

Adalimumab & Others

Technology from the group of Pradip Sen
at **CSIR-Institute of Microbial Technology,**
Chandigarh, India

Match Maker/ Biosimilars / 31 Aug 2021/DrSen CSIR-IMTech

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About Adalimumab

Adalimumab is a human monoclonal antibody that **treats autoimmune diseases** by **inhibiting tumour necrosis factor** (TNF); a soluble inflammatory cytokine.

- **Originator / reference product:** The originator product, AbbVie's Humira was approved by **USFDA in Dec 2002** and **EMA in Sept 2003**. Patent will **expire in US in 2023** and **expired in Europe in June 2017**. (Source: [GabiOnline](#))
- **Indications:** **Rheumatoid arthritis (RA)**, juvenile idiopathic and psoriatic arthritis, ankylosing spondylitis, **Crohn's disease**, **psoriasis** and ulcerative colitis.

Market & Industry Overview

Market:

Market size is estimated to reach **\$4.3 Billion by 2025**, growing at a CAGR of 4.98% during the forecast period 2020-2025. Geographically, **North America** registered for **highest revenue share of 37.1%** in 2019. (Source: [Industry Arc](#))

Industry players:

- **Global:** AbbVie, Boehringer Ingelheim, Cadila Pharma (EU)
 - **Approved and ready for launch** in US in 2023*: Amgen, Novartis Sandoz, Samsung BioEpiS, Pfizer, Mylan
- **Indian:** Zydus Cadila, Torrent Pharma, Reliance Lifesciences, Hetero Pharma, Glenmark Pharma

*With **AbbVie** announcing **settlement** of its **patent litigation with Boehringer Ingelheim** over Adalimumab in May 2019, **biosimilar entry** is set to **open up for US in 2023**. (Source: [Healio.com](#))

The Opportunity: Why you should be interested?

Market interesting: a) While EP patent on Adalimumab has expired, the US patent is set to expire in 2023. **Next generation Biosimilar** b) **Global prevalence** of RA is between **0.24-1%** and in **India** is **0.34%**. But for a population of 1.2 billion, it amounts to **5 million patients**, a significantly heavy burden. (Source: [Springerlink](#), [AcraaAbstracts](#)) c) **Humira** occupies an **outsized position in the biologic and biosimilar landscape**, as it netted \$16.11 billion in 2020, an increase of 8.4% over 2019.

New indications/applications: Being tested for chronic skin diseases such as eczema

Cost still high:

- Global cost between:
~\$2000-3000 per month
- India cost between:
~ \$2124 (~Rs. 1,56,000) per month (Humira)
~ \$164-328 (~Rs 15000-30000) per month (Biosimilar)

Annual Cost of treatment with Biosimilar: ~\$1966-4920 (Rs 1,44,000 - 3,60,000)

Sky-high prices

The U.S. has the highest medication prices in the world.

Country	Average monthly price: Humira
Japan	\$980
France	982
Canada	1,164
United Kingdom	1,180
Australia	1,243
Germany	1,749
United States	2,505

Sources: Bloomberg News, SSR Health, IHS Inc.

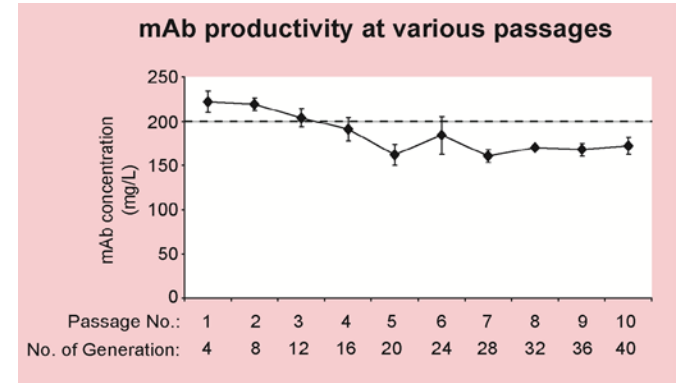
Source: [LAtimes](#)

Opportunities for process innovations to reduce costs: Higher mAb producing clone, innovation in upstream and downstream processing.

