CB 2782-PEG
A Complement Factor C3- Inactivating Protease for Dry AMD

Dry AMD Summit 2021
October 20th 2021
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CATALYST BIOSCIENCES

Forward-looking statements

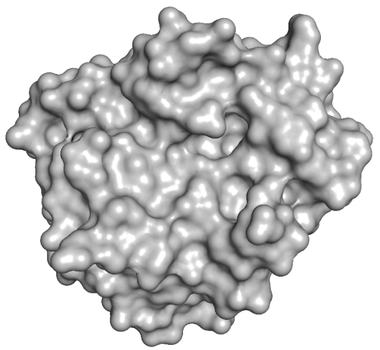
Certain information contained in this presentation and statements made orally during this presentation include forward-looking statements that involve substantial risks and uncertainties. All statements included in this presentation, other than statements of historical facts, are forward looking statements. 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 such as the potential for low dose intravitreal (IVT) eliminating C3 for 28 days; the potential for less frequent dosing and the potential for sustained suppression of complement, as well as the statements about the Company’s collaboration with Biogen for the development and commercialization of pegylated CB 2782 for the potential treatment of geographic atrophy-associated dry age-related macular degeneration. 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, 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 the Company's Quarterly Report 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.

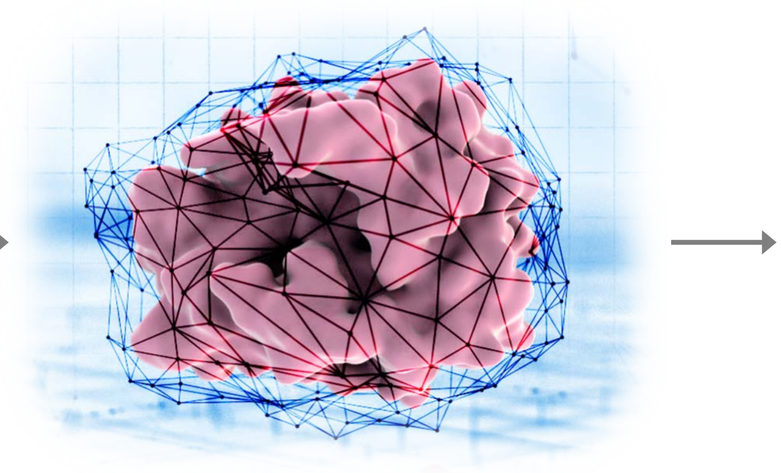
Catalyst protease platform

Unique expertise enables design of optimized & differentiated protease candidates

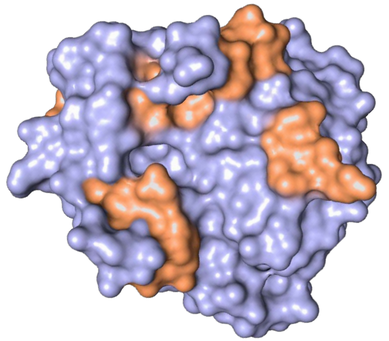
Discovery Platform

Protease Scaffold





Protease Candidate



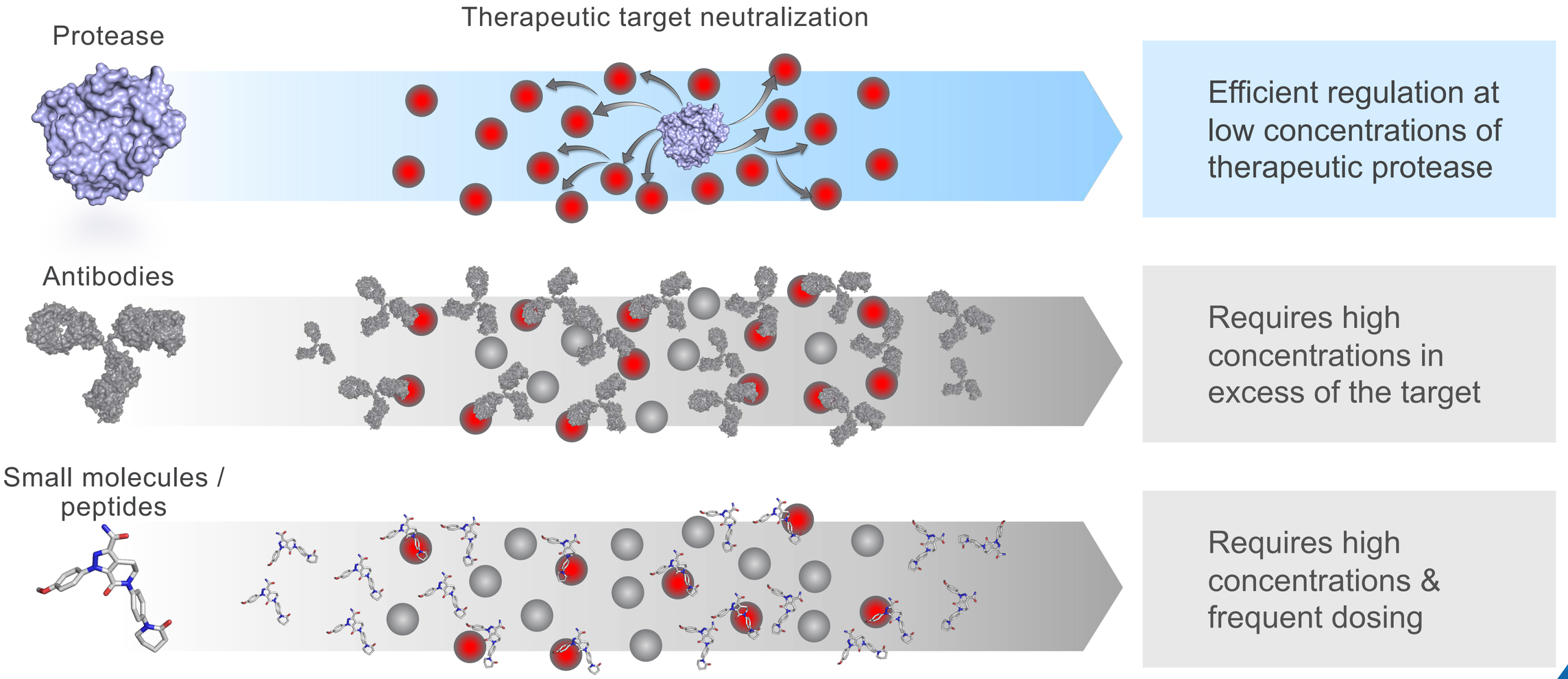
- **Structure Guided Design**
- **Molecular Evolution**
- **Engineered Regulation**
- **Pharmacokinetic Improvement**

