

IOCAB
2025
Conference

The 1st International Online Conference by Antibodies

13–14 October 2025 | Online



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13–14 October 2025 | Online



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Welcome from the Chair

We are pleased to announce the **1st International Online Conference by *Antibodies*–Therapeutic Antibodies: New Trends in Discovery, Developability and Characterization**, which will be held online on 13–14 October 2025 and promoted by the open access MDPI journal *Antibodies* (ISSN 2073-4468).

Discovered more than hundred years ago, antibodies have emerged as the most versatile and therapeutically effective class of biological drugs that we currently have. Since the approval of the first therapeutic antibody, muromonab-CD3, by the U.S. Food and Drug Administration (FDA) in 1986, and also the subsequent approval of the first recombinant humanized antibody, trastuzumab, in 1998, the number of monoclonal (or recombinant) antibodies (mAbs) in clinical use has grown exponentially, currently accounting for more than half of the top ten drugs according to global sales.

However, apart from this impressive success, many questions remain with regard to biomedical drug discovery and biopharmaceutical development, while new modalities and mechanisms of action have come into focus.

The journal *Antibodies* was launched 10 years ago to promote both fundamental research on this class of immunoglobulin (Ig) proteins and their application for human therapy, diagnostics and beyond. *Antibodies* has flourished since then, thanks to the continued support of many gifted Authors and our dedicated Editorial Board Members. Now the time has come to disseminate and discuss the latest insights in this field in regard to the broader scientific community with our inaugural electronic conference on antibodies.

We invite researchers from academia as well as the biopharmaceutical and biotech industry to contribute original findings, novel ideas, scientific concepts, as well as new technologies and experiences to deal with the molecular mechanisms of antibody activity, including novel multivalent or multispecific formats and drug conjugates, their discovery, manufacturing, in vitro characterization, and pharmacokinetic and pharmacodynamic properties in laboratory animals up to early clinical development.

Topics of the conference will be:

- Antibody Discovery and Engineering;
- Antibody-based Therapeutics;
- Immuno-oncology and Tumor Imaging;
- Humoral Immunity;
- Computational Antibody Engineering.

This conference will be organized as an online event in order to enable participation from all over the world, with no restrictions related to travel effort and expenditure. Furthermore, active participation and attendance in this online conference are free of charge. We extend our warmest welcome to you as Participants or Attendees of this virtual conference. We hope you can share this enthusiasm and help us to make this first *Antibodies* online conference a success.



Professor Arne Skerra
Conference Chair

School of Life Sciences, Technical
University of Munich, Munich, Germany



antibodies

an Open Access Journal by MDPI

Antibodies (ISSN 2073-4468) is an international, peer-reviewed open access journal that provides an advanced forum for scientific publications related to antibodies and antigens. It publishes reviews, research articles, communications and short notes. Our aim is to encourage scientists to report their experimental as well as theoretical results in as much detail as possible. There is no restriction on the maximum length of the papers. Full experimental and/or methodological details must be provided. Electronic files or software describing the full details of calculations and experimental procedures can be deposited as supplementary materials if unsuitable to be published in a normal way.

Impact Factor: 2.7 (2024); 5-Year Impact Factor: 4.7 (2024)

Keynote Speakers



Dr. Christian Klein

Biotech Startup, Zurich, Switzerland

Dr. Christian Klein is Distinguished Scientist and Department Head Cancer Immunotherapy Discovery at the Roche Innovation Center Zurich, specialized in the discovery, validation and preclinical development of antibody-based cancer immunotherapies and bispecific antibodies. During his 16 years at Roche he has made major contributions to the development and approval of obinutuzumab, the preclinical development of currently nine clinical stage bispecific antibodies/antibody fusion proteins, and the development of Roche's proprietary bispecific antibody platforms e.g. the CrossMAb technology and immunocytokine and T-cell bispecific antibody platforms. 2017 he completed his habilitation in biochemistry at the Ludwig-Maximilians University Munich and acts as external lecturer there.



Dr. Pietro Sormanni

Yusuf Hamied Department of Chemistry, University of Cambridge, Cambridge, UK

Dr Pietro Sormanni is a group leader supported by a Royal Society University Research Fellowship. His research focuses on the development of innovative data-driven technologies of rational antibody design, to obtain antibodies against targets that have been challenging to access using conventional approaches, and to improve or predict biophysical properties crucial for the successful development of antibody therapeutics. In his work he has established numerous collaborations and industrial partnerships, whose outcomes are beginning to demonstrate that computational approaches can be applied alongside established procedures to streamline antibody development, and to offer time- and cost-effective novel alternatives. Prior to taking up this post, Pietro held a postdoctoral Borysiewicz Biomedical Sciences Fellowship from the University of Cambridge, obtained a PhD in Chemistry from the University of Cambridge, and an MSc in Theoretical Physics from the University of Milan.



Prof. Dr. Christoph Schmidt

Institute of Experimental and Clinical Pharmacology, Toxicology and Pharmacology of Natural Products, University of Ulm Medical Center, Ulm, Germany

Dr. Christoph Schmidt is a Professor of Experimental Pharmacology at the Institute of Experimental and Clinical Pharmacology, Toxicology and Pharmacology of Natural Products, University of Ulm Medical Center. He studied pharmaceutical sciences at the LMU Munich (Germany) and received his Ph.D. at the University of Edinburgh (United Kingdom; under the guidance of Prof. Barlow), working on the structure and function of the complement regulator factor H. After his studies, Dr. Schmidt moved to the US for his postdoc, where he worked at the Innate Immunity/protein Chemistry laboratory (under the guidance of Prof. Lambris), focusing on developing a complement inhibitor. Since 2017 he has been a group leader at the Institute of Pharmacology of Natural Products and Clinical Pharmacology at Ulm University in Germany. After a short stay as a Professor of Biochemical Pharmacy at the Martin-Luther University of Halle-Wittenberg, he was appointed Professor of Experimental Pharmacology at the University of Ulm Medical Center. He and his team use numerous techniques to investigate the complement system to design new therapeutic molecules. His work has made fundamental contributions to the complement field, which includes extensive work on how the cascade is organized and regulated.