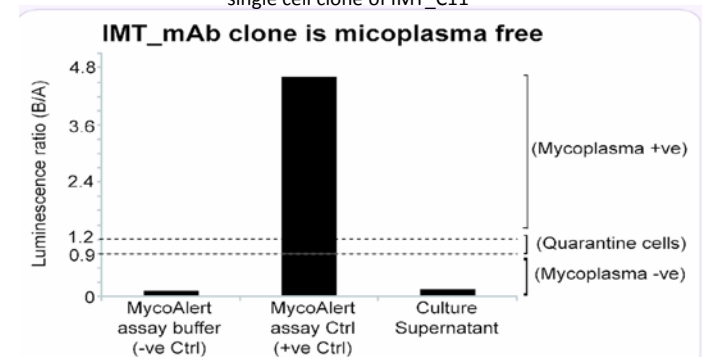
The Technology Offering

Clone Performance

- **Inhouse developed, stable, unencumbered CHO cell clone (IMT_C11)** (mycoplasma free and functional)
 - Produces : Adalimumab ~170-200 mg/L (100 ml culture vol. in 500 ml shake flask; unfed culture; repeated 3 times)
- Shows **stable mAb production through 40 generations**



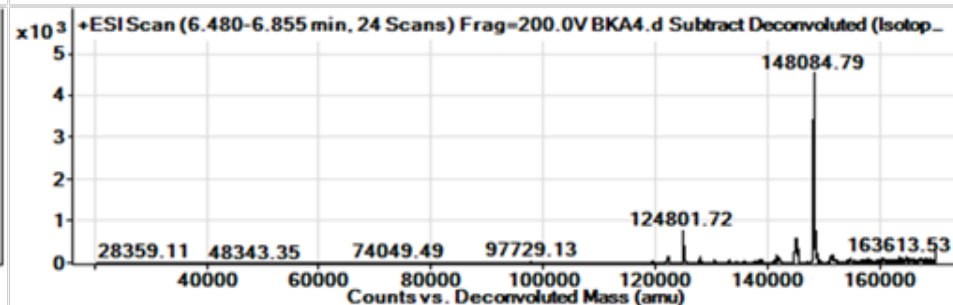
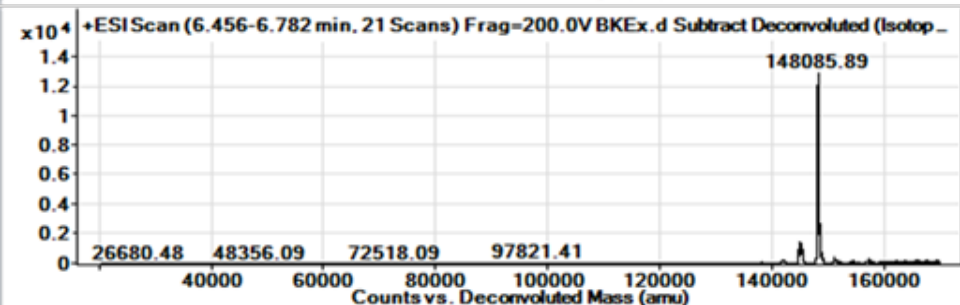
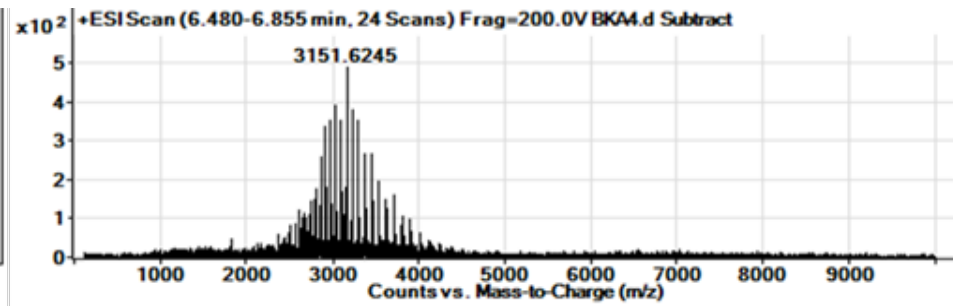
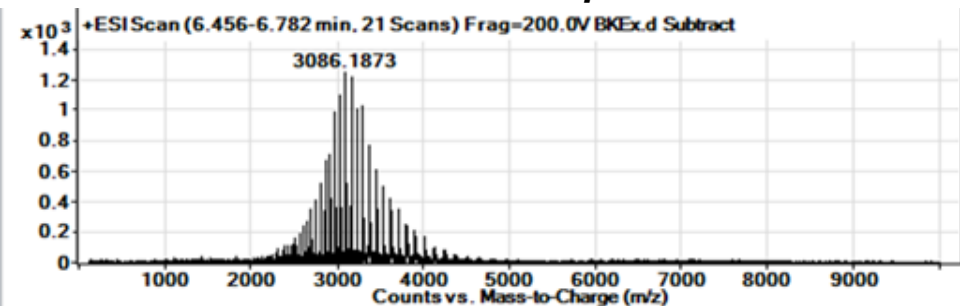
Consistent mAb production up to 10 passages observed from third round isolated single cell clone of IMT_C11



