Complement Factor I (CFI) as a protease medicine: engineered new therapeutics for complement-mediated disorders

Natacha Le Moan, Ph.D. | Executive Director

9 September 2021

CATALYST BIOSCIENCES

Forward-looking statements

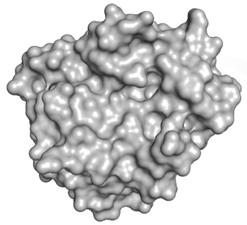
Certain information contained in this presentation and statements made orally during this presentation include forward-looking statements that involve substantial risks and uncertainties. All statements included in this presentation, other than statements of historical facts, are forward looking statements. Forward-looking statements include, without limitation, statements about the product candidates of Catalyst Biosciences, Inc. (the “Company”) and the benefits of its protease engineering platform; the potential markets for and advantages of the Company's complement product candidates, including C3b and C4b degraders; the ability of the ProTUNE™ platform to generate these or other product candidates; and the potential for C3b and C4b degraders to treat human disease. Actual results or events could differ materially from the plans, intentions, expectations and projections disclosed in the forward-looking statements. Various important factors could cause actual results or events to differ materially, including, but not limited to, the risk that pre-clinical studies may be delayed as a result of COVID-19 and other factors, that C3b and C4b degraders are not yet in human clinical trials and will require additional manufacturing validation and pre-clinical testing before entering human clinical trials, the risk that human clinical trial will not replicate the results of studies in mice or other animals, competition and other risks described in the “Risk Factors” section of the Company’s Annual Report on Form 10-K filed with the Securities and Exchange Commission ("SEC") on March 4, 2021, on Form 10-Q filed with the SEC on August 5, 2021, and in other filings with the SEC. The forward-looking statements in this presentation represent the Company's view as of the date of this presentation and the Company does not assume any obligation to update any forward-looking statements, except as required by law.

CATALYST BIOSCIENCES

Catalyst discovery platform of proteases

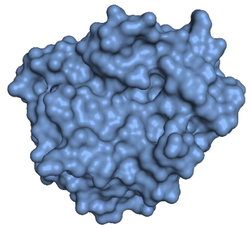
Unique design of optimized & differentiated protease candidates

Natural protease



- Structure Guided Design – Molecular evolution
- Modulate biological activation or inactivation
- Pharmacokinetic Improvement

Optimized protease candidate

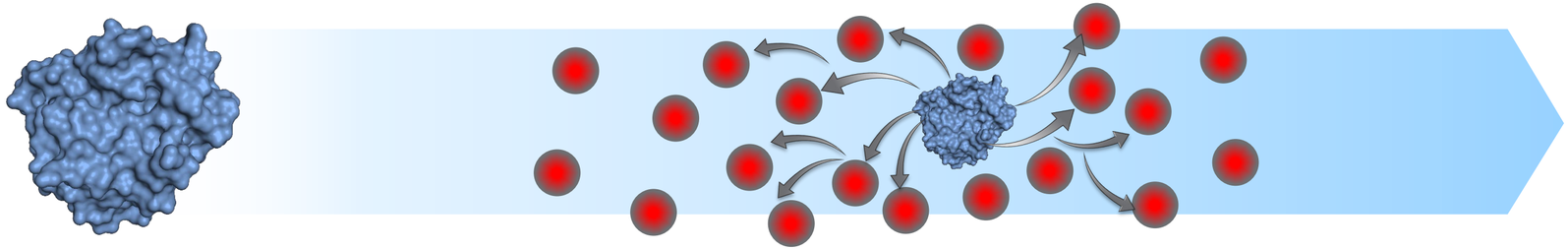


CATALYST BIOSCIENCES

Therapeutic advantage of proteases in regulating biological cascades

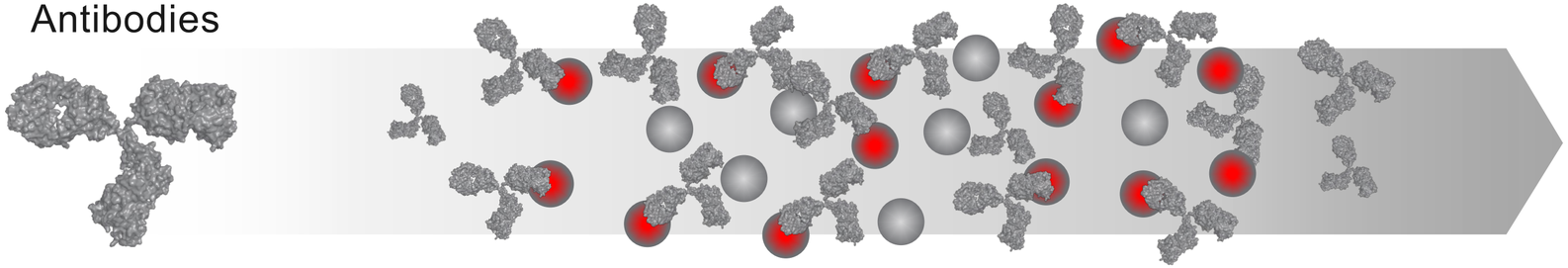
Protease

Therapeutic neutralization of target



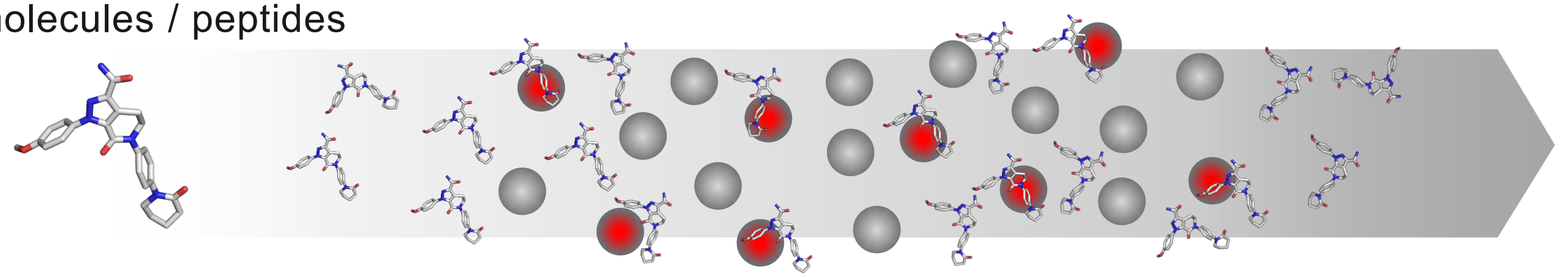
Efficient regulation at low concentrations of therapeutic protease