Our Proteases

+ Functionally enhanced natural proteases in the complement & coagulation cascades
+ Engineered novel protein degraders in the complement cascade
+ Modulate or target biological activation or inactivation

Proteases are ideal for high abundancy targets & cascades

A better way to regulate biological processes compared with antibodies & small molecules



The leading cause of blindness is geographic atrophy (GA)

There is no approved treatment for GA

Geographic atrophy is a high unmet need

- Advanced stage of dry age-related macular degeneration (dAMD)
- dAMD affects ~1M people in the US & >5M WW, no currently approved therapy
- Global market >$5B
- C3 is a clinically validated target for dry AMD
- New interventional modalities may offer improved efficacy

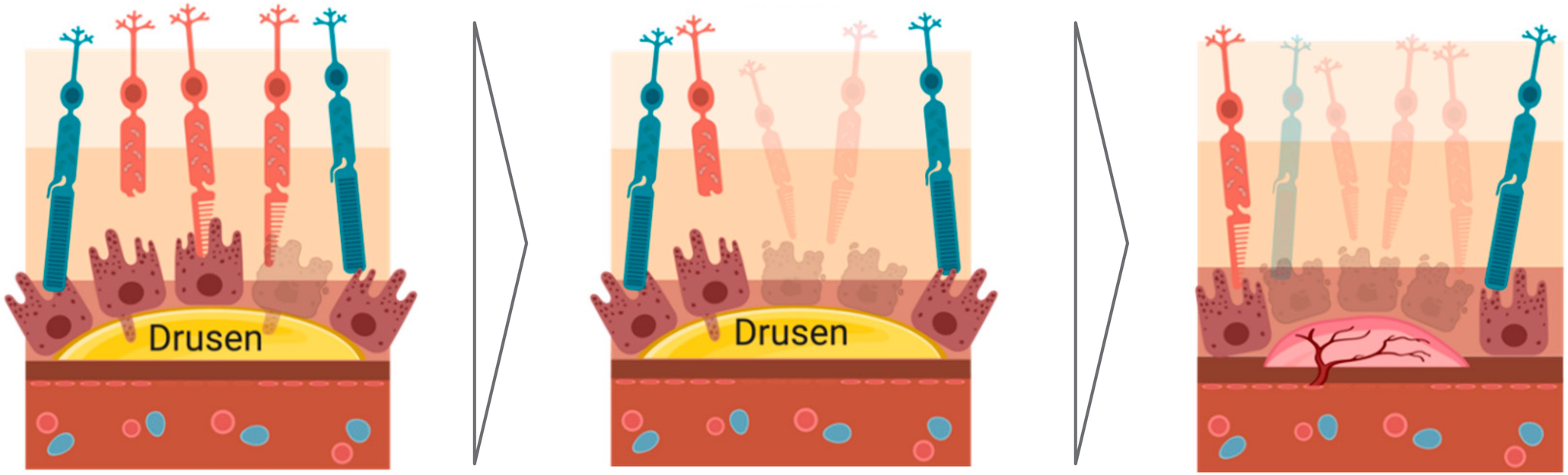
Progression of the healthy retina to AMD

Complement is implicated across the AMD spectrum

Age-Related Maculopathy

Dry AMD

Wet AMD

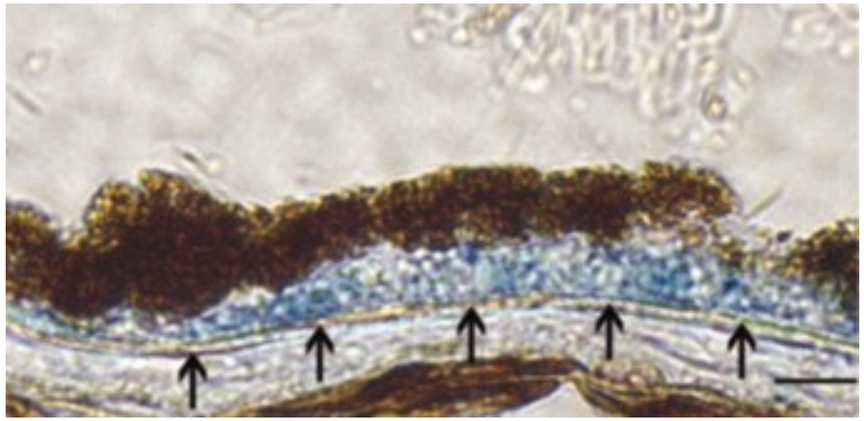


Jensen et al. (2020) Int. J. Mol. Sci. 21(24): 9752
Park et al. (2019) Front Immunol 10:1007

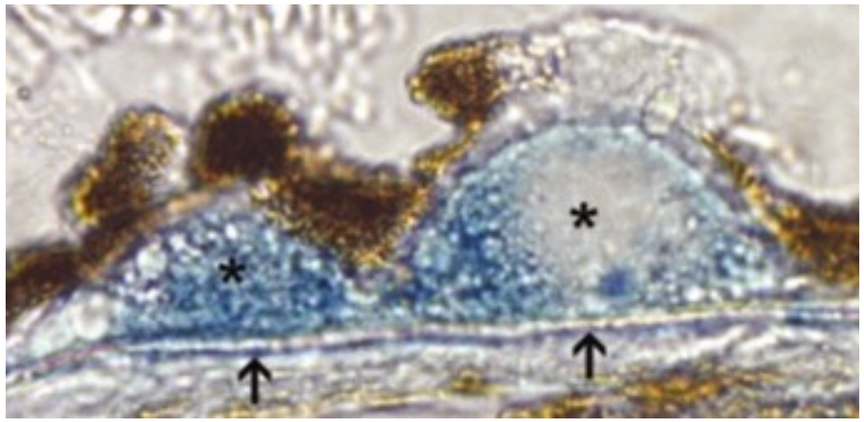
Complement is implicated in the progression of AMD