Select Data -Biosimilarity: Intact Mass Analysis

Exemptia

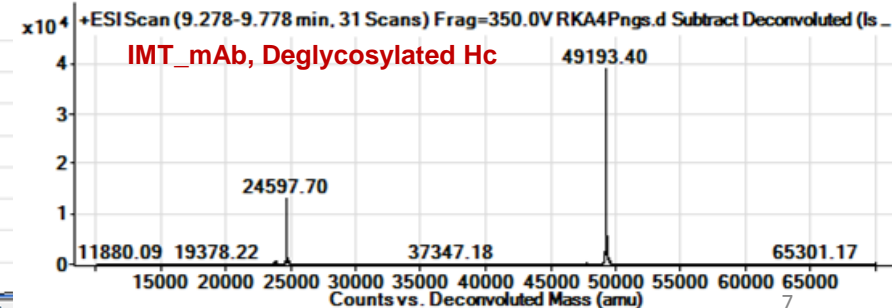
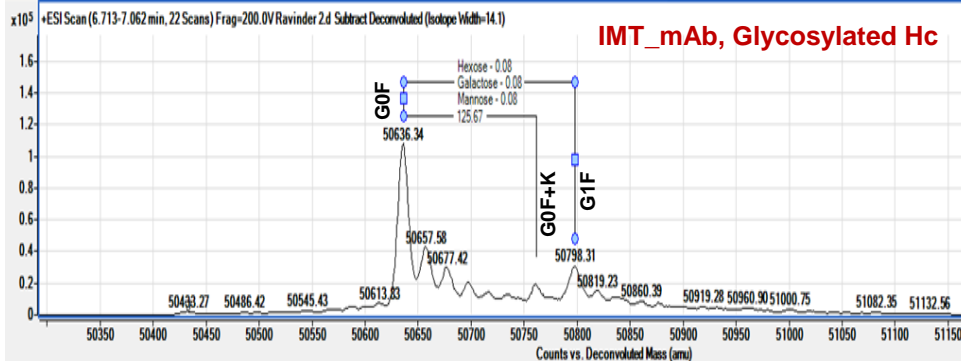
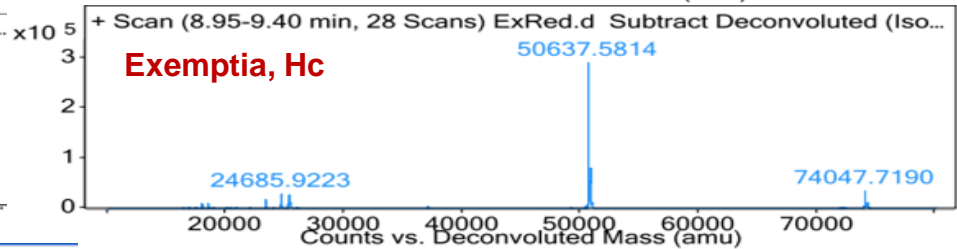
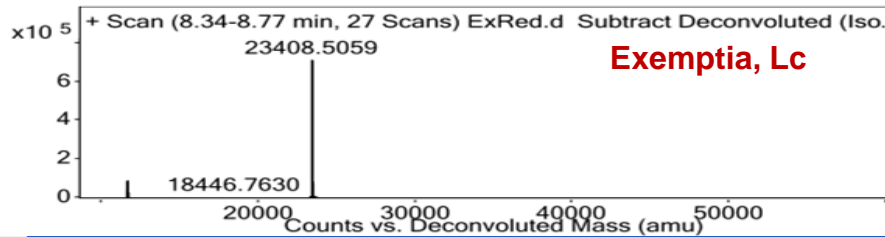
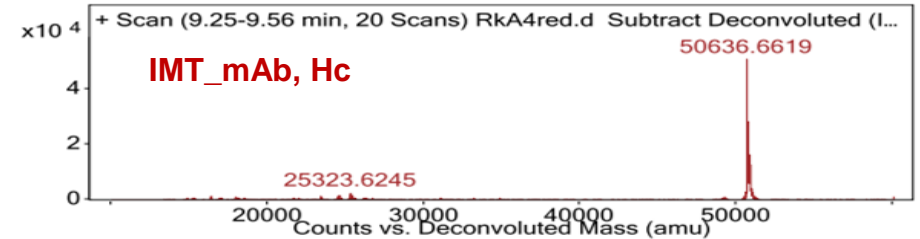
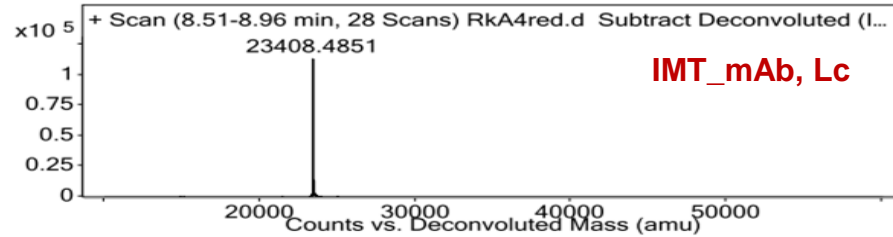
IMT_mAb