Antibodies



Requires high concentrations in excess of the target

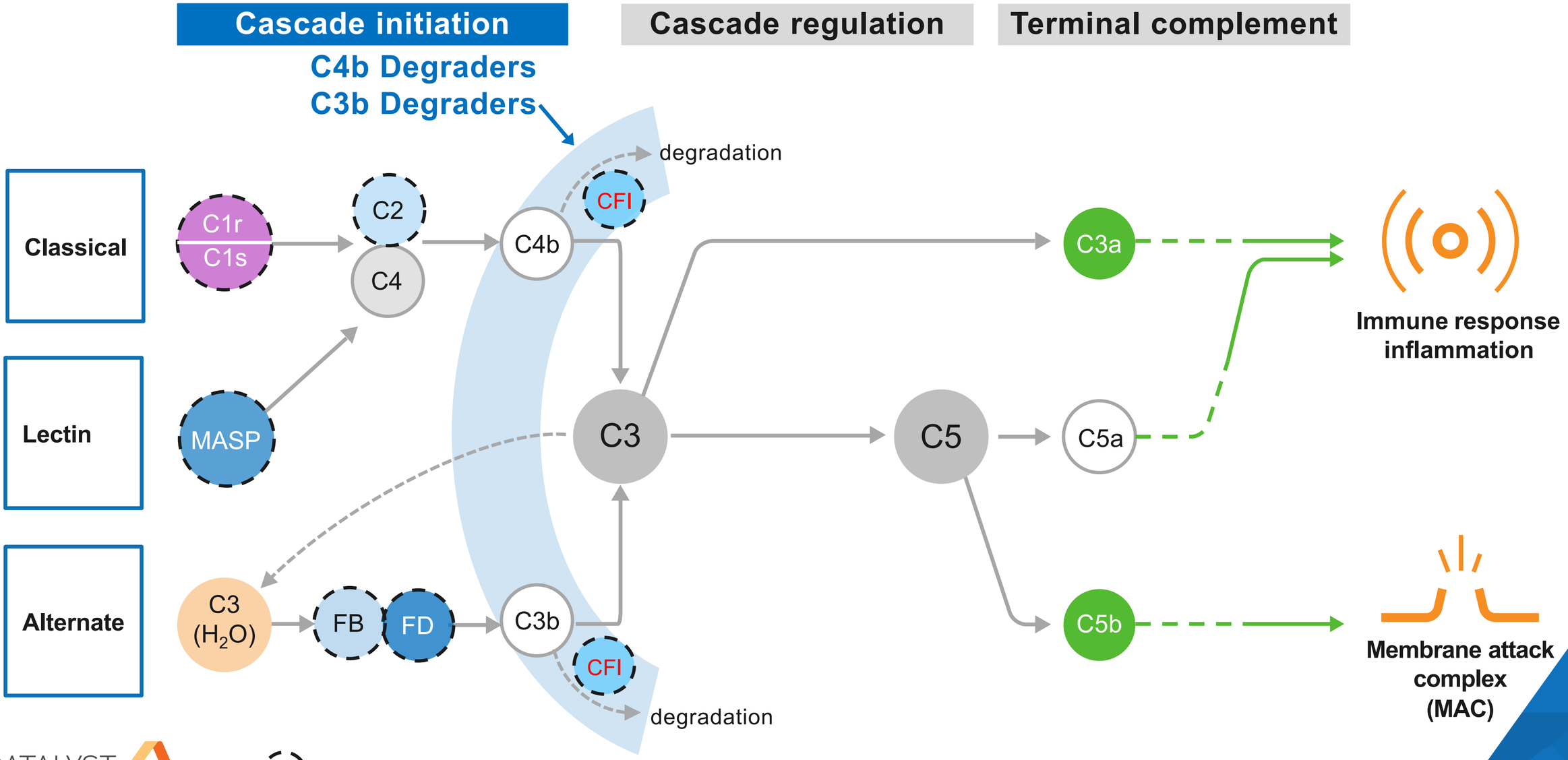
Small molecules / peptides



Requires high concentrations & frequent dosing

CATALYST BIOSCIENCES

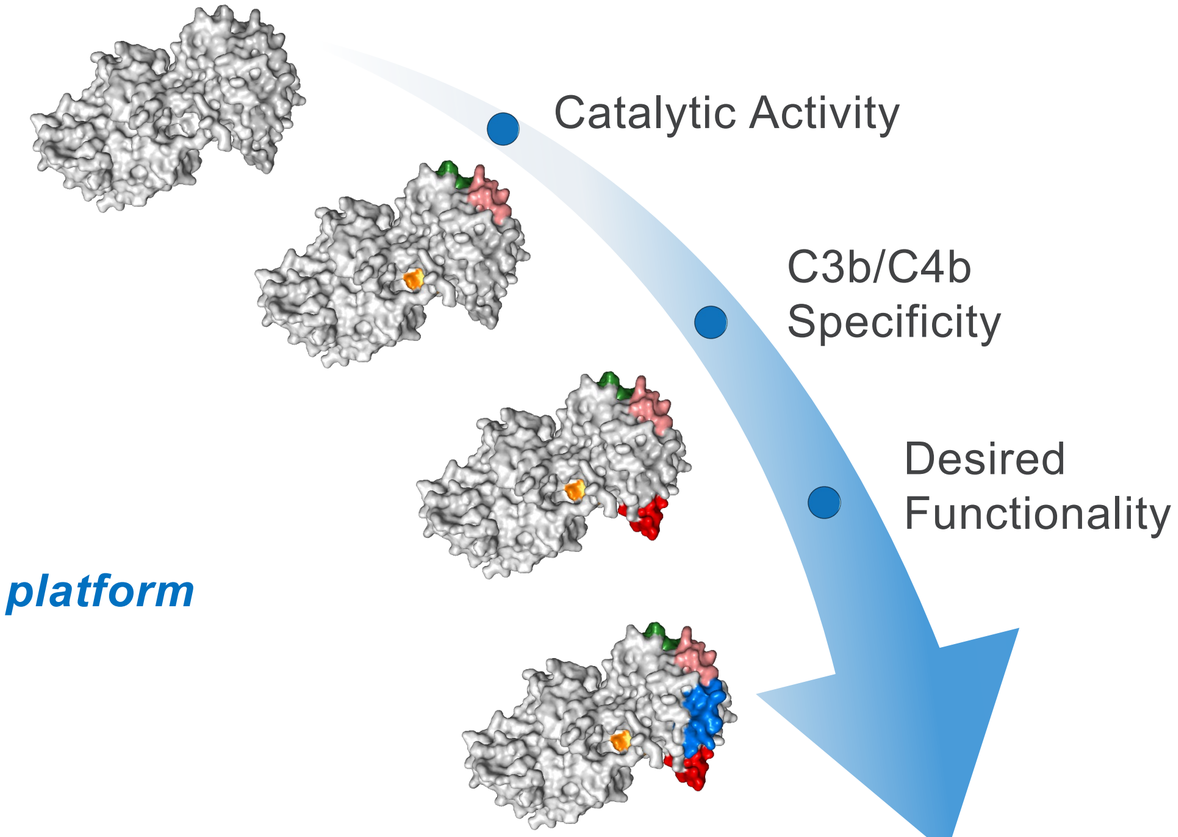
C3b-C4b degraders – unique approach to complement regulation



Dialing catalytic power & specificity into Complement Factor I (CFI)

