Stellabody®

ANTIBODY HEXAMERISATION TECHNOLOGY

Creating potent biologic therapeutics

Burnet
reach for the many

JUNE 2024

Non-confidential

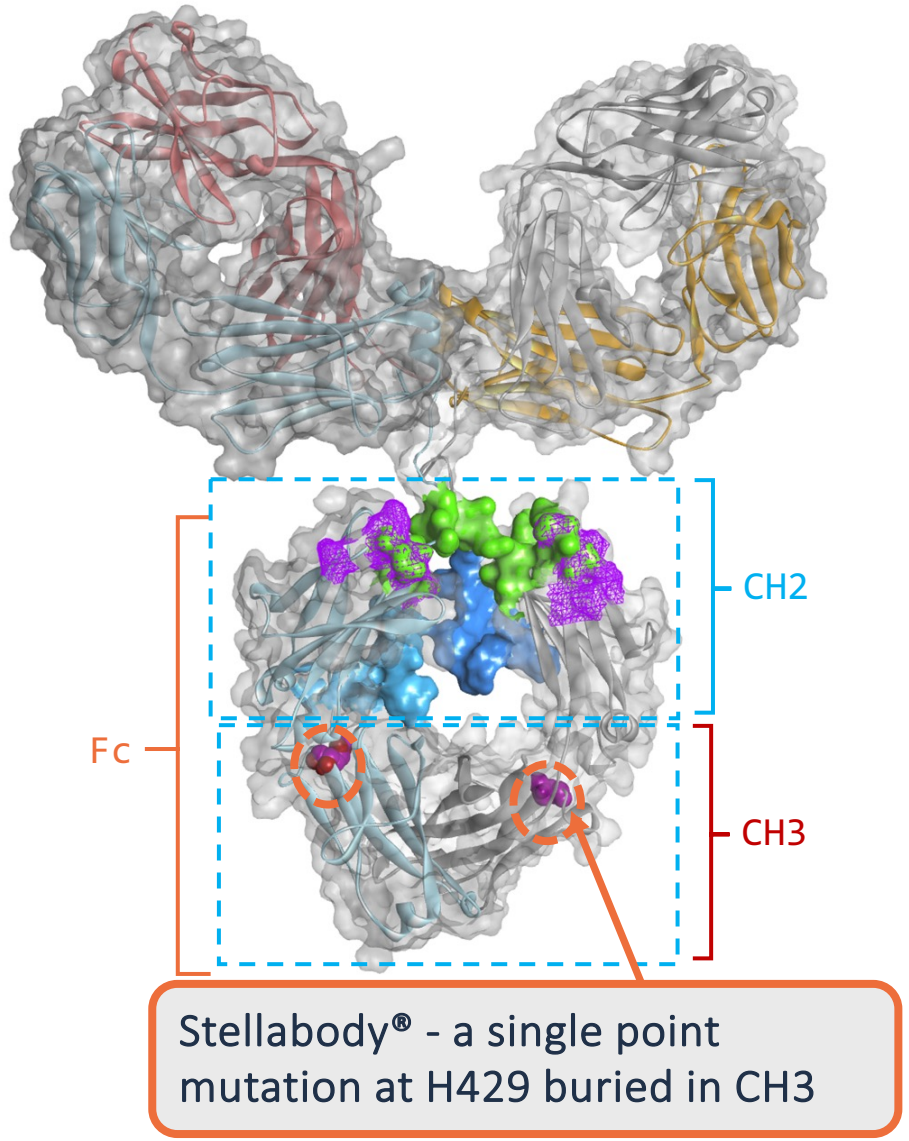
THE PROBLEM

- Still lacking biological treatments that achieve functional cures and dramatic improvement in patient survival
- Key issues
  - Insufficient potency
  - Limitation in dosing approaches (due to dosing restrictions)
  - Lack of/or limited efficacy

Stellabody®

Stellabody® provides a SOLUTION

- A **HEXAMERISING TECHNOLOGY** that enhances:
  - clustering of antibodies on target cell surface – in a hexameric format - for better cell signaling
  - complement killing (CDC)
- Leading to the development of better biologics