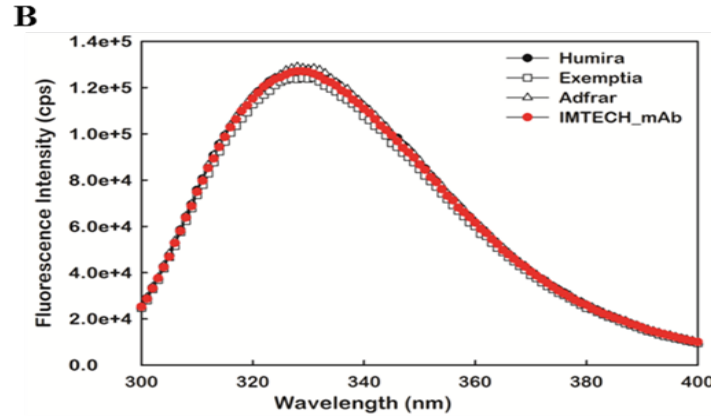
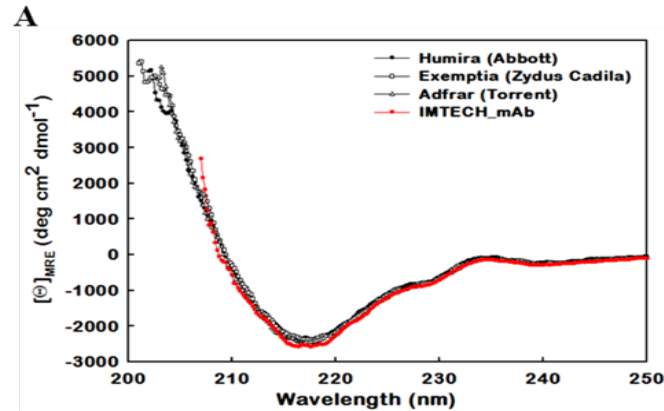
Confirms the correct molecular mass of Adalimumab.

