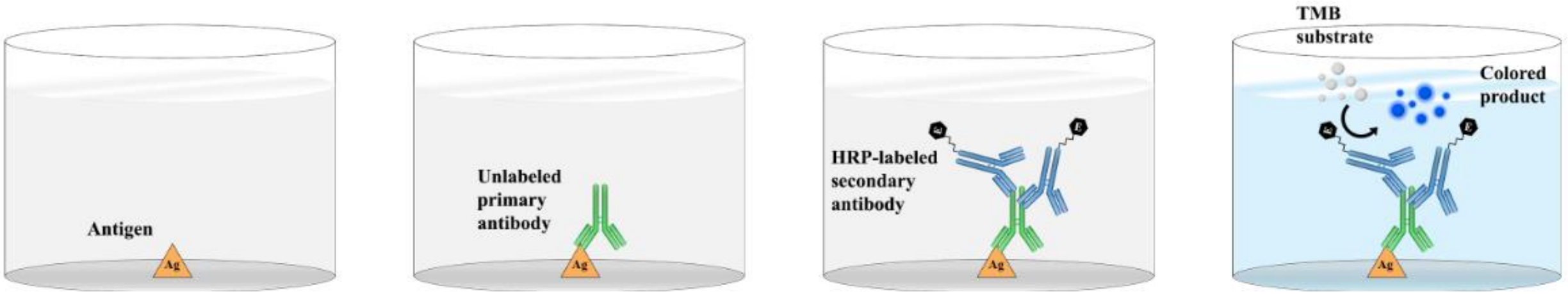
2015 Wingerchuk Criteria

- If AQP4+ by best available method (CBA)
  - ❑≥1 core clinical characteristic
  - ❑Alternatives excluded
- If AQP4- or unknown and ≥2 core clinical characteristics in one or more attacks
  - ❑At least one of ON, LETM, or AP syndrome
  - ❑Dissemination in space
  - ❑MRI criteria
  - ❑Alternatives excluded