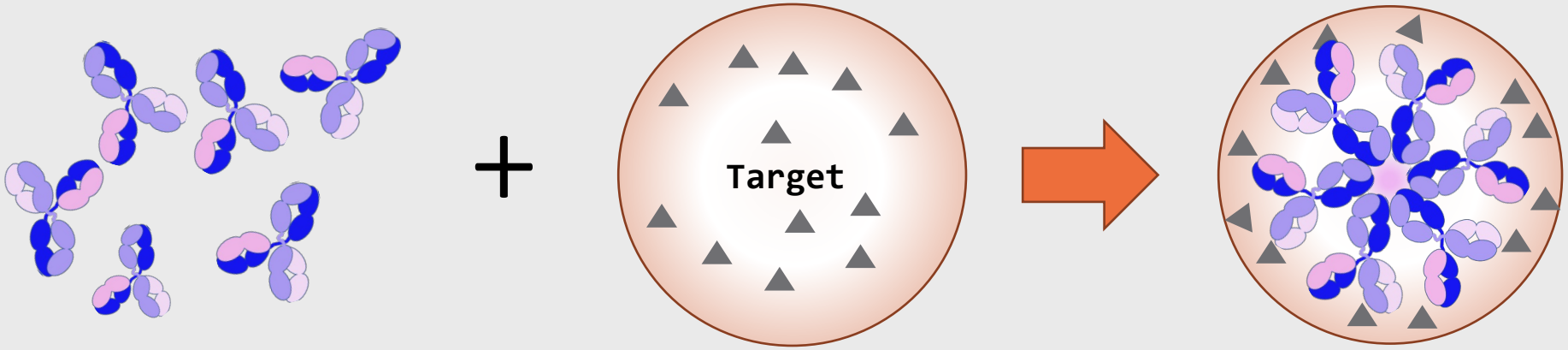
Stellabody® drives on-target hexamerisation

THE TECHNOLOGY: STELLABODY®

Modification at residue H429 of CH3 domain to H429F drives on-target hexamerisation, where antibodies form into clusters of six antibodies once bound to their target.

These hexamers can:

- Amplify signaling by enhanced target clustering
- Trigger or enhance the complement cascade via C1q binding to initiate immune protection, for example, killing of a target cell or pathogen



Stellabody®– enabling the development of better biologics

VALUE PROPOSITION

Dose benefit

- Enabling lower doses for:
  - Lower Cost of Goods (COG's)
  - Exploring challenging routes of administration
    - subcutaneous
    - intraarticular

Increased Potency

- Potential to dose lower
- Potential to explore low abundance targets
- Potential to rescue stranded assets