Engineering C3b & C4b degraders from CFI

Complement Factor I



ProTUNE™ platform

Tuned C3b-C4b Degraders

Precision CFI Therapeutics

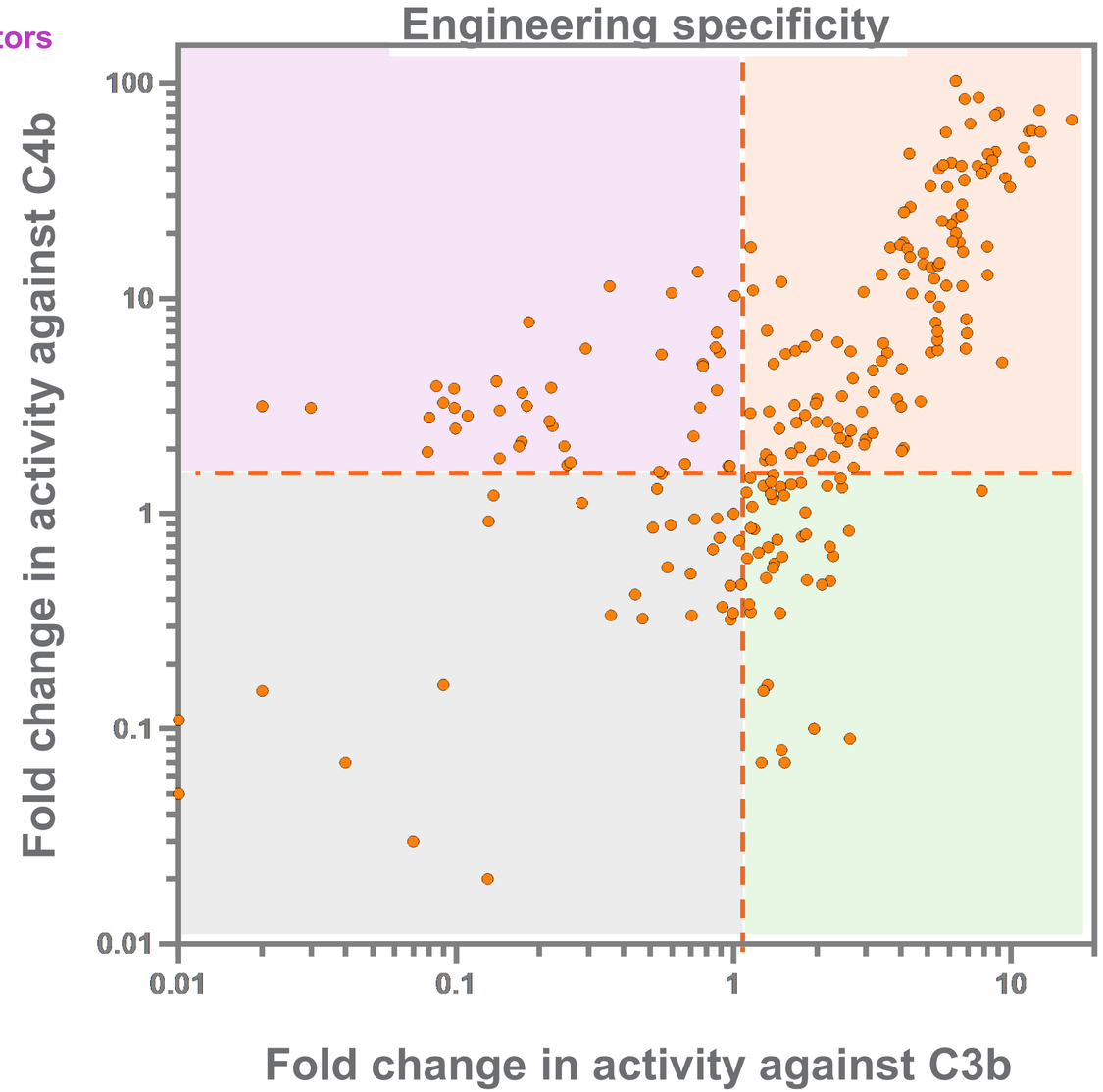
- Tunable **potency** to **control dysregulated** complement
- Tunable **specificity** toward C3b & C4b to restore the **right** balance to complement