Diagnostic Testing

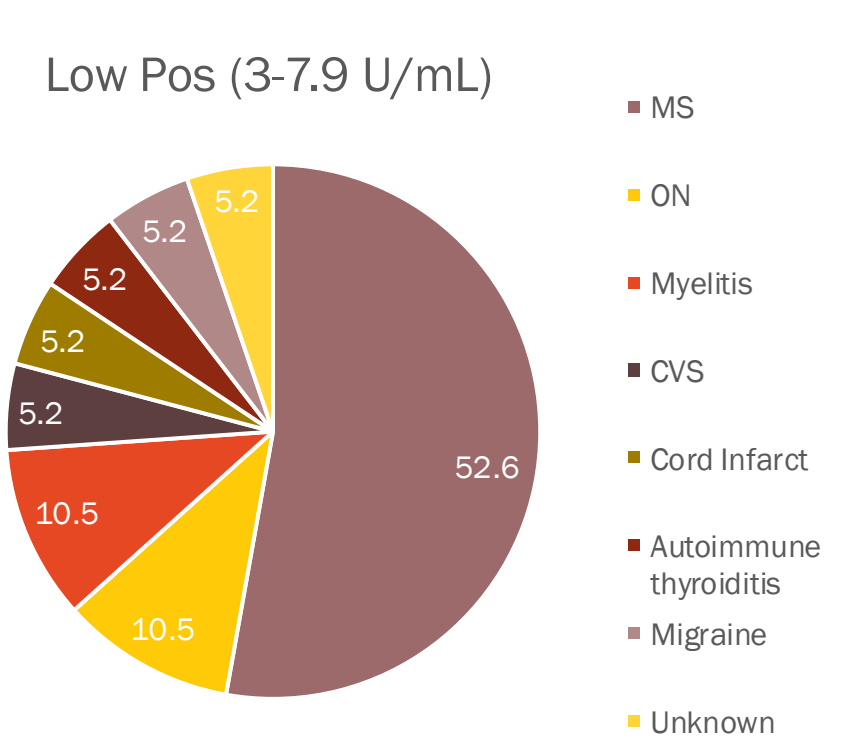
ELISA

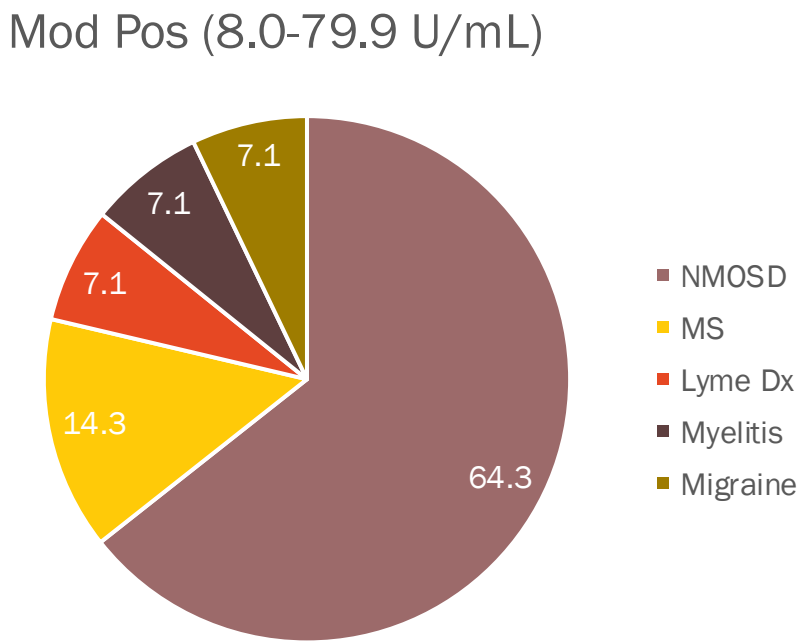


Adapted from aatbio.com

Issues with specificity (false positives) at low positive values make this a lousy option for modern testing