Efficacy benefit

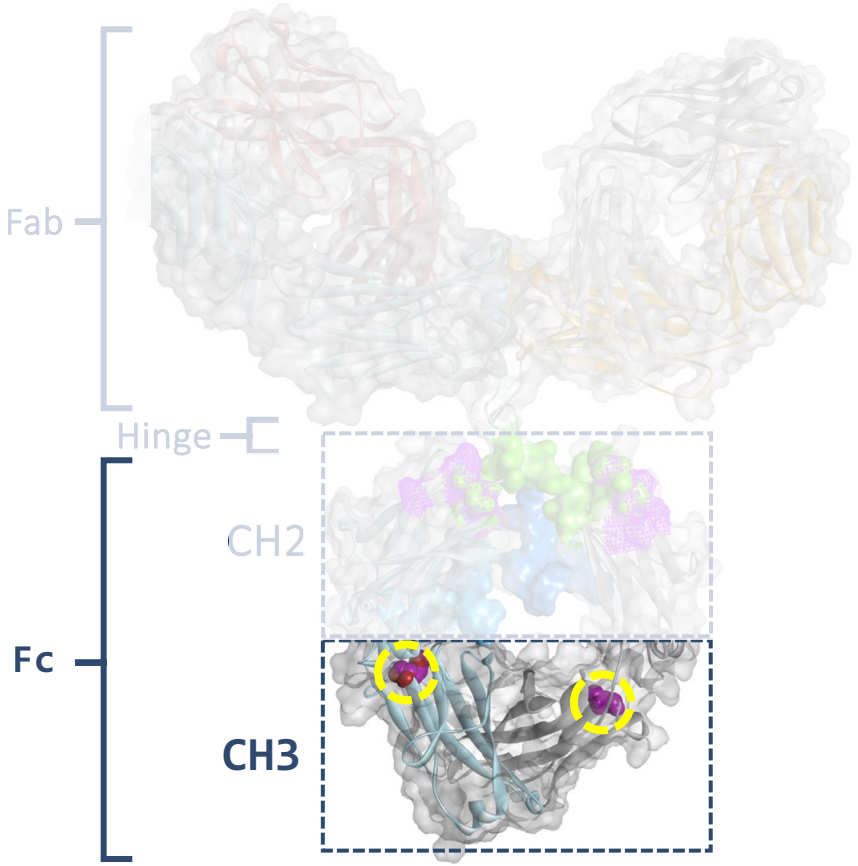
- Leading to increased therapeutic effects
- Rescuing assets with absent or low therapeutic effect
- Opens opportunity for exploring new targets

Safety benefit

- Lower potential for immunogenicity verses competitor

Stellabody®: Buried residue may lead to less risk of immunogenicity compared to competitor – Safety profile

THE TECHNOLOGY: STELLABODY®



A buried mutation:

Potentially less risk of immunogenicity versus a competitor hexamerisation technology (HexaBody®) that has mutated residues on the surface of Fc

Novel & Inventive:

International search report indicates Stellabody® substitution is novel & inventive over the prior art identified

Stellabody® has broad applicability

THE TECHNOLOGY: STELLABODY®

Signal amplification by target clustering

- Leading to enhanced agonism
- Example: Stellabody® DR5 mAbs enhanced cell killing *in vitro*
  - Colorectal cancer

Complement killing

- Leading to enhanced depletion of cells through:
  - Complement dependent cytotoxicity (CDC)
  - Phagocytosis
- Examples: Stellabody® CD38 mAbs and CD20 mAbs enhanced cell killing *in vitro and ex-vivo (CDC-mediated)*
  - Acute Lymphoblastic Leukemia (ALL)
  - B cell lymphoma (BLL)
  - Chronic Lymphocytic Leukemia (CLL)

Virus neutralisation

- Leading to enhanced killing of cells mimicking viral infection through:
  - CDC
  - Neutralisation
- Example: Stellabody ® ACE2-Fc fusion protein [SARS-CoV-2]:
  - Enhanced killing of spike trimer-positive cells *(CDC)*
  - Gain of neutralisation potency against immunoevasive SARS-CoV-2 strain *(% neutralisation)*

Multiple indications e.g. cancer, infection, autoimmunity, inflammation

Four patent families – All solely owned by Burnet Institute

INTELLECTUAL PROPERTY

#1

"Immunotherapeutic proteins comprising an Fc region component with a mutation at position 429"

- PCT application: PCT/AU2022/051287
- International filing date: 26 Oct 2022
- Overview: Stellabody® platform

#2

''Antiviral agent comprising a cellular entry receptor and Fc regions component''

- PCT application: PCT/AU2022/051285
- International filing date: 26 Oct 2022
- Overview: Stellabody® therapeutic against SARS-CoV-2 (i.e. ACE2-Fc)

#3

"Immunotherapeutic proteins"

- PCT application: PCT/AU2024/050463
- International filing date: 10 May 2024
- Overview: Stellabody®-modified bispecific antibodies

#4

"Immunotherapeutic proteins"

- PCT application: PCT/AU2024/050468
- International filing date: 10 May 2024
- Overview: Use of Stellabody® in combination with mutations and novel immunoglobulin backbones to modulate antibody function