CATALYST BIOSCIENCES

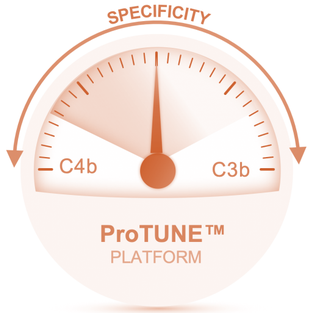
Using ProTUNE™ engineering platform to tune C3b & C4b degraders

Classical-Lectin pathway specific regulators

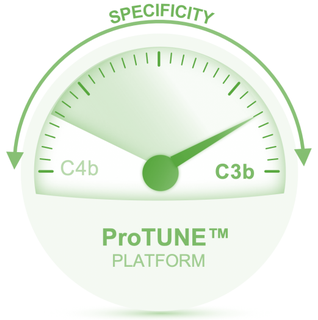
ProTUNE™ platform allows precision medicine



Dual regulators



Alternative pathway specific regulators



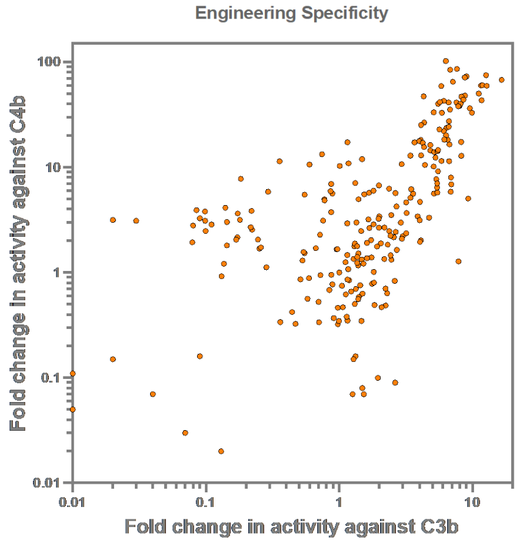
CATALYST BIOSCIENCES

Screening strategy for complement therapeutics

In vitro assays and *in vivo* models are used to evaluate C3b & C4b degraders

~1200 variants

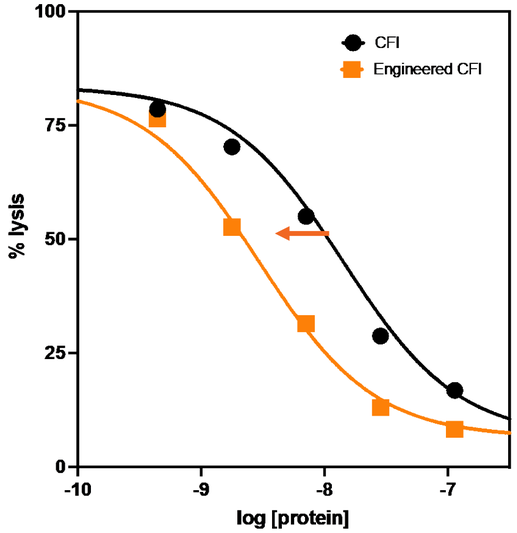
+ In vitro cleavage of C3b & C4b fragments by ELISA



Measure cleavage fragments of C3b (iC3b) and C4b (C4c)