Prof. Dr. Harald Kolmar

Clemens Schöpf-Institute of Chemistry and Biochemistry, Technical University of Darmstadt, Darmstadt, Germany

Harald Kolmar is full professor of Biochemistry at the Technische Universität Darmstadt. His current scientific interests mainly focus on protein engineering and design, nanobiotechnology, antibody engineering, chemical biology and development of tailor-made peptides and miniproteins for applications in diagnostics and therapy. His research interests are Peptides, Protein Engineering, Biochemistry, Protein Expression, Biotechnology, Proteins and Recombinant Fusion Proteins.



Prof. Dr. Nick Devoogdt

Vrije Universiteit Brussel, Brussel, Belgium

I obtained a MSc degree in Molecular Biology in 1997 and a PhD degree in Applied Biological Sciences in 2004, both at the Free University Brussels, working on cancer genetics and investigating the interaction between cancer cells and tumor-infiltrating macrophages. After my PhD, in 2004-2005, I joined a team at the USA National Cancer Institute in Bethesda, Maryland to study ovarian cancer genetics. I returned to the Free University Brussels to fulfill a number of postdoc positions, at first continuing my research on cancer genetics and the interplay between cancer cells and their microenvironment. During these studies I got acquainted with antibody engineering and became skilled in the art of nanobody technology. From 2007 on I started to apply nanobodies as tracers for molecular imaging. Currently I'm a full professor heading a team at the Free University Brussels applying nanobodies as vehicles for imaging and therapy in the fields of oncology, inflammation and cardiovascular diseases.



Prof. Dr. Sai Reddy

Department of Biosystems Science and Engineering, ETH Zurich, Zurich, Switzerland

Sai Reddy is an Associate Professor of Systems and Synthetic Immunology at ETH Zurich in the Department of Biosystems Science & Engineering (D-BSSE, Basel, Switzerland). He is the principal investigator of the Laboratory for Systems and Synthetic Immunology. Systems immunology uses quantitative measurements, computational biology and machine learning to describe and understand the complexity of the immune system. His group has developed a number of methods in systems immunology to greater understand adaptive immunity, in particular with a focus on antibody repertoire sequencing and analysis. Synthetic immunology is based on using methods in molecular and cellular engineering to control immune cell function and behavior. His group has established methods to reprogram immune cells for applications in directed evolution and cellular immunotherapy, with an emphasis on engineering the immunogenome.



Prof. Dr. Shohei Koide

Department of Biochemistry and Molecular Pharmacology, NYU Grossman School of Medicine, New York, NY, USA

Shohei Koide, Ph.D. is a synthetic protein scientist. His research integrates mechanistic biochemistry and directed evolution to create highly functional but still simple proteins. He is the inventor of the FN3 Monobody technology, and has made important contribution to synthetic antibody technologies. He has pioneered many applications of synthetic binding proteins to biology, chemistry and medicine. Previously he was Professor at University of Chicago and at University of Rochester School of Medicine and Dentistry. He is an elected fellow of the AAAS and the National Academy of Inventors. He is a co-founder of Aethon Therapeutics.



Prof. Dr. Stefan Dübel

Department of Biotechnology, Technical University of Braunschweig, Braunschweig, Germany

Stefan Dübel is Full Professor of Biotechnology and Director of the corresponding department at the Technical University of Braunschweig, Germany. He also heads the technology transfer office "Center for Molecular Engineering" at iTUBSmbH and works as a consultant for biotech/pharmaceutical companies and US/EU government institutions. His research topics are Antibody Engineering, Phage Display, Animal-Free Antibody Generation, Anti-Cancer-Antibodies, Intrabodies, in vitro Evolution, Synthetic Biology, Biosensors, Hyperphage, SARS-CoV-2 neutralizing antibodies.

Invited Speakers



Ms. Alessa Schaffrath
University Medical Center
Hamburg-Eppendorf,
Hamburg, Germany



Mr. Volker Morath
Clinic and Polyclinic for Nuclear
Medicine, Technical University
of Munich, Munich, Germany



Dr. Thomas Böldicke
Helmholtz Centre for
Infection Research,
Braunschweig, Germany



Professor Jan Steyaert
Technological University Dublin,
Dublin 7, Ireland



Prof. Dr. Guglielmo Lucchese
University of Milano-Bicocca,
Department of Materials
Science, Milano, Italy

Program Overview

	Day 1	Day 2
Morning	Session 2. Antibody-based Therapeutics	Session 1. Antibody Discovery and Engineering
Afternoon	Session 4. Humoral Immunity Session 3. Immuno-oncology and Tumor Imaging	Session 5. Computational Antibody Engineering Session 4. Humoral Immunity

IOCAB 2025 Program

13 October 2025 (Monday)

Session 2. Antibody-based Therapeutics

Time: 9:00 (CEST, Basel) | 03:00 (EDT, New York) | 15:00 (CST Asia, Beijing)

CEST Time	Speaker	Title
9:00-9:20		Welcome and Opening Remarks <i>Prof. Dr. Arne Skerra</i>
9:20-9:30		Welcome from the Session Chair <i>Dr. Patrick Chames</i>
9:30-10:00	Keynote Speaker Prof. Dr. Stefan Dübel	Remotely controlled Antibodies
10:00-10:25	Invited Speaker Dr. Thomas Böldicke	Recombinant Antibodies and Recombinant T-cells against Intracellular Neoantigens
10:25-10:40	Selected Oral Speaker Ainhoa Goenaga Aramendi	Antibody-Functionalized Nanoparticles: A Targeted Drug Delivery Strategy
10:40-10:55	Selected Oral Speaker Salman Shahid	Cryo-EM Structures of HCV E2 Bound to Neutralizing and Non-Neutralizing Antibodies Using Engineered Domain-Swapped Bivalent Fabs as Fiducial Markers
10:55-11:00	Selected Poster Presenter Inesa Stonkutė	Predictive Biomarkers for Monoclonal Antibody Therapy Response in Oral Squamous Cell Carcinoma: A Systematic Review
11:00-11:05	Selected Poster Presenter Archana Damavarapu	Role of Antibodies in HAV Vaccines and Therapeutic Approaches: Insights into Immunological Strategies
11:05-11:10	Selected Poster Presenter Empuluri Haritha	Antibodies Involved in Allergic Conditions: Mechanisms and Therapeutic Insights
11:10-11:15	Selected Poster Presenter Palla Nikitha	Antibody-Drug Conjugates: Redefining Chemotherapy with Targeted Precision
11:15-11:20	Selected Poster Presenter Peruri Likitha	Targeted Drug Delivery in Lung Cancer Using Antibodies: A Precision Approach to Therapy
11:20-11:25	Selected Poster Presenter Chinthu Krishnaveni	Architects of Immunity: Structural Insights into Antibodies for Novel Biomedical Applications
11:25-11:30	Selected Poster Presenter Aluru Uma Priyanka	Advancements in Antibody Technology: From Bispecifics to AI-Driven Therapeutics
11:30-14:00	Break	