C3a is deposited in soft and hard drusen of dAMD patients

Soft Drusen



Hard Drusen



Deposition in the proximity of the RPE & Bruch's membrane

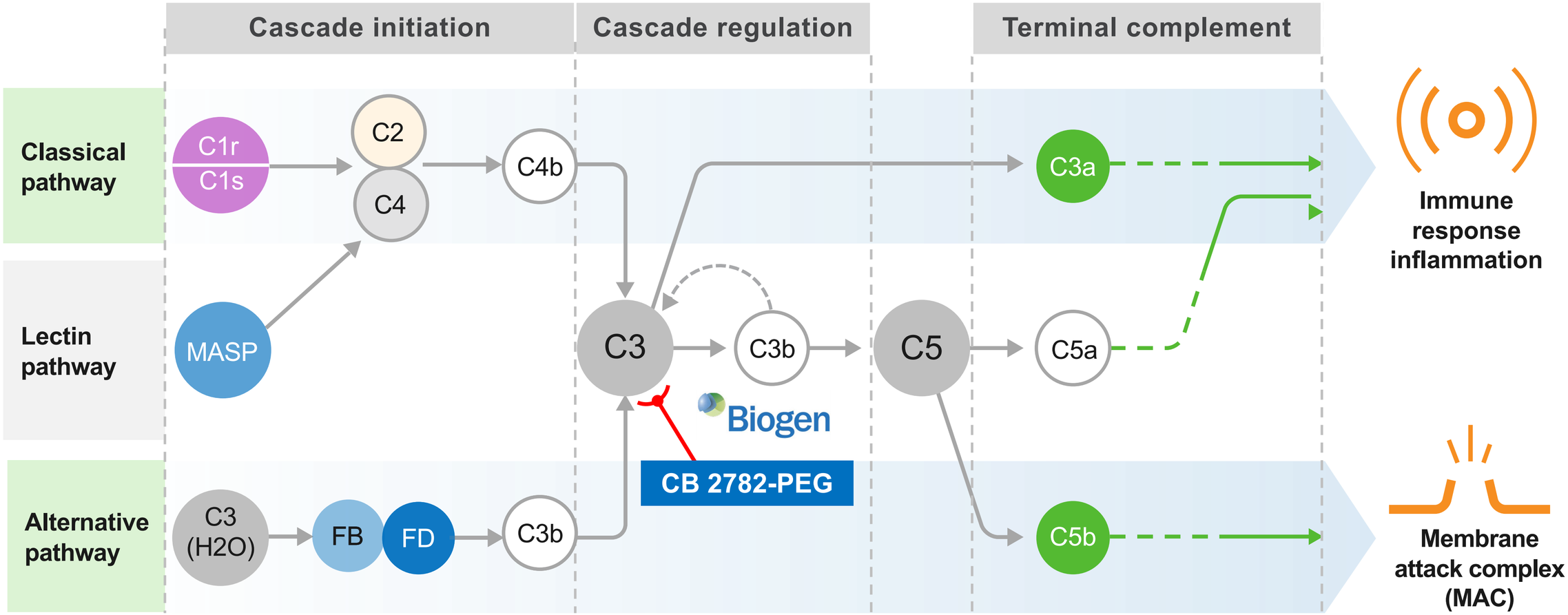
Dysregulated complement implicated in AMD progression

- Alternative pathway involvement
- Genetic association or dysregulation of:
  - Complement factor H (FH)
  - Complement factor 3 (C3)
  - Factor B (FB)
  - Factor D (FD)
  - Complement Factor I (CFI)
  - Complement factor 9 (C9)