~30 variants

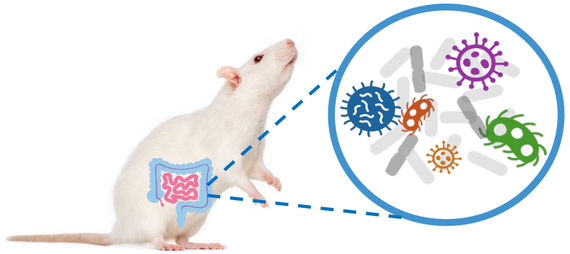
+ Hemolysis inhibition



Measure inhibition of red blood cell lysis

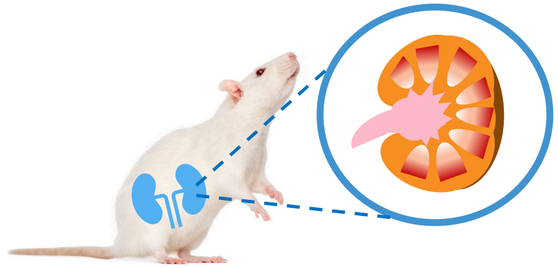
~10 variants

+ In vivo activity in **acute** rodent models



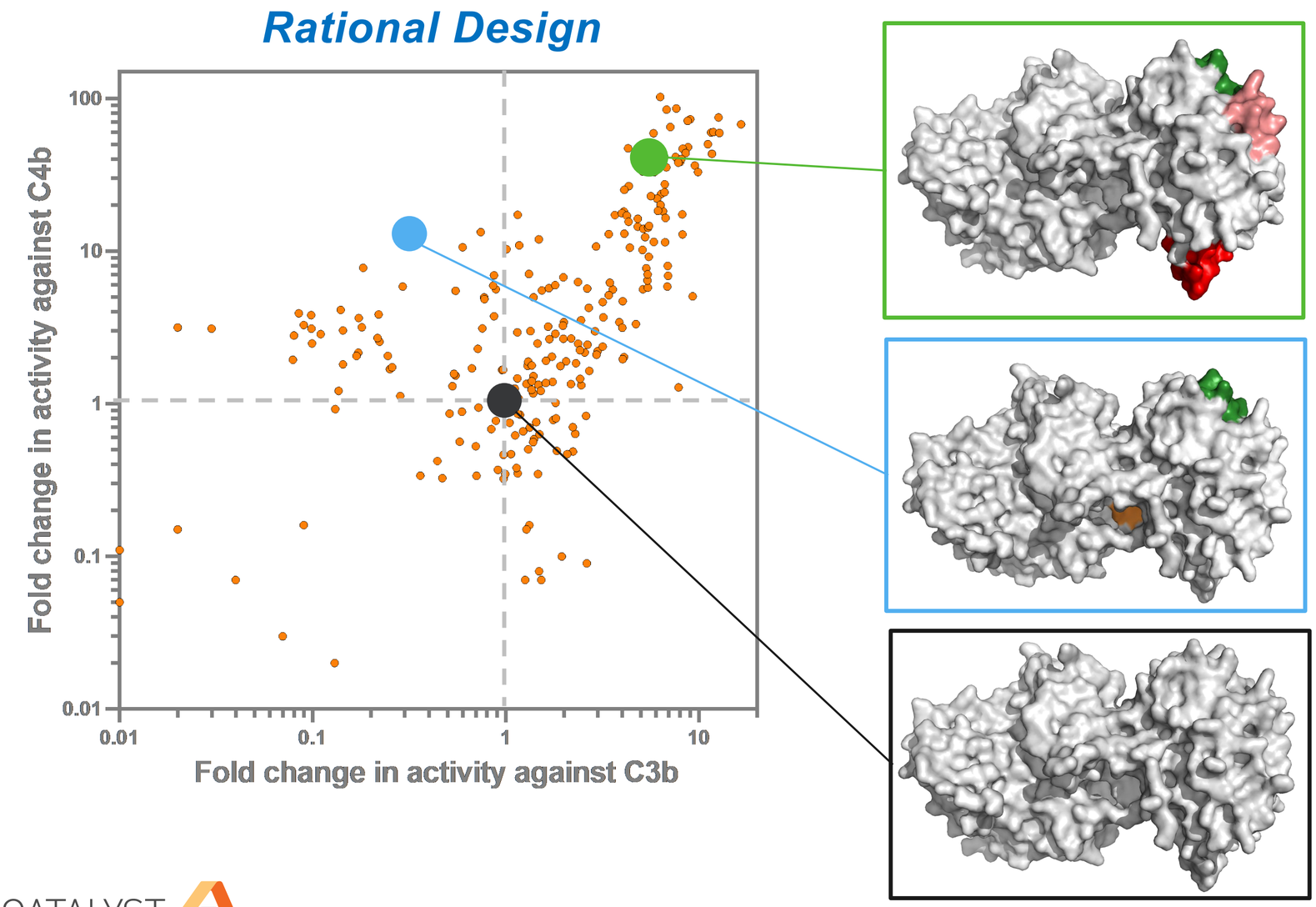
ongoing

+ In vivo activity in **chronic** rodent models



CATALYST BIOSCIENCES

Using ProTUNE™ Platform to tune C3b & C4b cleaving capabilities



Dual degrader:

High cleavage activity of C3b

High cleavage activity of C4b

Exclusive degrader:

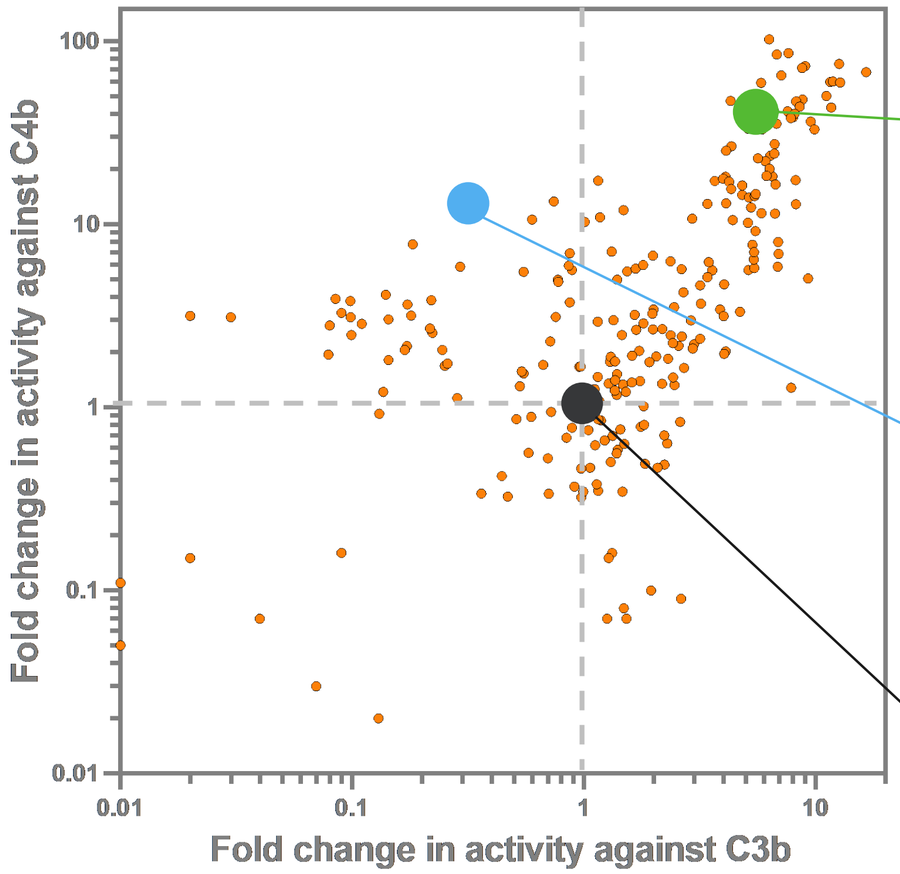
High cleavage activity of C4b

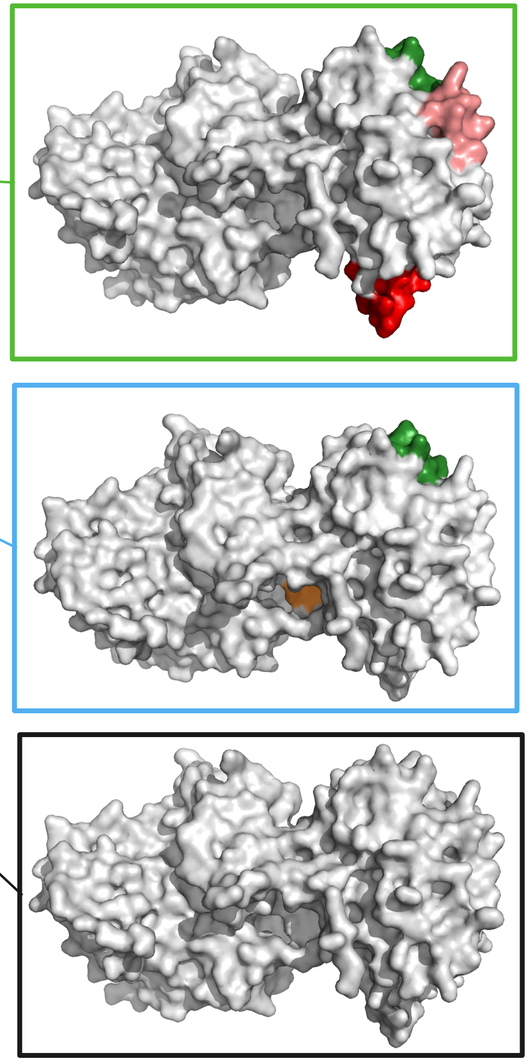
CFI base scaffold

CATALYST BIOSCIENCES

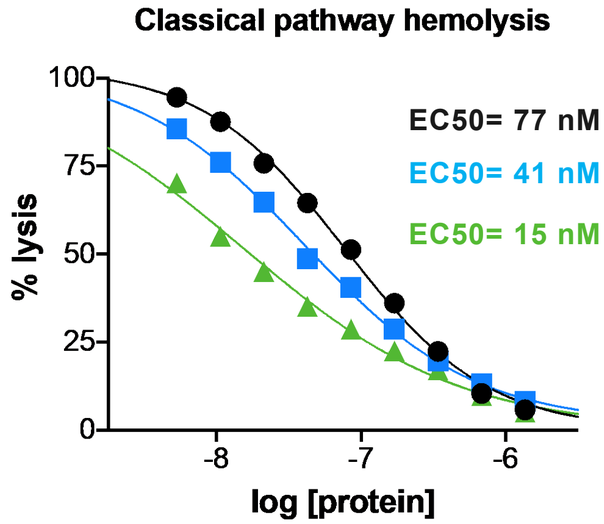
Using ProTUNE™ Platform to tune C3b & C4b cleaving capabilities

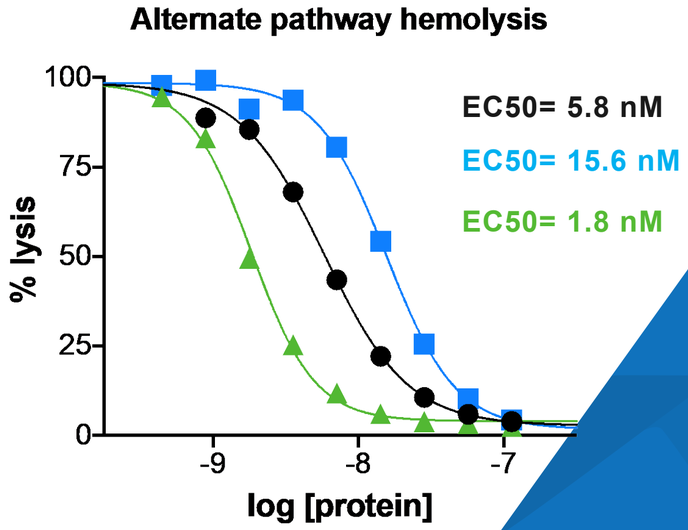
Rational Design





Reduction of hemolysis

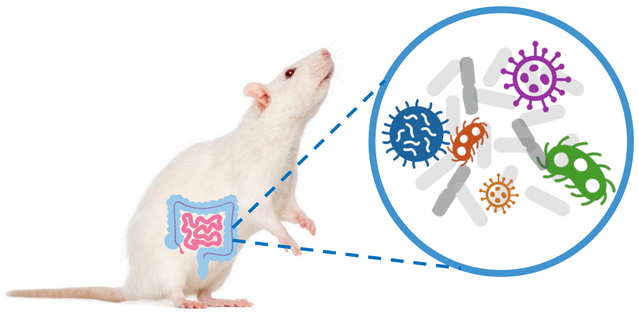




CATALYST BIOSCIENCES

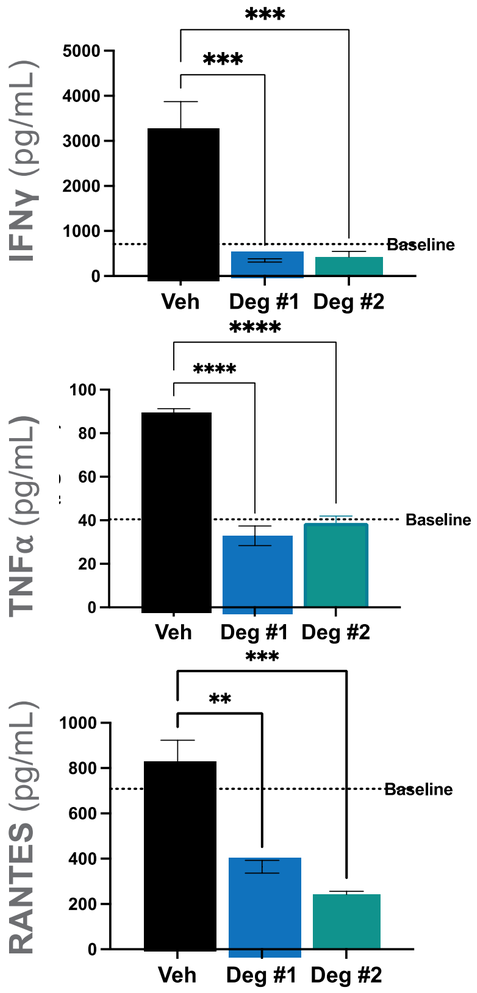
C3b & C4b degraders significantly reduce inflammation *in vivo*