AQP4 (ELISA) is not the recommended diagnostic test for NMO



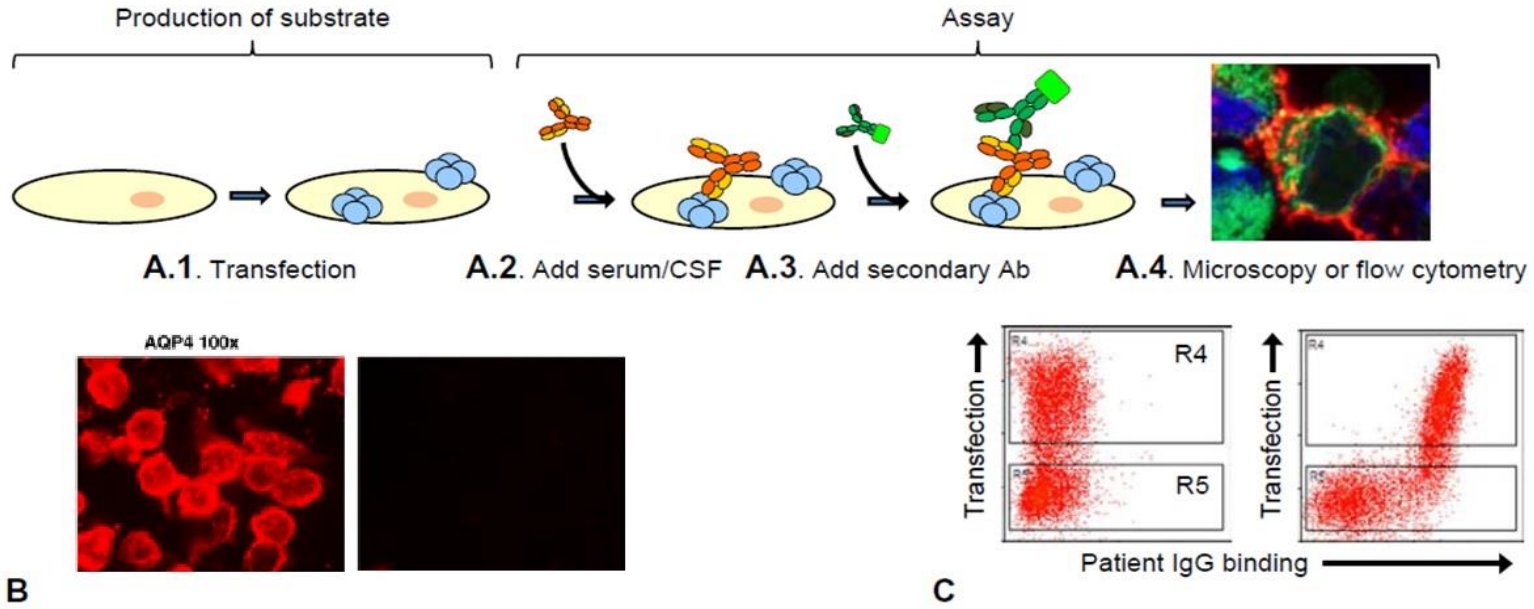


>80 U/mL 100% specific for NMOSD

Adapted from
doi: 10.1155/2021/8692328

Diagnostic Testing- Cell Based Assays are Preferred!