Session 4. Humoral Immunity

Session 3. Immuno-oncology and Tumor Imaging

Time: 14:00 (CEST, Basel) | 08:00 (EDT, New York) | 20:00 (CST Asia, Beijing)

CEST Time	Speaker	Title
14:00-14:10		Welcome from Session Chair <i>Dr. Cecile King</i>
14:10-14:40	Invited Speaker Professor Guglielmo Lucchese	Autoantibodies in post-COVID-syndrome
14:40-14:45	Selected Poster Presenter Madalen Arribas Galarreta	A broad-spectrum SARS-CoV-2 immunization strategy targeting the highly conserved MPER of the Spike protein
14:45-14:55		Welcome from Session Chair <i>Professor Sophia Karagiannis</i>
14:55-15:25	Keynote Speaker Prof. Dr. Nick Devoogdt	Imaging tumor immunity with nanobody tracers: from camel to bedside
15:25-15:55	Keynote Speaker Prof. Dr. Christian Klein	The present and future of bispecific antibodies for cancer therapy
15:55-16:20	Invited Speaker Volker Morath	PET Tracking of Cell and Gene Therapies Using a Novel Lanthanide•DTPA-Binding Anticalin Reporter Gene
16:20-16:25	Selected Poster Presenter Krishnaveni Manubolu	Targeting the Tumor Microenvironment with Radiolabeled Antibodies: Bridging Immunotherapy and Molecular Imaging

14 October 2025 (Tuesday)

Session 1. Antibody Discovery & Engineering

Time: 9:00 (CEST, Basel) | 03:00 (EDT, New York) | 15:00 (CST Asia, Beijing)

CEST Time	Speaker	Title
9:00–9:10		Welcome from the Session Chair Prof. Dr. Serge Muyldermans
9:10–9:40	Keynote Speaker Prof. Dr. Harald Kolmar	Discovery and optimization of bispecific antibodies with prescribed binding characteristics and biophysical properties
9:40–10:10	Keynote Speaker Professor Shohei Koide	Creating and targeting cancer-specific neoantigens by design
10:10–10:35	Invited Speaker Professor Jan Steyaert	Engineering Nanobodies for structural Biology, molecular pharmacology and drug discovery
10:35–11:00	Invited Speaker Alessa Schaffrath	Selection of nanobodies from LamaMice
11:00–11:05	Selected Poster Presenter Mattias Collin	Chemoenzymatically glycan engineered monoclonal IgG antibodies against Streptococcus pyogenes
11:05–14:00	Break	

Session 5. Computational Antibody Engineering

Session 4. Humoral Immunity

Time: 14:00 (CEST, Basel) | 08:00 (EDT, New York) | 20:00 (CST Asia, Beijing)

CEST Time	Speaker	Title
14:00–14:10		Welcome from Event Chair Prof. Dr. Arne Skerra
14:10–14:40	Keynote Speaker Prof. Dr. Sai Reddy	Generative design of antibody Fc variants with synthetic and programmable immune function
14:40–15:10	Keynote Speaker Dr. Pietro Sormanni	Antibody discovery and engineering by computational design
15:10–15:15	Selected Poster Presenter Sümeyla Ceren Elmaci	Computational Nanobody Design for Amyloid-Beta 42 Octamer in Alzheimer's Disease
15:15–15:45	Keynote Speaker Prof. Dr. Christoph Schmidt	Undue complement activation: Therapeutic strategies and hidden pitfalls
15:45–15:50	Event Chair Prof. Dr. Arne Skerra	Closing Remarks

Session 1. Antibody Discovery & Engineering

sciforum-142470: Chemoenzymatically glycan-engineered monoclonal IgG antibodies against *Streptococcus pyogenes*

Mattias Collin ^{1,*}, Berit Olofsson ¹, Andreas Naegeli ² and Pontus Nordenfelt ¹

¹ Division of Infection Medicine, Department of Clinical Sciences Lund, Lund University, Lund, SE-22184, Sweden

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Introduction

N-linked carbohydrate structures in the Fc-region of human IgG fine tune effector functions such as antibody-dependent complement activation and Fc-receptor-mediated phagocytosis. The Nordenfelt laboratory recently identified and characterized a human monoclonal (mAb) IgG antibody directed towards the M protein, a surface protein and virulence factor of *Streptococcus pyogenes* (GAS). These were isolated from memory B cells from an individual who had recovered from a GAS infection. One of the mAbs, Ab25, not only binds M protein with high affinity, but also promotes efficient phagocytosis of the bacteria in vitro. This is attributed to a natural bi-specificity towards two different M protein epitopes.

Methods

Chemoenzymatic engineering was used to remove all Fc glycans on Ab25, Ab49 (monospecific mAb against M protein), and omalizumab (IgG mAb against IgE) as the control, and then generate homogenous glycoforms (G0, G0-afuc, G2, G2S2) through click chemistry. Validation of glycosylation pre- and post engineering was performed using LC-MS. These were subsequently tested using flow cytometry-based bacterial binding, phagocytosis using THP-1 cells, and complement factor C1q deposition assays.

Results

Original mAb glycosylation and generated glycoforms were validated using LC-MS. Binding experiments revealed that only deglycosylation had any major effects of binding to bacteria; the phagocytosis experiment revealed that the internalization, but not association, of bacteria to THP-1 was influenced by antibody glycoform; and C1q deposition was gradually decreasing in correlation with the size and complexity of the glycans.

Conclusions

Human IgG mAbs against GAS, as well as omalizumab, could be converted to homogenous glycoforms. mAb glycoform clearly influences internalization into phagocytes as well as complement binding. This has important implications for the development of anti-infective mAbs, and highlights mAb glycan engineering as a modality when developing IgG-based therapeutic antibodies.