Rat model of complement activation

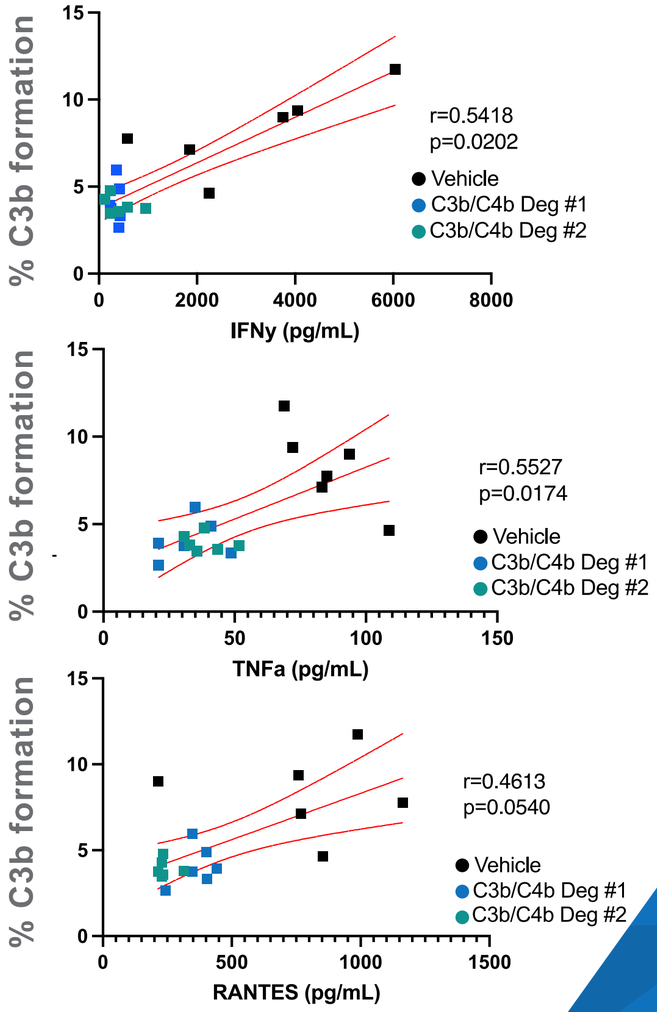


Reduction of **IFNγ, TNFα, & RANTES** involved in kidney damage & proteinuria in IgA nephropathy patients[1, 2, 3]

Inflammatory markers in IgA nephropathy



Concomitant reduction of inflammatory markers and complement C3 cleavage



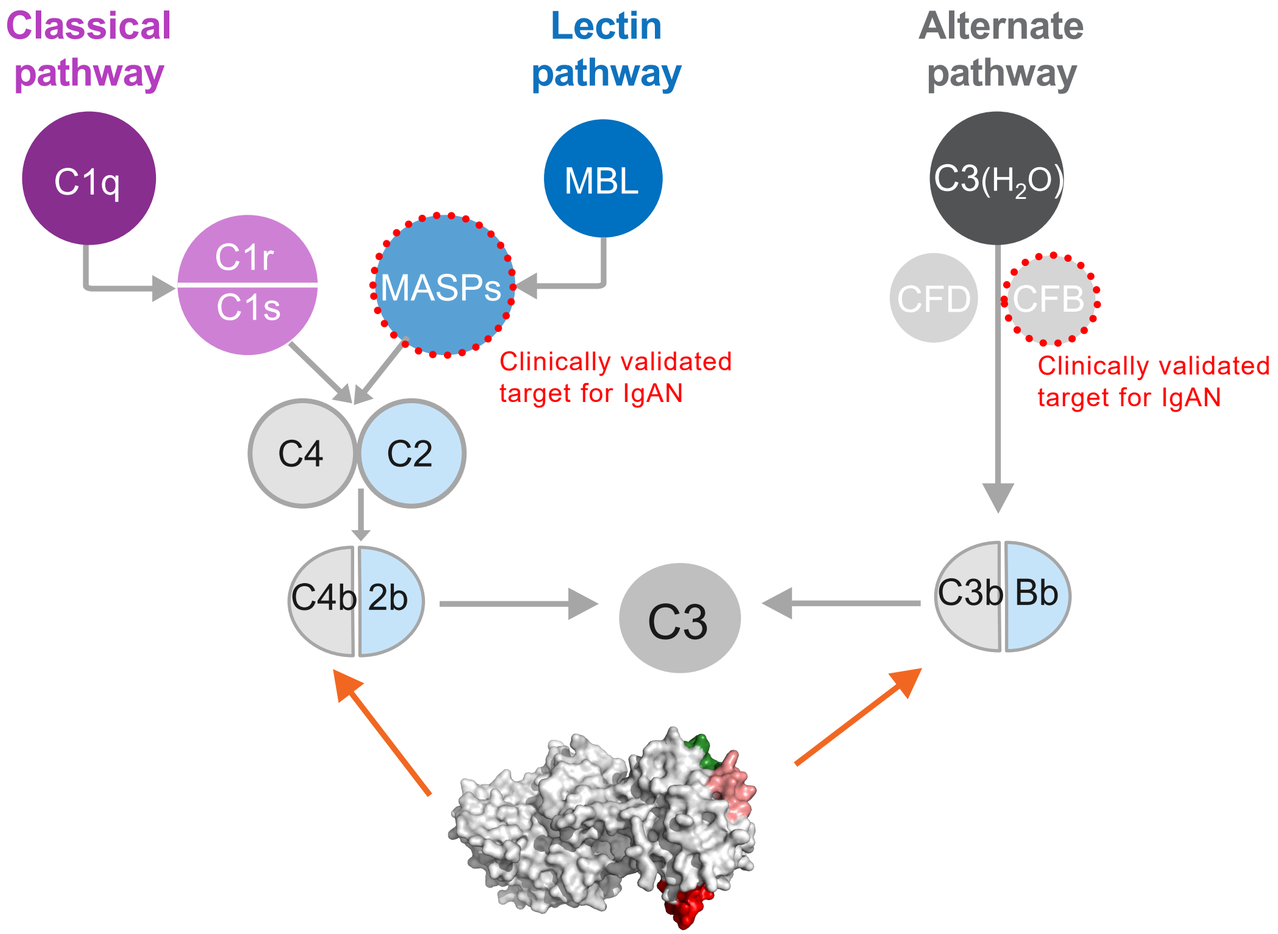
CATALYST BIOSCIENCES

1. Yano, N. *et al.* Phenotypic Characterization of Cytokine Expression in Patients With IgA Nephropathy. *J Clin Immunol* **17**, 396–402 (1997).
2. Lim, C. S. *et al.* Th1/Th2 predominance and proinflammatory cytokines determine the clinicopathological severity of IgA nephropathy. *Nephrol Dial Transpl* **16**, 269–275 (2001).
3. Brabcová, I. *et al.* Intrarenal gene expression of proinflammatory chemokines and cytokines in chronic proteinuric glomerulopathies. *Physiol Res* 221–226 (2007)