Selected Data - Biophysical characterization

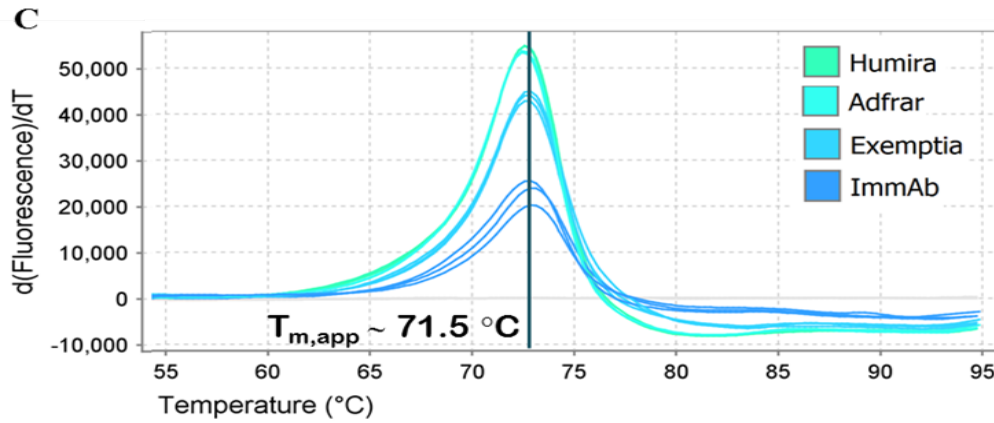
Mass spec analysis confirms IMT_C11 mAb contains single N-linked biantennary glycan in its heavy chain, similar to adalimumab and its known biosimilars.



Selected Data - Biophysical characterization

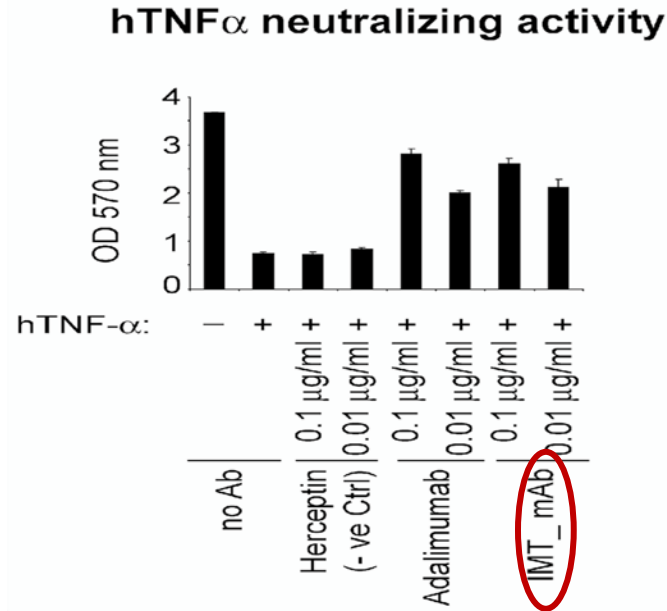


Comparison of (A) secondary structure by far-UV CD spectrum, (B) tertiary structure by fluorescence, and (C) thermal stability of purified IMT_mAb with that of commercially available anti-TNF α mAbs

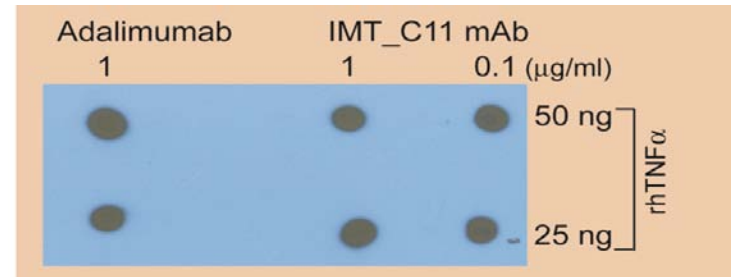


In-solution secondary and tertiary structure and thermal stability results for IMTECH_mAb found similar to the Zydus's Adalimumab biosimilar Exemptia