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sciforum-145186: Detection of Anti-HEV IgM and IgG Antibodies among Antenatal Women Attending a Tertiary Care Center

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Hepatitis E virus (HEV) is recognized as one of the leading causes of acute viral hepatitis (AVH) in developing countries, where it is primarily transmitted through the consumption of contaminated food and water. Although often self-limiting, HEV infection poses a significant public health concern, particularly among pregnant women, due to its potential complications. The present study aimed to determine the seroprevalence of HEV infection in asymptomatic antenatal women attending a tertiary care center in South Punjab, Pakistan.

A total of 100 asymptomatic pregnant women were screened for anti-HEV antibodies (IgM and IgG) using an ELISA kit (DIA PRO, Italy). The overall seropositivity rate was found to be 12%, indicating prior exposure to HEV infection in this cohort. Specifically, IgG antibodies were detected in 6% of women and IgM antibodies in 5%, while two women showed evidence of both IgG and IgM positivity, suggestive of recent or ongoing infection. Notably, the majority of participants reported reliance on untreated water sources irrespective of educational background, highlighting environmental risk factors.

Although HEV is generally self-limiting, these findings underscore the importance of routine serological screening in antenatal populations to prevent adverse pregnancy outcomes. In addition, increased community awareness regarding transmission routes and preventive measures is essential. Given the scarcity of regional data, this study emphasizes the need for larger-scale epidemiological investigations to better understand the burden of HEV in South Punjab, Pakistan.

Keywords: Hepatitis E Virus, Antenatal Women, Seroprevalence, Immunoglobulins, South Punjab



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Session 2. Antibody-based Therapeutics

sciforum-138915: Advancements in Antibody Technology: From Bispecifics to AI-Driven Therapeutics

Aluru Uma Priyanka *, Budidhavaka Yashika, Chintham Jayesh and Akkidasari Charanteja

B.Pharmacy 4th Year Student, Narayana Pharmacy College, Nellore, India-524003

Antibody technology has rapidly evolved beyond conventional monoclonal antibodies, transforming the landscape of diagnostics, immunotherapy, and precision medicine. These advancements have led to the development of highly specialized antibody formats and engineering platforms that address complex diseases, including cancers, viral infections, and autoimmune conditions.

One of the most significant breakthroughs is the development of **bispecific antibodies**, which are designed to simultaneously bind to two different antigens or epitopes. This dual-targeting capability enhances therapeutic specificity, as seen in bispecific T-cell engagers (BiTEs), which redirect immune cells to tumor cells, offering greater efficacy in cancer immunotherapy.

Antibody-drug conjugates (ADCs) represent another innovation, combining the specificity of antibodies with the potency of cytotoxic agents. By selectively delivering chemotherapy drugs to tumor cells, ADCs such as trastuzumab deruxtecan have shown marked success in treating HER2-positive cancers, with reduced systemic toxicity.

During the COVID-19 pandemic, antibody technology played a pivotal role in the development of **neutralizing antibodies** against SARS-CoV-2. Monoclonal antibodies targeting the spike protein helped reduce viral load and disease severity in infected patients, demonstrating the rapid applicability of antibody platforms in pandemic response.

AI-driven antibody design is emerging as a revolutionary approach in drug development. Machine learning algorithms are being used to predict antibody-antigen interactions, optimize binding affinities, and design novel antibody sequences with high precision and speed, significantly reducing time and cost in therapeutic discovery.

Moreover, **CAR T-cell therapy**, a form of cellular immunotherapy based on engineered antibodies, has shown remarkable success in treating hematologic malignancies. By fusing an antibody-derived recognition domain with a T-cell signaling domain, CAR T-cells specifically target and kill cancer cells, offering durable responses in refractory cases.



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sciforum-138932: Antibodies in the War Against Cancer: Precision Weapons in Targeted Therapy

Shaik Masthani Farhana *, Shaik Tabassum, Sarangam Padmavathi, Syed Muskaan
and Shaik Zaiba Firdose

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Among the arsenal of therapeutic strategies, antibodies have emerged as potent tools in the war against cancer due to their exceptional specificity and adaptability. Antibodies are protective glycoproteins that are synthesized by the immune system in response to foreign substances known as antigens. Their unique ability to selectively recognize and bind to tumor-associated antigens has positioned them as a cornerstone in targeted cancer therapy. The mechanism by which antibodies act against cancer cells can be either direct—by inducing apoptosis or inhibiting cellular proliferation—or indirect, by recruiting immune effector functions such as antibody-dependent cellular cytotoxicity (ADCC) or complement-dependent cytotoxicity (CDC). Monoclonal antibodies (mAbs), the most commonly used therapeutic format, have shown considerable success in treating cancers such as breast cancer (e.g., trastuzumab) and lymphomas (e.g., rituximab). Based on their structure and action, antibody therapies can be classified into naked antibodies, conjugated antibodies (linked to toxins or radionuclides), immune checkpoint inhibitors, and engineered formats such as bispecific and trispecific antibodies, which can bind to two or more targets simultaneously, thereby enhancing therapeutic outcomes. Personalized antibody therapy has gained momentum, guided by tumor profiling and molecular diagnostics. This approach enables the selection of antibody treatments based on the unique genetic and proteomic signature of an individual's tumor, ensuring improved efficacy and minimized toxicity. Moreover, combining antibodies with chemotherapy, radiotherapy, or other immunotherapies (like CAR-T cells or checkpoint inhibitors) offers synergistic effects and overcomes tumor resistance.



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sciforum-138943: Antibody–Drug Conjugates: Redefining Chemotherapy with Targeted Precision

Palla Nikitha *, Pralayakaveri Kalyani and Rudrakota Swaruparani

B.Pharmacy 4th Year Student, Narayana Pharmacy College, Nellore, Inida-524003

Antibody–drug conjugates (ADCs) represent a groundbreaking advancement in cancer therapeutics, combining the high specificity of monoclonal antibodies with the potent cytotoxic effects of chemotherapy. This innovative approach aims to selectively target cancer cells while minimizing damage to healthy tissues, thereby overcoming the limitations of traditional chemotherapy.

ADCs are engineered molecules composed of three critical components: a monoclonal antibody that specifically binds to tumor-associated antigens, a cytotoxic payload capable of killing cancer cells, and a chemical linker that ensures the stability of the drug until it reaches the target. Upon binding to the target antigen on the surface of cancer cells, the ADC is internalized, and the cytotoxic drug is released intracellularly, leading to targeted cell death.