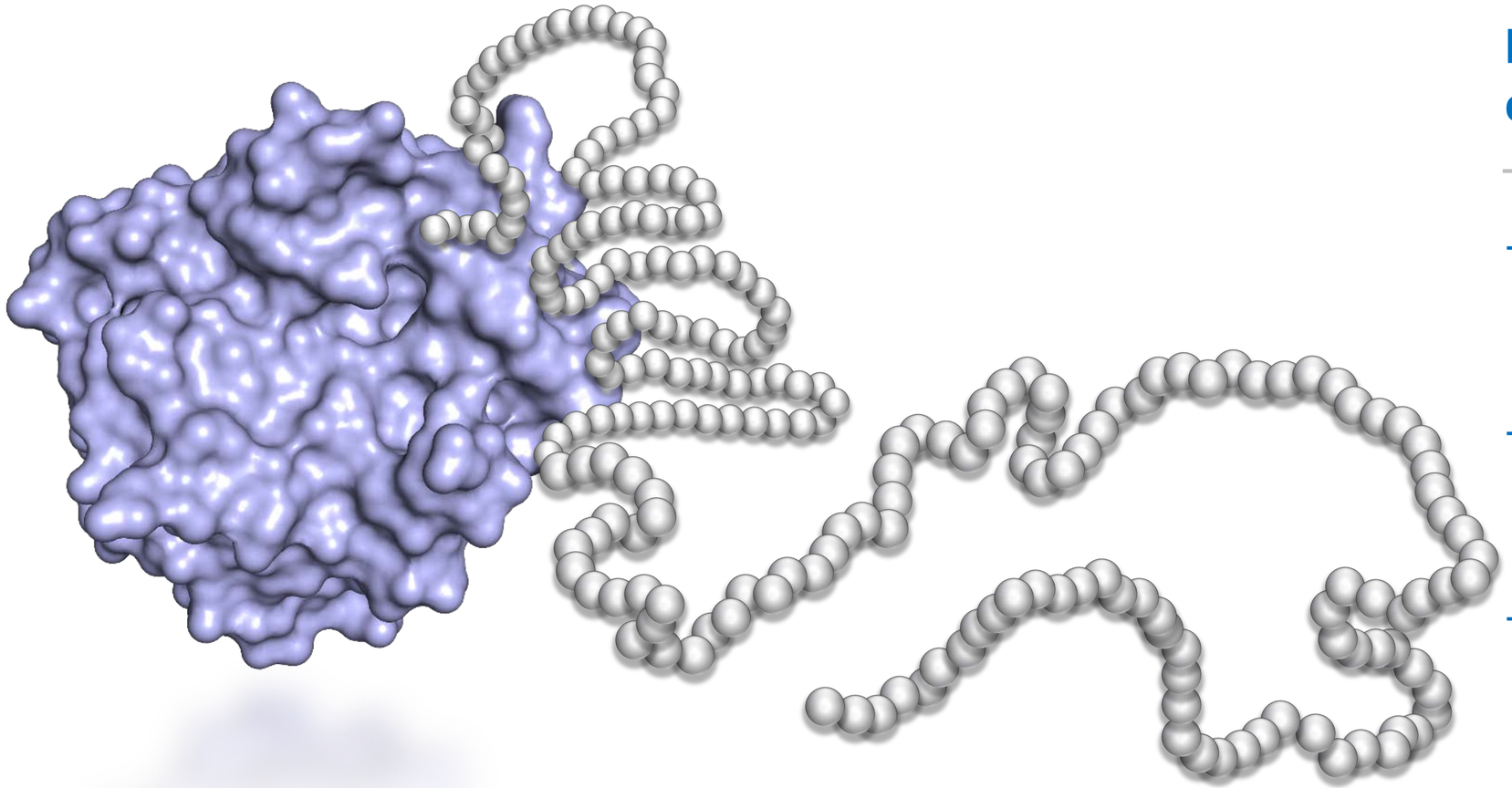
Nozaki et al. (2006) PNAS 103(7):2328-33
Park et al. (2019) Front Immunol 10:1007
RPE: retinal pigment epithelium

Targeting the central axis of complement at C3

CB 2782-PEG targets the central regulator of the complement cascade



CB 2782-PEG: Long acting anti-C3 protease for dry AMD



- Cysteine specific 40 kDa PEG (maleimide) conjugated
- Site specific labeling on an engineered free Cysteine

Potential best-in-class C3 degrader for dry AMD

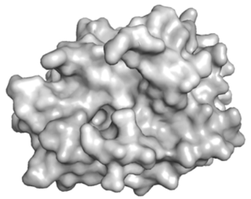
+ Generated from Catalyst's proprietary **protease engineering platform**
+ Potent, selective & long acting, degrades C3 into inactive fragments
+ NHP PK & PD data predict potential **best-in-class** human intravitreal product

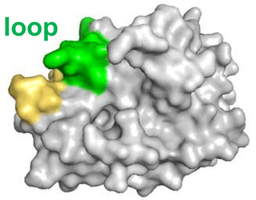
CB 2782-PEG: Potential best-in-class treatment for dAMD

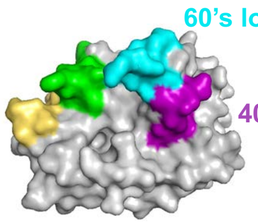
Designed as a differentiated molecule in C3 regulation

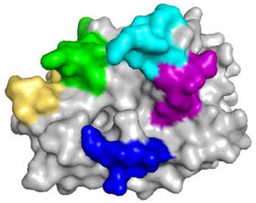
Differentiated attributes	CB 2782-PEG Designed to address
Potential for less frequent dosing	✓
Low intraocular dose	✓
Effectively “sweeps away” the targeted C3	✓
Degrades C3 in a manner that removes both C3b & C3a	✓
Offers sustained suppression of complement	✓

Molecular evolution of CB 2782 for C3-specific cleavage









MTSP-1

CB 2013

CB 2426

CB 2470

CB 2782
(lead candidate)

Select ⇧ Catalysis

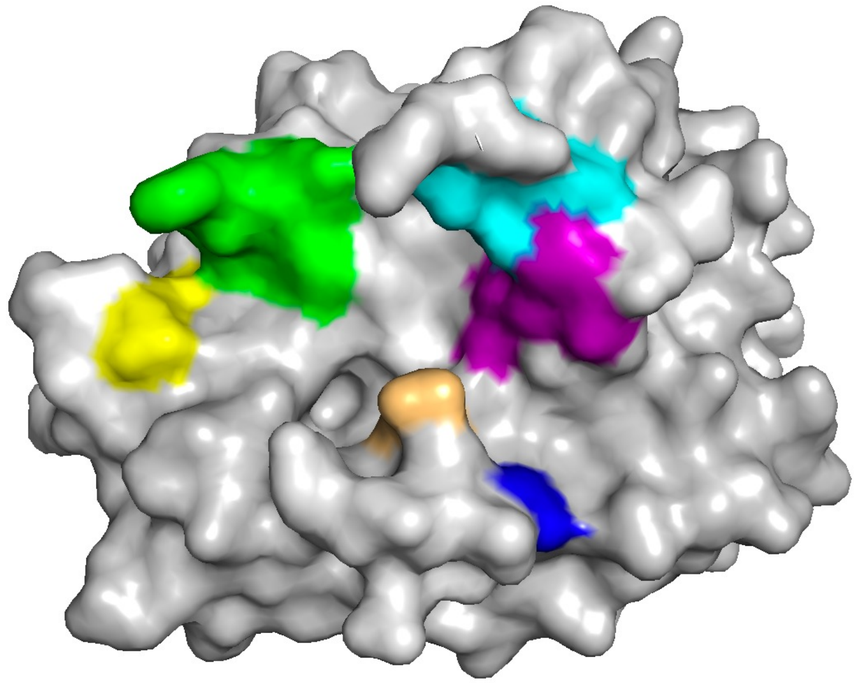
Human Plasma
(counter selection)