Values are mean +/- SEM, **p<0.01 ***p<0.001 p<0.0001 using One Way or Two-way ANOVA.

C3b & C4b degraders for IgA nephropathy patients

Dual targeting of alternate & lectin pathways



Differentiation

+ Dual targeting mode of action: lectin & alternate pathways

Rationale for IgA nephropathy

+ Both lectin & alternate pathways are involved in IgA nephropathy & correlate with severe clinical manifestation [1, 2, 3]

Clinically validated targets

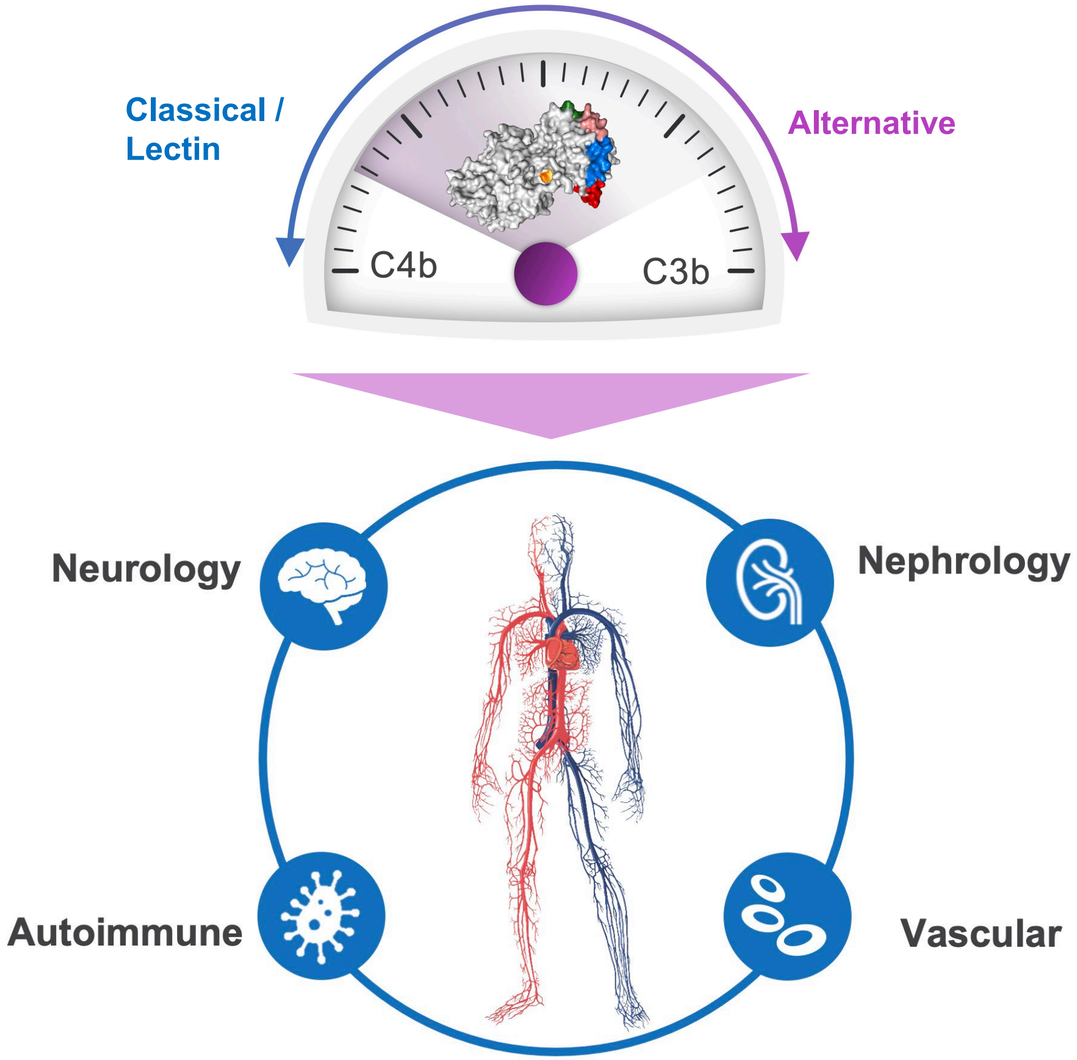
+ Inhibition of only MASP2 or Factor B may be insufficient to reduce proteinuria in IgA nephropathy patients

CATALYST BIOSCIENCES

1. Medjeral-Thomas et al. Kidney International Reports (2018); 2. Bi et al. BMC Nephrology (2019); 3. Roos et al. J Am Soc Nephrol (2006)

C3b & C4b degraders for precision medicine in complement disorders

Diseases in which classical, lectin and/or alternative pathways drive pathogenesis



Specific inhibition of complement components at different sites of the complement cascade allows a personalized approach to treating complement disorders

CATALYST BIOSCIENCES

Acknowledgements

Catalyst Biosciences

Lauren Kelly
Shyam Rajan Iyer
Jim McGuire
Grant E. Blouse

Aarhus University

Emil Oldenburg
Agnieszka Jendroszek
Christine R. Schar
Jan K. Jensen

Newcastle University

Thomas Hallam
Kevin Marchbank

IPST

Camille Simard
Emilie Dupré