Selected Data - Biosimilarity: Neutralizing activity



Dot blot assay for rhTNF α -binding

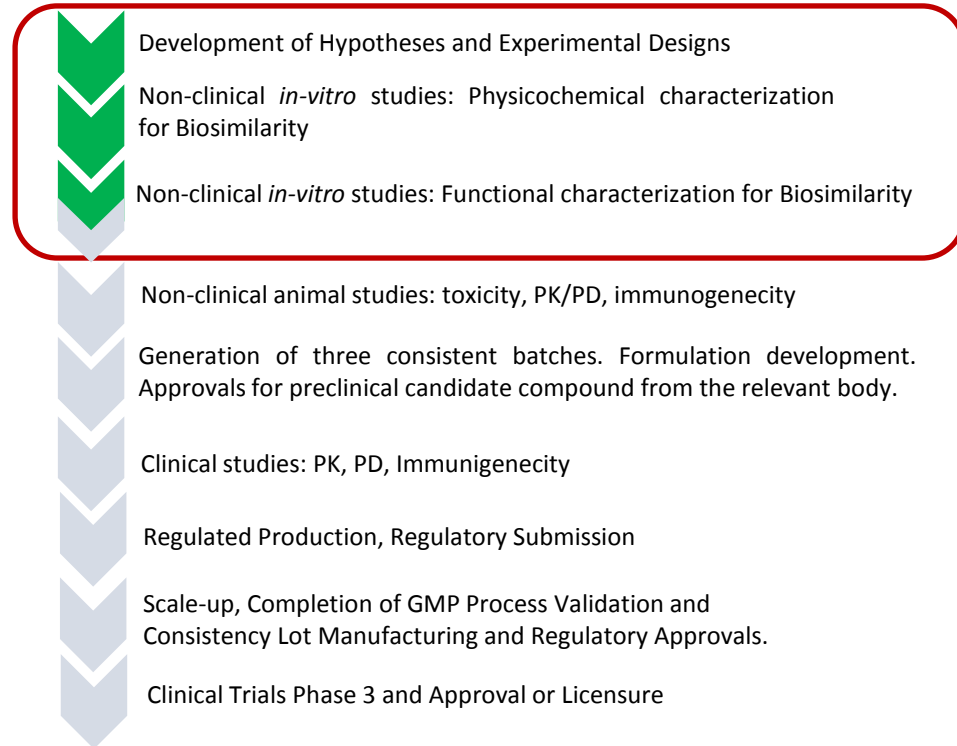


Preliminary results shows **comparable TNF α neutralizing ability and demonstrate biosimilarity of IMT_C11 mAb** with the originator molecule.

Cell-based assay for neutralization of rhTNF α -induced cell toxicity shows IIMT_C11 mAb is **functionally equivalent** to Adalimumab

Current Status of Technology and Path Ahead

- Stage of Development
 - mAb production at shake flask level (unfed culture)
- Clone and construct developed inhouse (unencumbered)
- Vector and cell lines in-licensed from invitrogen
- Key process parameters —
 - IMT_C11 clone 100% purity
 - Yield: ~170-200 mg/L (100 ml culture vol. in 500 ml shake flask; unfed culture; repeated 3 times)



What are we seeking?

Seeking Industrial partners interested in:

- ❖ **Technology Transfer of clone:** IMTech shall license out clone IMT_C11 along with SOP's and protocols as per CSIR Tech Transfer Guidelines.
- ❖ **Co-development partners:** To carry out further development/validation work like functional characterization of biosimilarity and upscaling on mutually agreeable terms.
- ❖ **Sponsored R&D and research collaborations:** Any R&D program leveraging the capabilities at IMTech

CSIR-IMTECH mAb based Biotherapeutics Group



Lead Scientist: Dr Pradip Sen

EXPERIENCE

Academic:

- **Current affiliations** : Senior Principal Scientist, monoclonal antibodies based biotherapeutics group
- **Network collaborator** - Global Challenge Research Fund project with Durham University (UK) for neglected and tropical diseases.
- **Past affiliations:** University of Northern Carolina and Humboldt University, Berlin

Fact file of IMTECH Biotherapeutics Group:

- **Dr. Pradip Sen** (lead PI) has authored more than **20 publications** in his areas of expertise.
- **Team members**
 - **Dr. Raj Kumar:** Cell and molecular biologist
 - **Dr. Beena Krishnan:** Protein Biochemist
 - **Dr. Grish Vashney:** Immunologist
- State-of-the-art **bioprocess development till 5 L scale, analytical and functional characterization facilities.**
- Group capable of performing complete **end-to-end research for select protein-based biotherapeutics** (biosimilar, biobetters and/or novel molecules)

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