Anti-thrombin (AT)
(counterselection)

Directed Engineering

α_2-Macroglobulin
(counterselection)

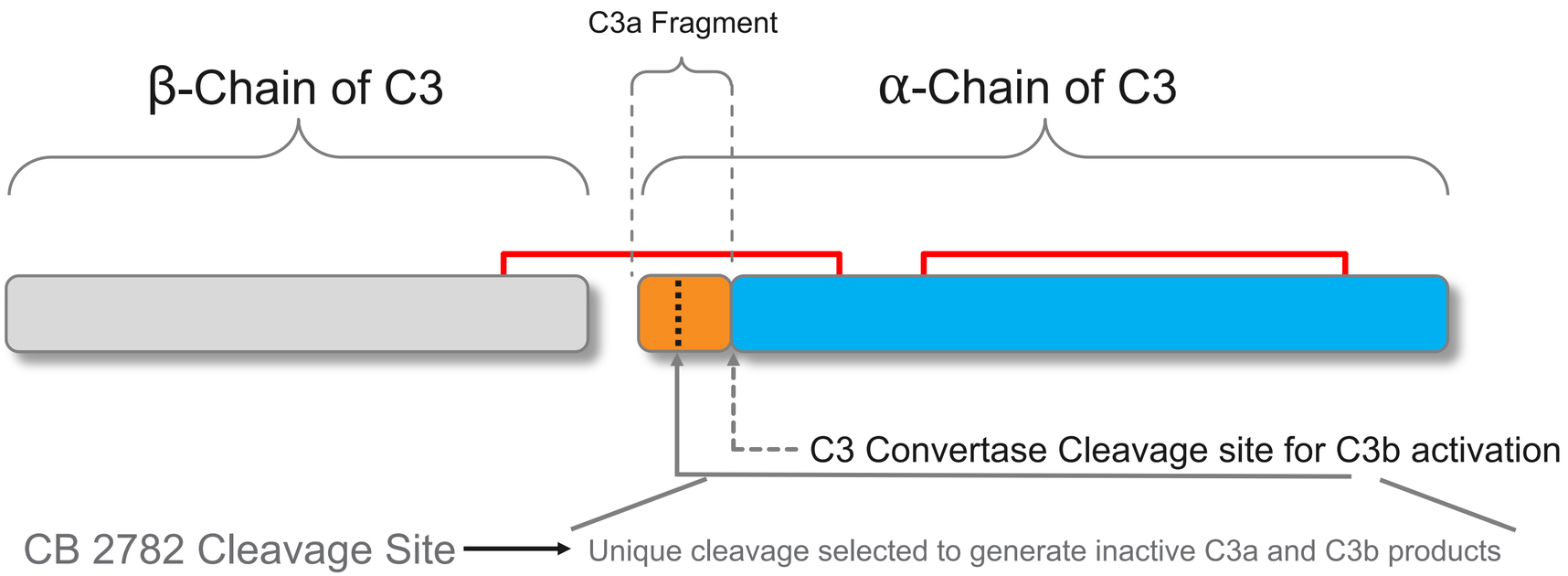
Evolved Protease Candidate



CB 2782

Selection of a specific “inactivating” cleavage site

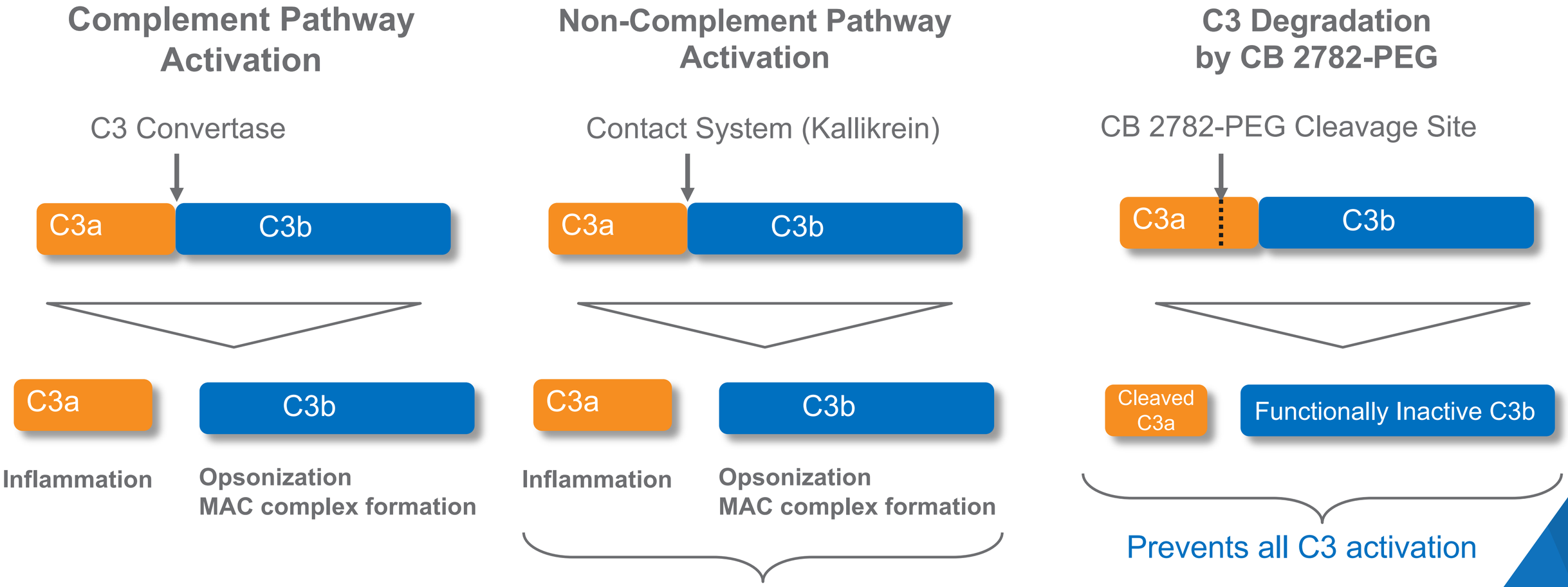
Schematic of C3 structure and the C3 convertase cleavage site