Clinically approved ADCs such as **trastuzumab emtansine (T-DM1)**, targeting **HER2** in breast cancer, and **gemtuzumab ozogamicin**, targeting **CD33** in acute myeloid leukemia, have demonstrated substantial improvements in treatment outcomes, including enhanced progression-free survival and reduced systemic toxicity. These successes underscore the importance of precise antigen selection and the continuous evolution of ADC design strategies.

Despite their promise, ADC development is challenged by factors such as tumor antigen heterogeneity, multidrug resistance, and the need for stable yet cleavable linkers. However, advancements in antibody engineering, site-specific conjugation, and next-generation payloads are rapidly addressing these hurdles. Novel ADCs with bispecific targeting capabilities and innovative payload mechanisms are currently in development, further expanding their therapeutic potential.

This work emphasizes the role of HER2 and CD33-targeted ADCs as models of precision oncology, illustrating how these agents are redefining the landscape of chemotherapy. As research progresses, ADCs are expected to play an increasingly vital role in personalized cancer treatment, offering a powerful blend of specificity, efficacy, and safety.



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sciforum-138963: Role of Antibodies in HAV Vaccines and Therapeutic Approaches: Insights into Immunological Strategies

Archana Damavarapu *, Chilakapati Pragnasri Harshini and Nakka Venkata Pallavi

B.Pharmacy 4th Year Student, Narayana Pharmacy Collge, Nellore, India-524003

Hepatitis A virus (HAV) remains a global health concern, especially in regions with poor sanitation and limited access to clean water. Although self-limiting in most cases, HAV infection can result in acute liver failure, particularly in adults and immunocompromised individuals. The immune response, particularly the production of antibodies, plays a central role in both natural immunity and vaccine-induced protection against HAV. Antibodies generated against HAV surface antigens are crucial in neutralizing the virus and preventing infection. Licensed inactivated and live-attenuated HAV vaccines have been highly successful in inducing long-lasting immunity by stimulating robust antibody responses. The role of neutralizing IgG antibodies is well established in conferring lifelong protection, and vaccine-induced memory B cells contribute to rapid response upon re-exposure. In addition to prophylactic vaccination, antibody-based interventions can support antiviral therapies, particularly in post-exposure prophylaxis. The use of passive immunization through HAV-specific immunoglobulins provides temporary protection and is especially useful for individuals at high risk or those with contraindications to vaccination. Animal models have significantly contributed to understanding the immunogenicity of HAV vaccines and the mechanisms of antibody-mediated viral clearance. While antiretroviral therapy (ART) is primarily associated with HIV, HAV-HIV coinfection presents a unique challenge where ART's immune modulation may influence HAV infection outcomes. Monitoring antibody titers and HAV vaccine responsiveness in ART-treated individuals is essential for effective immunization strategies in immunocompromised populations. Novel approaches such as monoclonal antibody development targeting HAV capsid proteins are under exploration, offering potential in both treatment and prophylaxis. These innovative therapies could be particularly valuable during outbreaks or in regions with limited vaccine access. In conclusion, antibodies are at the core of effective HAV prevention and therapeutic strategies. Continued research into vaccine optimization, monoclonal antibody therapy, and immune response modulation is essential to combat HAV infections across diverse populations.



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sciforum-125772: Antibody–drug conjugates (ADCs) and their journey to autoimmune disease immunotherapy

Angel Justiz-Vaillant

Department of Pathology, Microbiology and Pharmacology, Faculty of Medical Sciences, University of the West Indies, St. Augustine 330912, Trinidad and Tobago

Antibody–drug conjugates (ADCs) represent a novel and rapidly evolving class of targeted therapeutics that combine the high specificity of monoclonal antibodies (mAbs) with the potent cytotoxic effects of small-molecule drugs. These engineered molecules are designed to selectively deliver cytotoxic agents to specific cells, thereby reducing off-target toxicity and enhancing therapeutic efficacy. In oncology, ADCs have already demonstrated significant clinical success, particularly in the treatment of hematological malignancies and solid tumors. Agents such as trastuzumab emtansine and brentuximab vedotin exemplify how ADCs can effectively target cancer cells while limiting damage to healthy tissues. Over the past decade, the development of new linkers, payloads, and antibody engineering technologies has further refined the safety and effectiveness of ADCs, leading to an expanded pipeline of approved and investigational compounds. Following their success in oncology, interest has grown in repurposing ADCs for the treatment of non-malignant diseases, including autoimmune disorders. These conditions are characterised by inappropriate immune responses in which autoreactive cells and inflammatory mediators attack host tissues. ADCs offer a promising solution by enabling the selective depletion or modulation of these pathogenic immune cell subsets without broadly suppressing the entire immune system. Preclinical and early clinical studies have shown encouraging results. For instance, ADCs targeting CD19 or CD22 are being explored for systemic lupus erythematosus and other B-cell-driven diseases, while anti-CD3 ADCs have shown potential in type 1 diabetes. As knowledge of disease-specific immune targets increases, ADCs may provide a new avenue for achieving durable remission in autoimmune diseases with improved safety profiles compared to conventional immunosuppressants. This presentation comprehensively explores the evolving landscape of ADCs in autoimmune therapeutics.



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sciforum-138945: Antibodies Involved in Allergic Conditions: Mechanisms and Therapeutic Insights

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Allergic conditions are immune hypersensitivity reactions triggered by otherwise harmless environmental substances such as pollen, dust, food, or insect venom. Central to these reactions are specific antibodies—particularly **Immunoglobulin E (IgE)**—which mediate **Type I hypersensitivity**. IgE is produced upon initial exposure to an allergen through the activation of B cells, aided by T helper 2 (Th2) cells and cytokines like IL-4 and IL-13. Once synthesized, IgE binds to **high-affinity FcεRI receptors** on mast cells and basophils, sensitizing them to future exposures.

Upon re-exposure, allergens cross-link the IgE molecules on these sensitized cells, leading to **degranulation** and the release of **inflammatory mediators** such as histamine, prostaglandins, leukotrienes, and cytokines. These mediators are responsible for the hallmark symptoms of allergy, including itching, wheezing, swelling, and in severe cases, **anaphylaxis**.