Cell-based assays



Both live and fixed assays have excellent sensitivity and specificity for AQP4; know where and how your testing was done to enable interpretation in the future.

Adapted from Waters et al. Handbook of Clinical Neurology, Vol. 133, Chapter 9, pgs.147-163 and doi:10.1111/cen3.12107

Diagnosis Confirmed- What now?

PREVENTING RELAPSES WITH IMMUNOTHERAPY: HOW TO CHOOSE!

- Risk of immunosuppression vs risk of relapse
- Vaccination history
- Family Planning
- Cost
- Convenience (dosing and monitoring)

BUILDING A CARE TEAM TO PARTNER WITH YOU

- Neurologist
- PT/OT/Rehab docs
- Medical specialists (sleep, urology, GI, pain, psychistry)

Immune Modulating Treatments

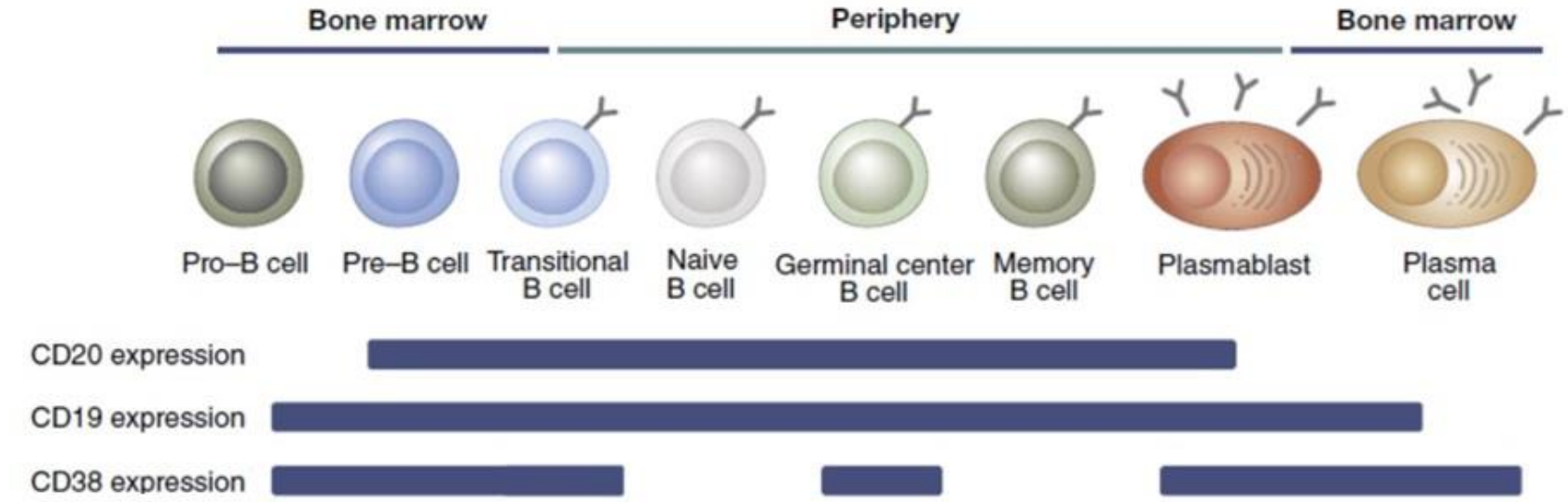
FDA-Approved

- Eculizumab
- Inebilizumab
- Ravulizumab
- Satralizumab

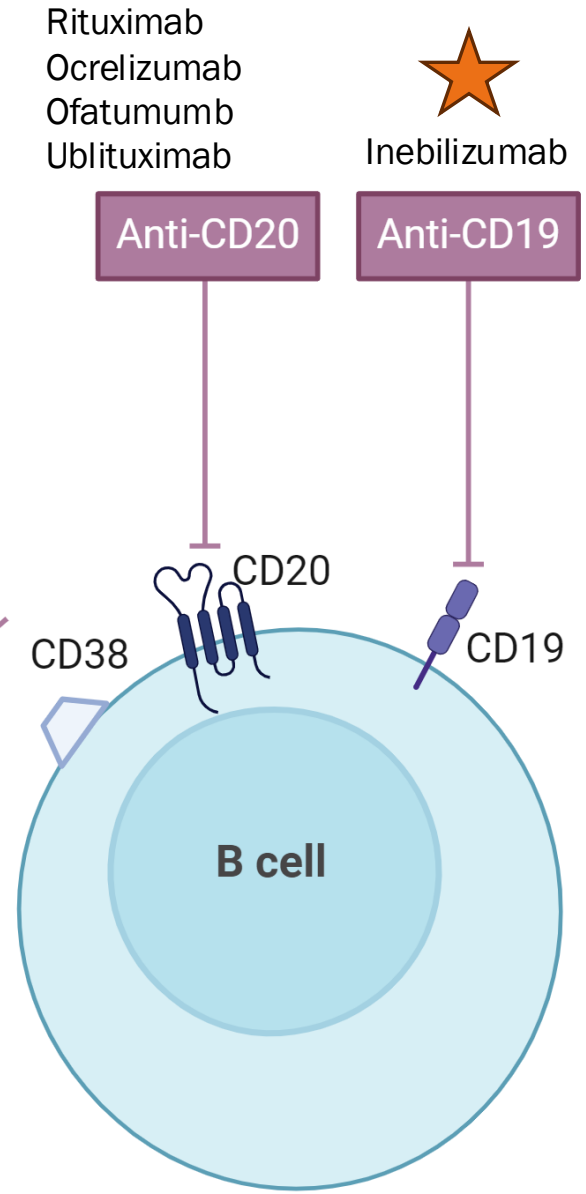
Off-label

- Rituximab
- Azathioprine
- Mycophenolate

B-cell Depleting Therapies



Adapted from https://doi.org/10.1016/j.kint.2019.12.025



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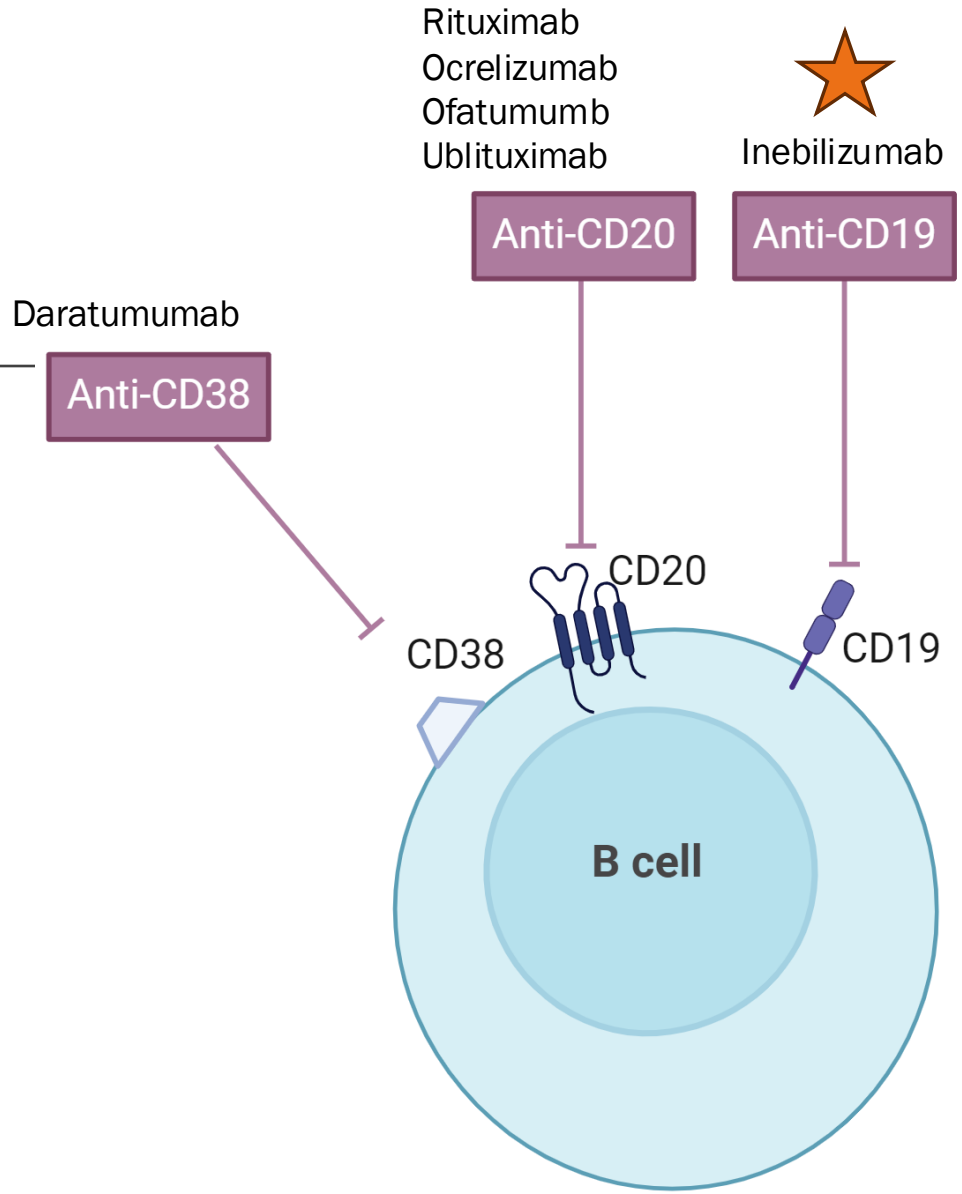
FDA-Approved for NMOSD