+ CB 2782 was engineered to specifically cleave a single site in C3
  - Divergent from that which is cleaved by the C3 convertases
+ Cleavage of C3 results in an inactive C3a and C3b-related species
  - Cannot be further activated by the C3 convertases

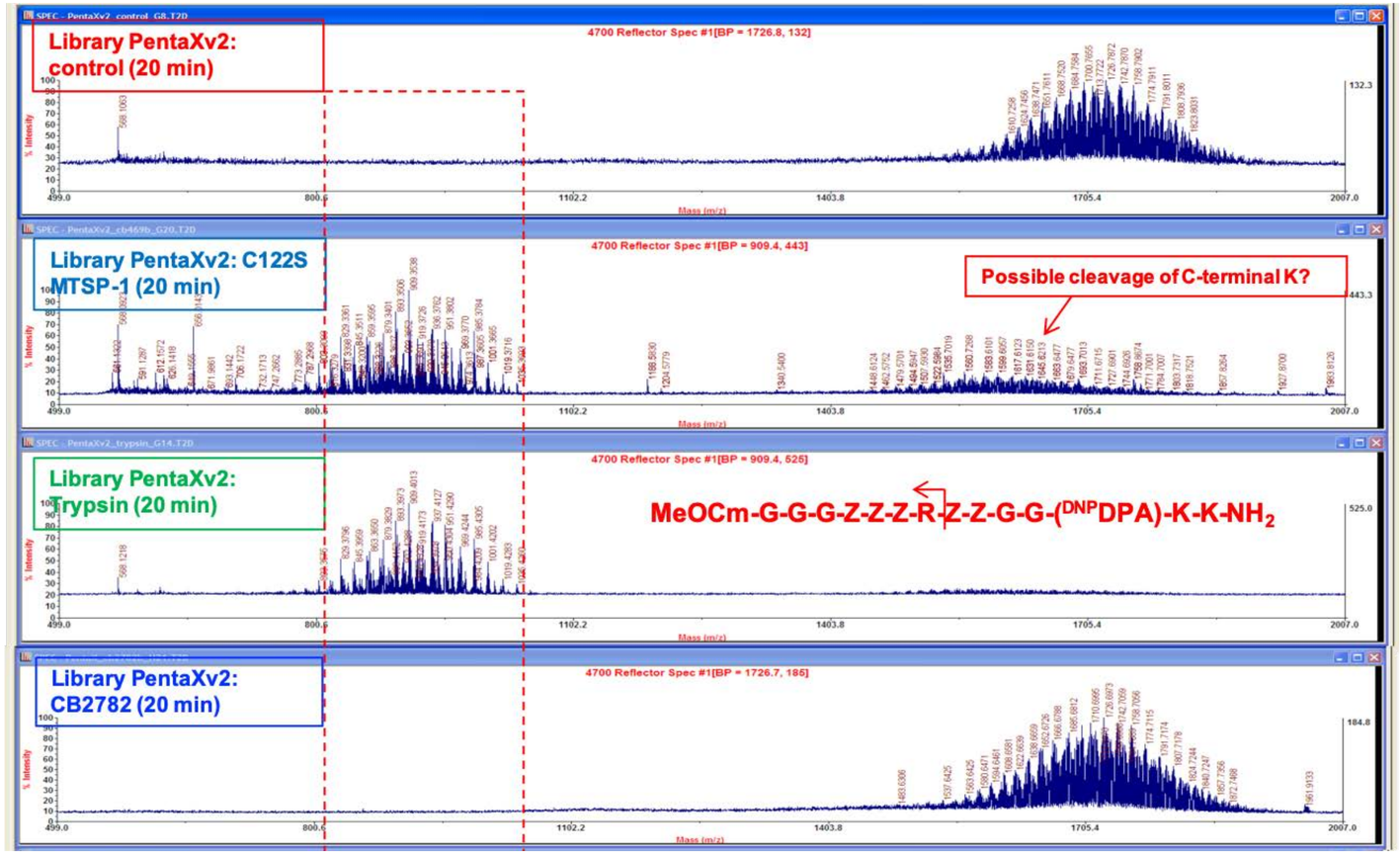
C3 can be activated by multiple mechanisms

Activation of plasma kallikrein provides an alternate mechanism of dysregulation



Irmscher et al. (2018) J Innate Immun:10:94–105

CB 2782 shows high specificity



Cleavage of PentaXv2 Library

P_4 P_3 P_2 P_1 $P_{1'}$ $P_{2'}$

▲-G - G - G - Y – Y – Y – R – Y – Y - G - G - ■ - K - K - NH_2

Y	Any of 18 AAs (excluding R, C)
▲	N-terminal 7-methoxycoumarin-4-acetyl
■	dinitrophenyl-diaminopropyl