Beyond IgE, emerging research suggests roles for **IgG subclasses**, particularly **IgG4**, in immunomodulation during allergen-specific immunotherapy, and **IgA** in mucosal immune responses, adding complexity to our understanding of antibody function in allergic diseases.

Therapeutically, targeting IgE has revolutionized allergy management. **Monoclonal antibodies** like **omalizumab** bind free IgE, preventing its interaction with FcεRI receptors and thus reducing mast cell and basophil activation. Newer approaches are exploring **anti-IL-4/IL-13 therapies**, Fc receptor blockers, and allergen desensitization strategies to reduce IgE synthesis and allergic inflammation.

Understanding the antibody-mediated immune mechanisms in allergy not only improves diagnosis and risk stratification, but also facilitates the development of **personalized therapies** that are safer and more effective. Continued research into antibody dynamics in hypersensitivity responses holds promise for reducing the global burden of allergic diseases, which are on the rise due to urbanization, pollution, and changing lifestyles.



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sciforum-144658: Antibody-Functionalized Nanoparticles: A Targeted Drug Delivery Strategy

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Introduction

Monoclonal antibodies (mAbs) have become pivotal in cancer therapy due to their ability to recognize tumor-associated antigens, triggering immune responses or disrupting signaling pathways essential for tumor growth and survival. Over recent decades, mAbs have been engineered as carriers for cytotoxic agents, enabling targeted delivery, reducing off-target toxicity, and expanding the therapeutic window of chemotherapeutics. Since antitumor efficacy often correlates with drug payload, this study explores a strategy to enhance drug delivery by conjugating a mAb to a drug-loaded nanostructured lipid carrier (NLC) via a maleimide-based reaction.

Methods

NLCs were produced consisting of a disordered solid lipid matrix (comprising blended solid and liquid lipids) and a surfactant-containing aqueous phase, designed to encapsulate poorly soluble drugs. After loading the maleimide lipid containing NLCs with the topoisomerase I inhibitor SN-38, nanoparticles were incubated with Denintuzumab, a CD19 specific antibody, in the presence of a reducing agent. The mixture was next purified through size exclusion chromatography.

Results

The resulting antibody-NLC conjugates are monodisperse (with a PDI of 0.27), exhibit a hydrodynamic diameter of ~140 nm, and retain high target specificity.

Conclusions

It is feasible to conjugate monoclonal antibodies to drug-loaded NLCs. Ongoing work focuses on loading these nanoparticles with the topoisomerase I inhibitor SN-38 and evaluating the targeted delivery efficacy of these nanoparticles in tumor models.



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sciforum-138927: Architects of Immunity: Structural Insights into Antibodies for Novel Biomedical Applications

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Antibodies, or immunoglobulins, are Y-shaped glycoproteins produced by B cells, playing a central role in immune defense. Their unique structural characteristics, particularly the variable (V) and constant (C) regions, have made them indispensable not only in traditional immunology, but in a broad spectrum of modern biomedical applications. Advances in structural biology and protein engineering have enabled the rational design of antibody-based tools for diagnostics, therapeutics, and targeted drug delivery.

The antigen-binding fragment (Fab) of an antibody, comprising variable regions of the heavy and light chains (VH and VL), is responsible for high-affinity binding to specific epitopes. Meanwhile, the crystallizable fragment (Fc) mediates effector functions such as antibody-dependent cellular cytotoxicity (ADCC) and complement activation. Modifications in these regions allow for tailoring antibodies to specific therapeutic needs, including half-life extension, reduced immunogenicity, or enhanced tissue penetration.

In novel applications, structural insights have facilitated the development of **single-chain variable fragments (scFvs)**, **nanobodies**, and **bispecific antibodies**, offering reduced size, improved tissue access, and dual-targeting capabilities. These engineered formats are now being explored in targeted cancer therapies, neurodegenerative disease treatment, biosensor design, and infectious disease management. The understanding of hinge flexibility, epitope–paratope interactions, and glycosylation patterns has further enhanced the functional versatility of antibodies.

Monoclonal antibodies, owing to their specificity and modularity, are now employed in precision medicine, including checkpoint blockade therapy, antibody-drug conjugates (ADCs), and CAR-T cell engineering. Moreover, structural mapping using tools such as X-ray crystallography, cryo-electron microscopy, and molecular dynamics simulations is paving the way for the next generation of antibody-based modalities.

This work explores the structural foundations that empower antibodies to serve as precision instruments in diverse biomedical fields. By integrating structural design with innovative applications, antibodies are transitioning from natural immune defenders to engineered molecules with immense therapeutic and diagnostic potential.



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sciforum-137976: Cryo-EM Structures of HCV E2 Bound to Neutralizing and Non-Neutralizing Antibodies Using Engineered Domain-Swapped Bivalent Fabs as Fiducial Markers

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The high-resolution cryo-EM of small antigen-antibody complexes remains a major challenge due to low molecular weight, conformational flexibility, and particle heterogeneity. To address this, we engineered a bivalent Fab from the broadly neutralizing antibody HC84.26.5D, which targets the hepatitis C virus (HCV) E2 glycoprotein. By deleting a single residue (VH Ser113) in the Fab elbow region, we induced stable dimerization (~80% in solution) and confirmed dimer formation by solving its crystal structure at 1.8 Å resolution. The resulting Fab dimer adopts a domain-swapped conformation with ~25 Å separation between the VL/VH domains, forming a doughnut-shaped molecule with a rectangular central hole. This architecture enables the simultaneous binding of two E2 molecules and improves symmetry, effective mass, and particle alignment—key parameters for high-resolution cryo-EM reconstruction. Using this fiducial marker approach, we solved cryo-EM structures of E2 bound to three monoclonal antibodies with distinct neutralization profiles, a broadly neutralizing, moderately neutralizing, and non-neutralizing antibody, at resolutions of 3.8 Å, 3.3 Å, and 3.7 Å, respectively. Epitope mapping revealed that the broadly neutralizing antibody targets the conserved front layer of E2, while the non-neutralizing antibody binds to the back layer. Notably, the moderately neutralizing antibody spans both regions, defining a previously unrecognized cross-layer epitope associated with partial neutralization. This work establishes a generalizable strategy for domain-swapped Fab design that preserves antigen-binding integrity while enabling the structural analysis of small or flexible antigen-antibody assemblies by cryo-EM. In addition, it provides mechanistic insights into how epitope location influences neutralization potency, offering a molecular blueprint for rational HCV vaccine design focused on conserved, functionally critical epitopes of E2.