B-cell Depleting Therapies

- Infusion every 6 months (after initial dose at 0, 2weeks)
- Common side effects: nausea, joint aches, headache, back pain
- Infections: URI, UTI, HepB reactivation, opportunistic infections (including PML)
- Risks: Infusion-related reactions, lymphopenia, neutropenia, hypogammaglobulinemia
- Monitor CBC with differential, serum immunoglobulins, CD19/20 B-cell counts



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FDA-Approved for NMOSD

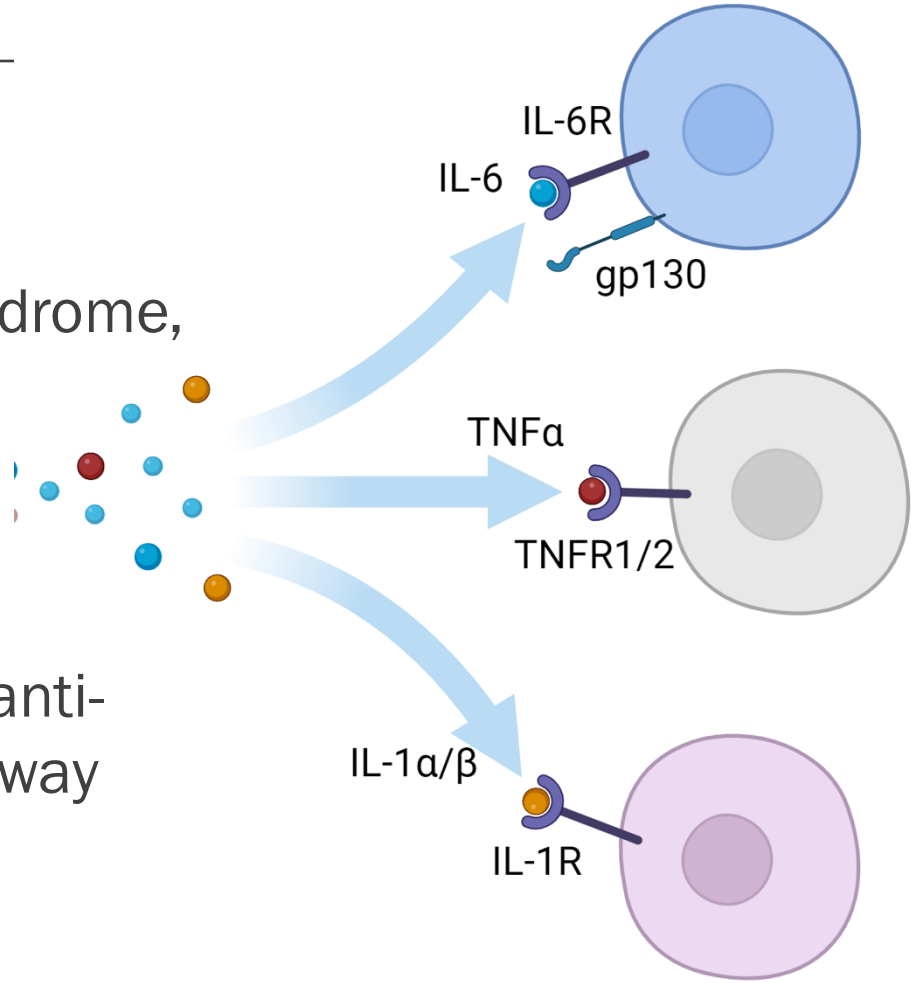
IL-6 Receptor Inhibitors

Tocilizumab

- Used for cytokine release syndrome, systemic autoimmunity

Satralizumab ★

- Approved for NMOSD
- Clinical trial in anti-LGI1 and anti-NMDAR encephalitis is underway (CIELO)



IL-6 signaling can promote B cell survival, stimulate antibody production, support helper T cell proliferation and differentiation, and increase BBB permeability

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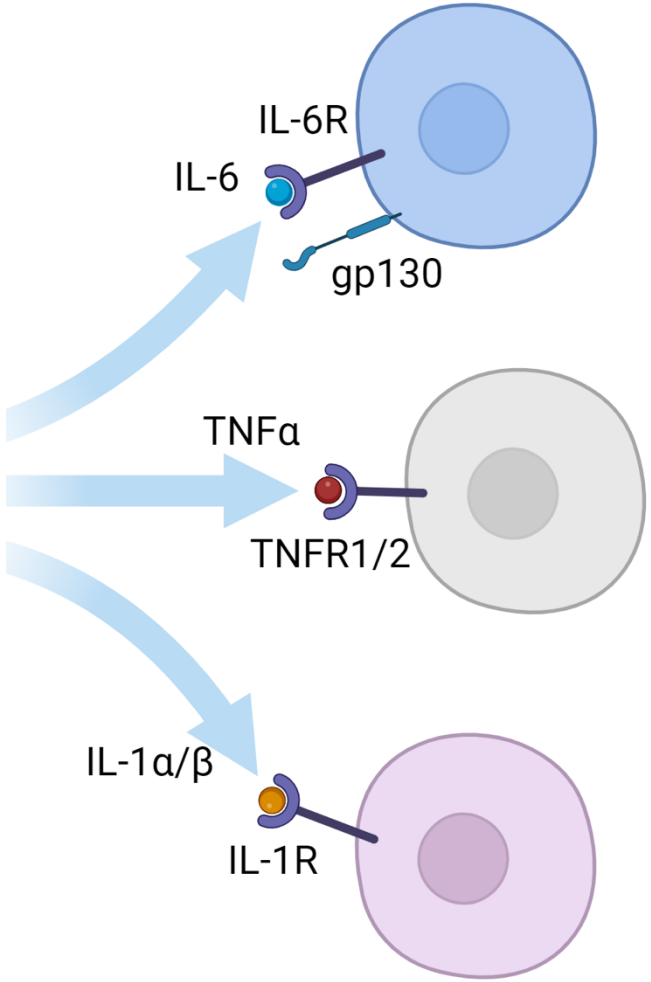
IL-6 Receptor Inhibitors

Satralizumab

- SQ dosing every 4 weeks (after 0, 2, 4)- self administered!
- Common side effects: injection-related reactions, headache, joint aches
- Associated with mild to moderate infections
- Risks: low neutrophils, low platelets, elevated liver enzymes, elevated cholesterol, decrease C3/C4/fgn
- Monitor with CBC with differential, liver enzymes, lipids