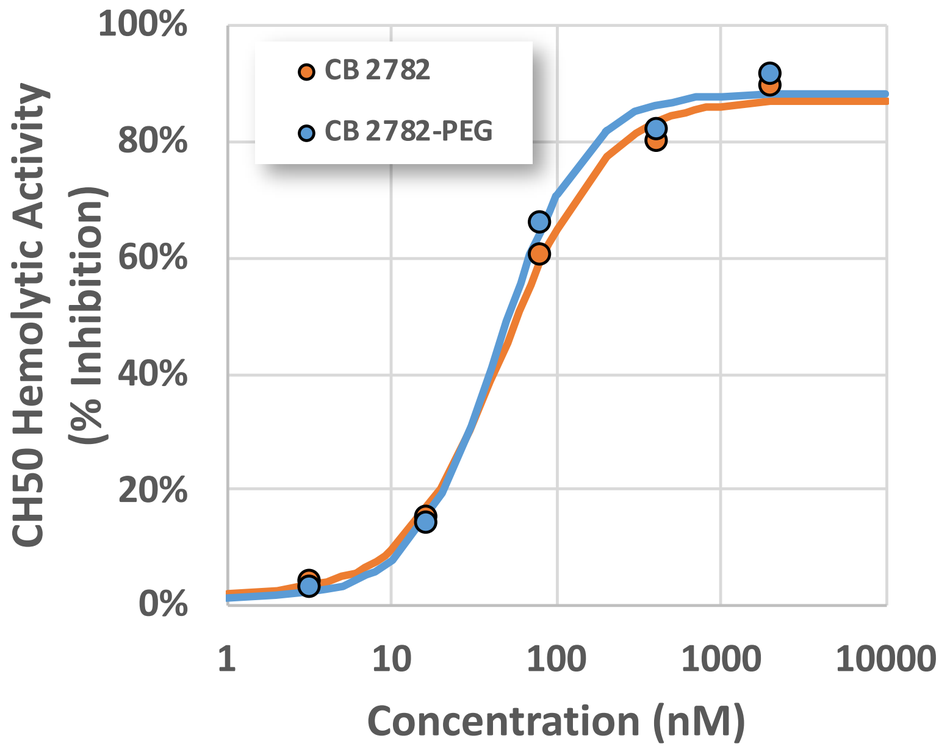
 # Peptides

1,889,568 (18^5)

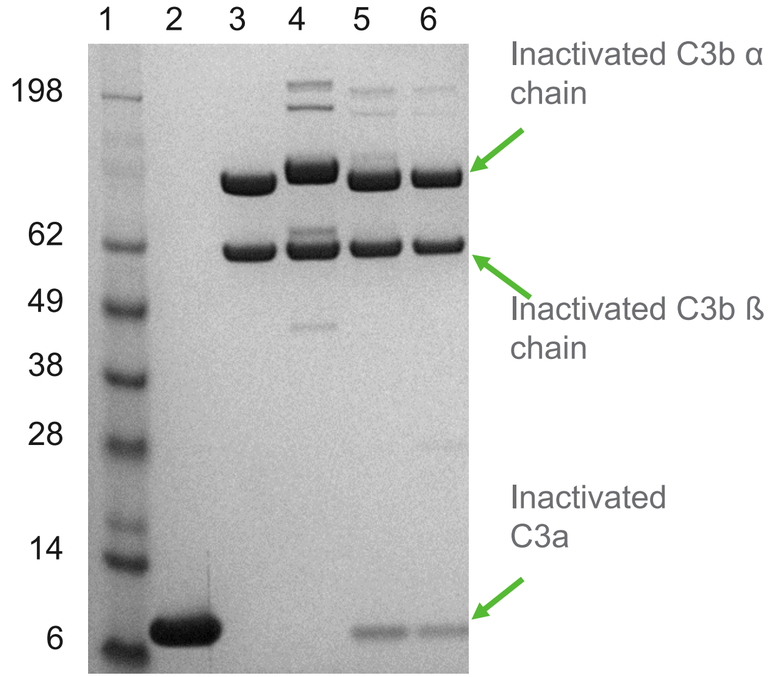
+ Essentially no detectable cleavage of the PentaXv2 library by CB 2782
+ Near complete cleavage by MTSP-1
+ Complete cleavage by trypsin

CB 2782-PEG has indistinguishable activity *vs* CB 2782

CB 2782 and CB 2782-PEG inhibit complement-mediated hemolysis *in vitro*



Sub-stoichiometric CB 2782 & CB 2782-PEG specifically cleave C3 at a single site into inactive fragments