Opportunity to partner on a promising platform technology

NEXT STEPS

Burnet is seeking partners to incorporate Stellabody® technology in mAbs and mAb-like therapeutics

Current focus: Target-by-target partnerships

NB. We are open to other models

POTENTIAL PARTNERSHIPS

- Research evaluations
- Co-development of new Stellabody®- containing biologic therapeutics
- Licensing

Stellabody®: Current development status

Strengthening and furthering scope of Stellabody® technology

Burnet Institute is advancing Stellabody® internally

Validation studies

Overall aim:

To assess preclinical efficacy of Stellabody® in *in vivo* and human clinical samples

Models

- Human clinical samples
- Animal models

BACK

Human clinical samples

VALIDATION STUDIES – HUMAN CLINICAL SAMPLES

AIM

To demonstrate efficacy of Stellabody® antibodies in patient samples

MODELS

Samples selected based on clinical stage and risk

- B Cell Lymphoma
- Leukaemia
- Multiple myeloma

READOUT

Complement killing (CDC) [Preliminary data available]

ANTIBODIES TESTED

Unmodified antibody, Stellabody® antibodies, competitor antibodies (HexaBody®)

ANTIBODY TARGETS

- CD38
- CD20
  - Comparing to hexamerisation competitor (HexaBody®)

TIMEFRAME

- Preliminary data from chronic lymphocytic leukemia (CLL) generated

BACK

Stellabody® CD20 mAb showed greater killing potency on cell samples from CLL patients

Study

- CD20 mAb (ofatumumab) was enhanced for potency using Stellabody®
- Stellabody® ofatumumab, HexaBody® ofatumumab and unmodified/wild-type ofatumumab were tested for their ability to induce cell death of leukaemic cells.

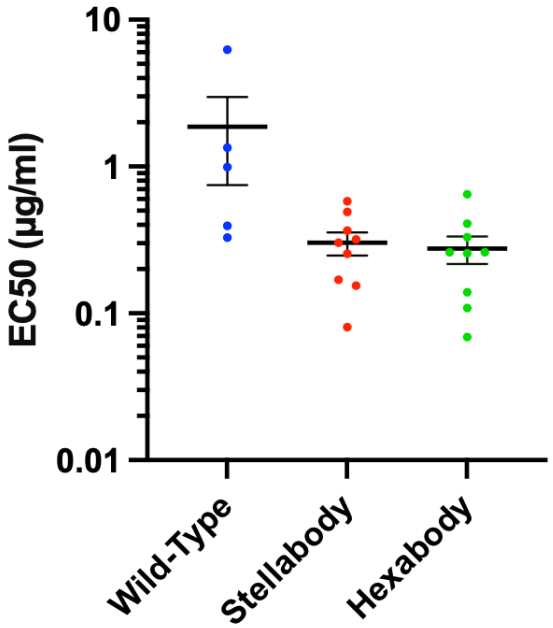
Cells: Blood samples from CLL patients

Assay: EC50 values were measured in a CDC assay

Key Results

- Stellabody® ofatumumab exhibited greater potency on CLL patients' cells than wild-type (as shown by EC50 in graph to right)
- Stellabody® also exhibited equivalent potency to its direct competitor HexaBody®.

PRELIMINARY RESULTS:
9 PATIENTS



Versions of ofatumumab tested on CLL patient cells

*Data on file

BACK

Animal studies

VALIDATION STUDIES – ANIMAL STUDIES

AIM

To test efficacy Stellabody® antibodies in *in vivo* mouse models, initially focusing on cancer

MODELS (Xenograft models)

- Solid cancer (planned)
  - Colon cancer
- Blood cancers (in progress)
  - B Cell Lymphoma
  - Leukaemia

⇒ Patient-derived cells (pdx) & Cell line-derived (cdx)

TIMEFRAME

Commenced November 2023

ANTIBODY TARGETS

- DR5
- CD38
- CD20

READOUTS

- Tumour volume / growth
- Animal weight
- Metastases

BACK

Burnet
reach for the many

Thank you

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