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sciforum-125774: Development of IgY-Based Vaccine for *Salmonella* Control in Layer Chickens

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Salmonella infections in poultry represent a significant public health and economic burden, particularly in regions where poultry serves as a major source of animal protein. Traditional control methods often rely on antibiotics, which contribute to antimicrobial resistance and raise consumer health concerns. This study developed a novel, sustainable strategy by integrating indigenous plant-based bacterial attenuation with immunotherapy using IgY antibodies. Specifically, garlic (*Allium sativum*) and onion (*Allium cepa*) extracts were employed to attenuate wild-type *Salmonella* serovars. These plant-derived agents exhibited strong antimicrobial properties, effectively inhibiting bacterial growth in vitro. The attenuated strains were then used to vaccinate chickens, which led to the induction of high levels of anti-*Salmonella* IgY antibodies, as confirmed by an enzyme-linked immunosorbent assay (ELISA). Functional assays revealed that the harvested IgY antibodies possessed robust agglutination activity, highlighting their potential role in passive immunisation strategies. Importantly, the vaccine was found to be both safe and immunogenic, with no adverse effects observed in the immunised birds. This dual approach—combining natural antimicrobial agents with immune-based protection—offers a cost-effective and environmentally friendly alternative to conventional methods. It holds particular promise for improving poultry health and food safety in the Caribbean, where locally available resources and affordable interventions are crucial. This strategy may also be applicable to broader global contexts, especially in low-resource agricultural settings.



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sciforum-136263: Evaluation of anti-drug antibody formation in response to AAV-mediated monoclonal antibody expression in sheep

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Vectored Immunoprophylaxis (VIP) is a gene-based approach to vaccination that delivers genetic instructions for an antibody, enabling the host to produce an immune response without engaging the traditional humoral pathway. Adeno-associated virus (AAV) vectors are well-suited for in vivo antibody gene delivery due to their low pathogenicity, minimal genome integration, sustained transgene expression, and liver/muscle tropism—optimal sites for monoclonal antibody (mAb) production. AAV has been used in non-human primates (NHPs) and clinical trials, but studies report transient antibody expression due to anti-drug antibodies (ADAs) and anti-capsid immune responses, limiting repeat dosing.

A study by the Wootton lab demonstrated AAV6.2FF-mediated expression of the anti-Marburg virus mAb MR191 in sheep for over 1100 days with low ADA and anti-capsid responses, contradicting findings in NHPs. This discrepancy may be due to differences in AAV serotype, host age, or the sequence divergence from the germline of the expressed mAb. Notably, NHP studies primarily tested highly somatically hypermutated broadly neutralizing HIV mAbs (bNAbs), whereas MR191 was derived from a patient recovering from acute Marburg infection and would therefore have undergone less hypermutation. The higher divergence from the germline in bNAbs may contribute to increased immunogenicity.

This study will assess these factors in a sheep model to better understand their role in ADA development. Determining how mAb sequence divergence, host age, and AAV serotype influence immune responses to VIP will hopefully help decrease the incidence of ADAs and improve the durability of AAV-mediated antibody expression.



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sciforum-138881: Monoclonal Antibodies in Cervical Cancer: Advancing Targeted Immunotherapy

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Cervical cancer remains one of the leading causes of cancer-related mortality among women worldwide, particularly in developing countries. While early screening and HPV vaccination have significantly reduced incidence rates, advanced and recurrent stages of cervical cancer still pose major treatment challenges. Conventional therapies such as chemotherapy and radiotherapy often result in systemic toxicity and limited efficacy. In this context, monoclonal antibodies (mAbs) have emerged as a powerful and targeted therapeutic option, capable of offering greater precision with fewer side effects.

Monoclonal antibodies are engineered proteins that bind specifically to antigens expressed on tumor cells or within the tumor microenvironment. In cervical cancer, several key targets have been identified, including **vascular endothelial growth factor (VEGF)** and **programmed death-ligand 1 (PD-L1)**. The anti-VEGF mAb **bevacizumab** was the first to be approved for advanced cervical cancer and has shown to significantly improve progression-free and overall survival when combined with chemotherapy by inhibiting tumor angiogenesis.

Checkpoint inhibitors such as **pembrolizumab** and **nivolumab**, which target the PD-1/PD-L1 axis, have demonstrated promising results in restoring T-cell activity and enhancing immune-mediated tumor cell killing in patients with recurrent or metastatic disease. These immune-based therapies mark a paradigm shift toward precision oncology in cervical cancer treatment.

Furthermore, antibody–drug conjugates (ADCs) represent an evolving strategy, combining monoclonal antibodies with potent cytotoxic drugs to deliver targeted therapy directly to cancer cells. Emerging targets such as tissue factor (TF) and epidermal growth factor receptor (EGFR) are currently under clinical investigation to further expand the treatment arsenal.

This paper explores the structural and functional aspects of monoclonal antibodies in the context of cervical cancer, detailing their mechanisms, clinical relevance, and future prospects. With continued research and development, monoclonal antibodies are poised to redefine the therapeutic landscape of cervical cancer by offering safer, more effective, and personalized treatment options.



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sciforum-144737: Predictive Biomarkers for Monoclonal Antibody Therapy Response in Oral Squamous Cell Carcinoma: A Systematic Review

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Introduction

Monoclonal antibody (mAb) therapies, including immune checkpoint inhibitors and anti-epidermal growth factor receptor (EGFR) agents, are increasingly used in oral squamous cell carcinoma (OSCC) [1]. Response rates vary, highlighting the need for predictive biomarkers to guide patient selection [2,3]. This review summarises current evidence linking biomarker profiles with mAb outcomes in OSCC.

Methods

A PRISMA-guided search of PubMed, ScienceDirect, and Web of Science identified English-language studies published within the past five years on adult OSCC treated with mAbs, reporting biomarker associations with clinical outcomes. Of the 502 records screened, 5 met inclusion criteria.