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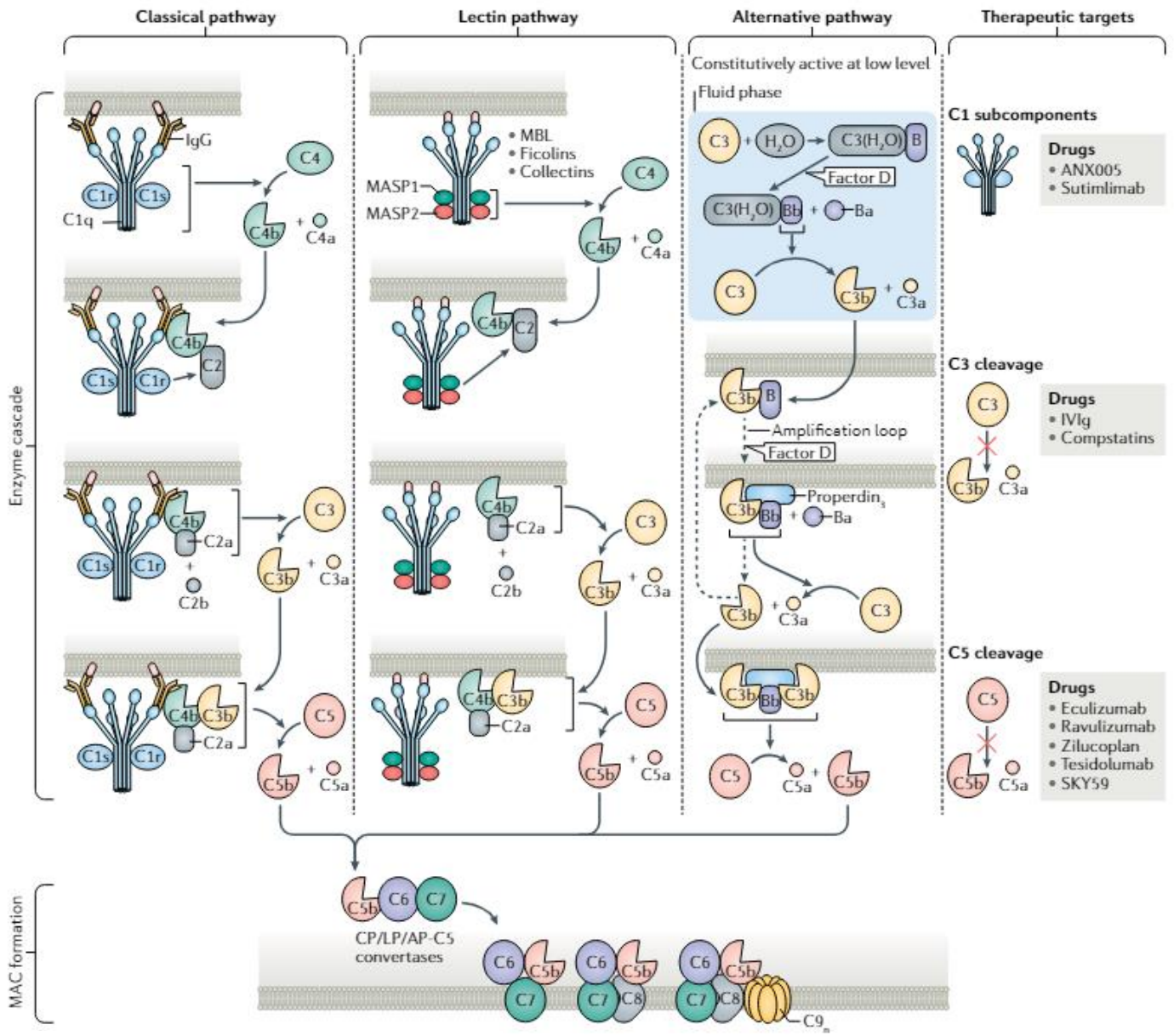
C5 Inhibitors