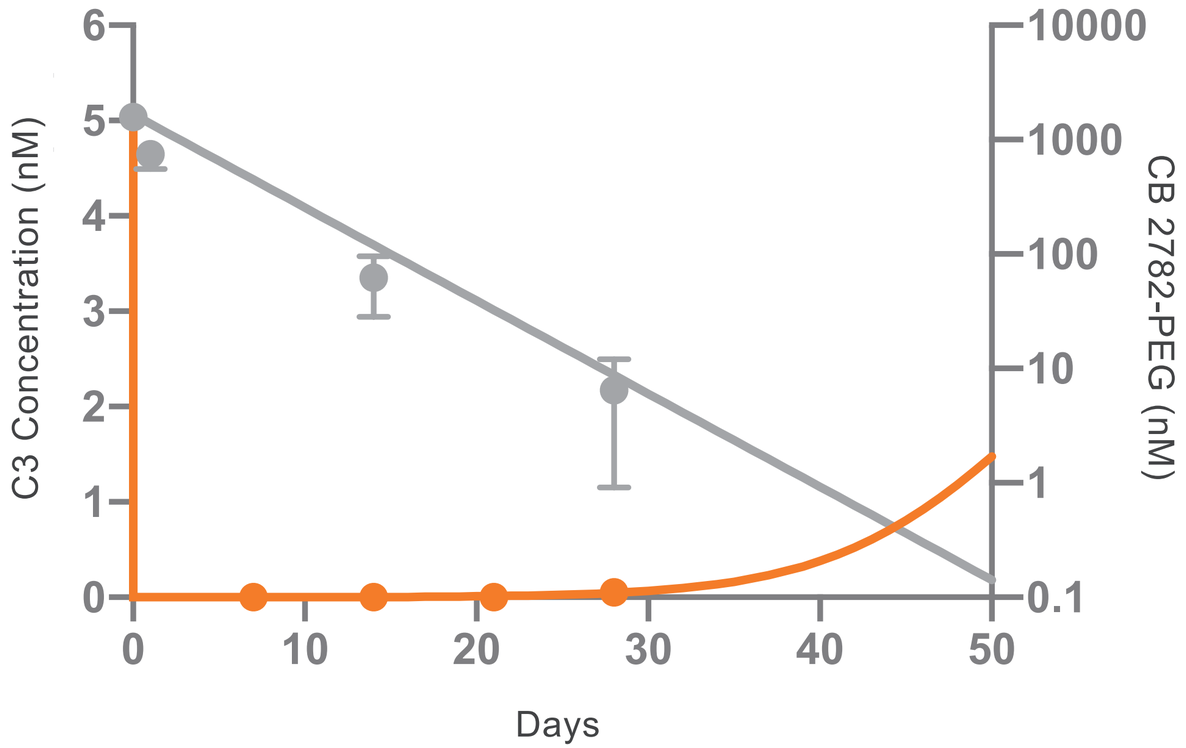


Reduced SDS-PAGE	
Lane	Sample
1	Ladder
2	C3a
3	C3b
4	C3
5	2 µM C3 treated with 0.2 µM CB 2782-PEG
6	2 µM C3 treated with 0.2 µM CB 2782

CB 2782-PEG: Best-in-class C3 degrader for dAMD

Protease advantage demonstrated *in vivo*

CB 2782-PEG degrades C3 levels in the eye for at least 28 days in a non-human primate model

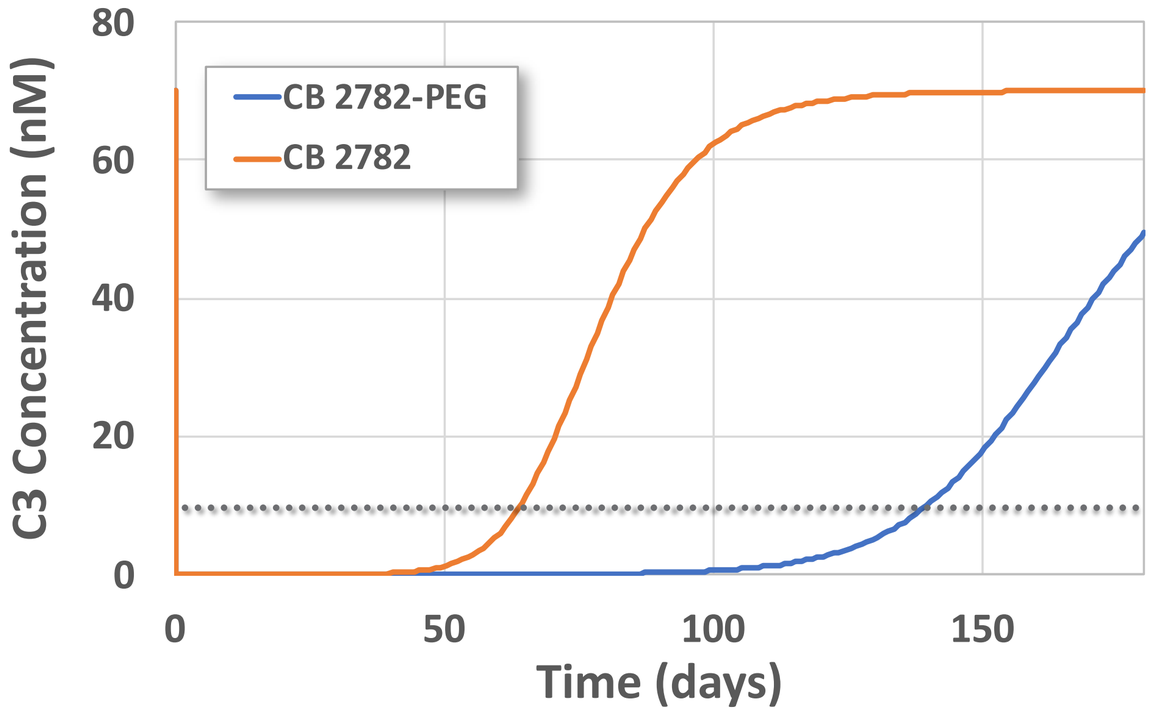


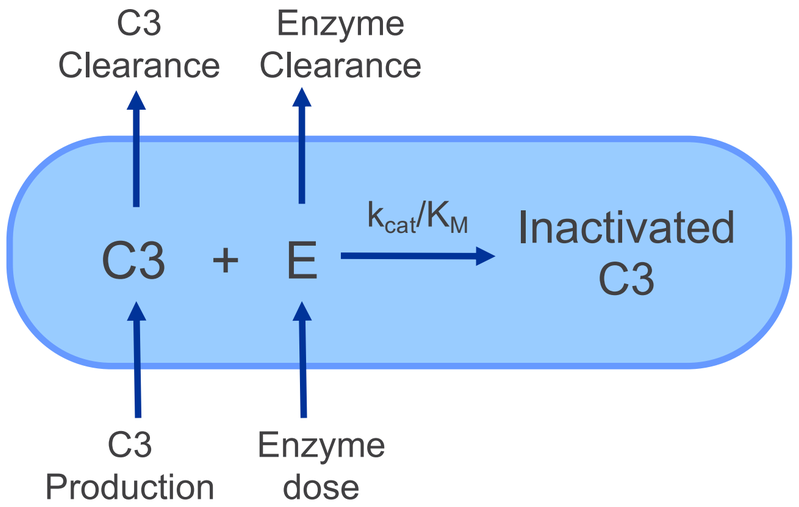
Catalytic advantage of proteases

- One therapeutic molecule neutralizes 1000s
- Fast & potent response
- Extended pharmacodynamic effect
- Can activate or degrade therapeutic targets
- Engineered novel protein degraders “sweep away” difficult to drug targets

Predicted low infrequent human dose

Fit to observed primate PK/PD data and scaled to the human condition





Key takeaway messages

- Engineered novel specificity through molecular evolution and rational design
- Nonclinical studies resulted in 99% elimination of C3 for 28 days
- Predicted efficacious and less frequent dosing
- CB 2782-PEG has potential for best-in-class efficacy and convenience in dry AMD
- Offers sustained suppression of complement

THANK YOU

Nasdaq: CBIO

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