Block the cleavage of C5 into

- C5a- proinflammatory factor
- C5b- part of the MAC

Eculizumab and Ravulizumab, infusion monoclonal abs ★

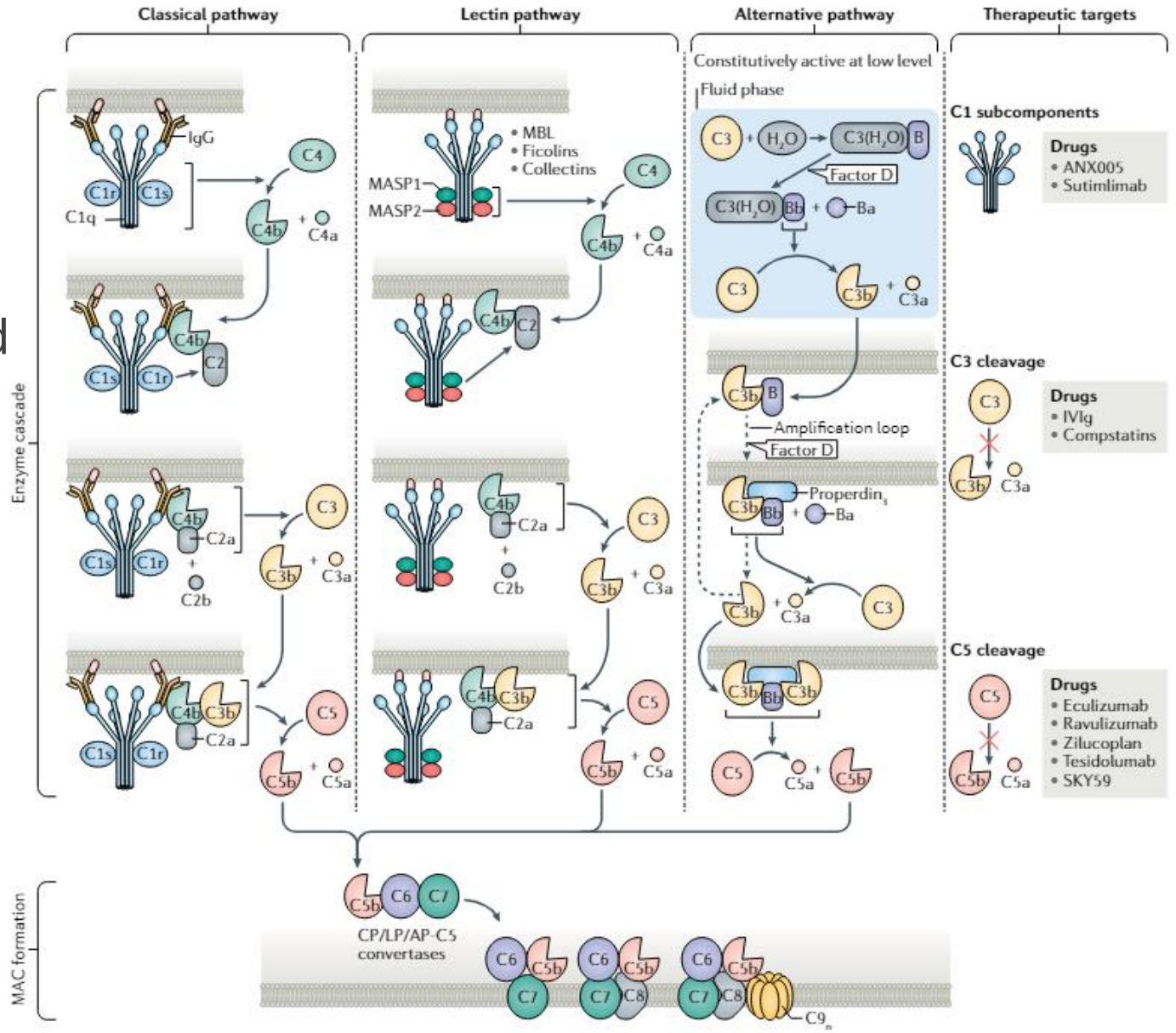
Zilucoplan is a peptide inhibitor of C5, subQ injection



https://doi.org/10.1038/s41582-020-0400-0

C5 Inhibitors

- Eculizumab: infuse Q2w after initial load
- Ravulizumab: infuse Q8w after initial load
- Common side effects: headaches, URI
- Serious infection risk: meningococcal infections- REMS!
- Risks: anemia, leukopenia, fungal infections, infusion-related reactions
- Monitoring: CBC with differential



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Symptom Management

Physical disabilities

Visual impairment

Pain

Fatigue

Bowel/bladder

Cognition, concentration

Sleep

Psychological

Build Your Care Team To Address ALL of Your Concerns

Physical disabilities

Visual impairment

Pain

Fatigue

Bowel/bladder

Cognition, concentration

Sleep

Psychological

Future Therapies and Research

- Biomarkers to predict relapse
- Stem Cell Transplant, CAR T-cell therapy targeting B-cell antigens (CD19, BCMA), Telitacicept, bortezomib, BTK inhibitors, FcRn inhibitors, immune tolerance therapies- STAY TUNED!
- We need more data from long-term registries, patient-reported outcome measures, and partnerships between clinicians, scientists, and people living with rare diseases