Results

Analysis of recent evidence highlights several biomarkers with predictive value for mAb and immunotherapy response in OSCC. In recurrent disease treated with nivolumab (n = 64), Tachinami et al. found that a post-treatment neutrophil-to-lymphocyte ratio (NLR) ≥ 5 was associated with poorer survival [4]. Dou et al. reported that EGFR mutations and chromosome 11q13 amplification correlated with reduced progression-free survival (PFS) and a lack of clinical benefit in patients receiving anti-PD-1 therapy [5]. In locally advanced OSCC, Xiang et al. achieved a major pathological response (MPR) rate of 69.0% and pathological complete response (pCR) rate of 41.4% with camrelizumab plus chemotherapy, with higher rates in programmed death-ligand 1 (PD-L1)-positive patients [6]. Huang et al. reported MPR 60% and pCR 30% with toripalimab plus chemotherapy, with a PD-L1 combined positive score (CPS) > 10 and increased tertiary lymphoid structures predicting response [7]. Ju et al. observed MPR 40% with camrelizumab and the vascular endothelial growth factor receptor 2 (VEGFR2) inhibitor apatinib, with all PD-L1 CPS > 10 patients responding [8].

Conclusion

PD-L1 expression, tertiary lymphoid structures, NLR, and genomic alterations may guide mAb therapy selection in OSCC. Evidence is limited by few studies and heterogeneity; larger prospective trials are needed to confirm clinical utility.



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sciforum-133344: Recombinant Antibodies against intracellular neoantigens

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Recombinant antibodies targeting MHC/neoepitope complexes include TCR-like antibodies, bi-specific T-cell engagers (BITEs) in the format of CD3 x TCR-like antibodies, or CD3 x soluble TCR. Several T cell receptor-mimetic antibodies (TCRms) demonstrated therapeutic effects in xenograft mouse models. The advantage of IgG TCRm antibodies is their stability compared to soluble TCRs. But in contrast to TCRs, TCRm antibodies demonstrate more cross-reactivity through binding to hotspots on the HLA/peptide complex surface, whereas the binding of the T cell receptor is dispersed over multiple residues. Over 100 BITEs are under clinical investigation and 7 of them are FDA-approved. In addition, intrabodies neutralizing neoantigens inside tumor cells have recently been developed. They seem to be a very promising additional tool to inhibit cancer growth because of their easy selection and high specificity compared to TCR-like antibodies and soluble TCRs. In the near future, a transfer of intrabodies embedded in lipid-nanoparticles should bring them into clinical practice. Most promising T cell-based therapies targeting cell surface proteins or neoantigens use T cells expressing a chimeric antigen receptor (CAR) or a recombinant complete TCR (TCR-T cell). Seven CAR T-cell therapies and one TCR-T cell therapy have been FDA-approved. The effectivity of therapies with BITEs and CARs are similar, such as with BITE Mosunetuzumab (CD3 x CD20), which produces similar high response rates in patients compared to CAR T-cell therapy, as demonstrated in relapsed/refractory follicular lymphoma therapy. The most important adverse events were cytokine release syndrome (CRS), fatigue, neutropenia, immune-effector-cell-associated neurotoxicity syndrome (ICANS) and infections with a lower risk of CRS or ICANS than in patients who had received CAR-T cell therapy.

Overall, T-cell therapy is particularly limited by complex manufacturing processes and the necessity for lymphodepleting chemotherapy, restricting patient accessibility, which will not be of concern in intrabody therapy.



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sciforum-138922: Smart Weapons Against Cancer: The Role of Monoclonal Antibodies in Targeted Therapy

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Monoclonal antibodies (mAbs) have revolutionized the landscape of cancer therapy by offering highly specific, targeted treatment options that differ significantly from conventional chemotherapeutic approaches. These laboratory-engineered antibodies are designed to recognize and bind selectively to antigens expressed on the surface of cancer cells, leading to direct or immune-mediated tumor cell destruction.

The therapeutic mechanisms of mAbs include blocking growth factor receptors, inducing apoptosis, recruiting immune effector functions such as antibody-dependent cellular cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC), and delivering cytotoxic agents via antibody-drug conjugates (ADCs). Notable examples include **trastuzumab**, which targets the HER2 receptor in breast cancer, and **rituximab**, which binds to CD20 in non-Hodgkin's lymphoma. These treatments have significantly improved clinical outcomes, including progression-free survival and overall response rates.

Monoclonal antibodies can be classified based on their function: **naked antibodies** that act without a drug payload; **conjugated antibodies** linked to toxins or radionuclides; and **bispecific antibodies** designed to bind to two different antigens simultaneously. Additionally, **immune checkpoint inhibitors** such as **nivolumab** and **pembrolizumab** block PD-1/PD-L1 pathways, restoring the immune system's ability to recognize and attack cancer cells.

Ongoing research in molecular oncology and immunotherapy is paving the way for **personalized cancer therapy**, in which monoclonal antibodies are selected based on the genetic and molecular profile of the tumor. Despite their success, challenges remain, including tumor antigen heterogeneity, resistance development, and adverse immune reactions.



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sciforum-138901: The Art of Immune Suppression: An Antibody Perspective

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The immune system serves as the body's defense mechanism against pathogens and abnormal cells. However, in autoimmune conditions or transplant scenarios, it becomes essential to suppress the immune response to prevent tissue damage or graft rejection. This delicate balance is achieved through targeted immunosuppressive therapies. Antibodies, particularly monoclonal and engineered types, have emerged as potent tools in this domain, offering precision in modulating immune activity while minimizing generalized immunosuppression.

In diseases such as **Neuromyelitis Optica Spectrum Disorder (NMOSD)**, where the immune system mistakenly targets the aquaporin-4 water channels in the central nervous system, antibody-mediated immune suppression plays a pivotal role. Drugs like **eculizumab**, a complement inhibitor, and **inebilizumab**, an anti-CD19 monoclonal antibody, exemplify the effectiveness of tailored antibody therapies in mitigating disease progression while preserving general immune function.

The **need for immune suppression** arises not only in autoimmune conditions but also in organ transplantation, allergic reactions, and certain chronic inflammatory diseases. Traditional immunosuppressants affect multiple immune pathways, often leading to an increased risk of infections and malignancies. In contrast, **antibody-based suppression** provides a targeted approach—binding to specific immune cells, receptors, or cytokines to downregulate overactive responses.

However, concerns remain regarding **long-term safety and immune compromise**. The prolonged use of immune-suppressing antibodies can lead to opportunistic infections, diminished vaccine response, and the reactivation of latent diseases. Yet, with proper dosing, monitoring, and patient stratification, these risks can be significantly reduced. Clinical trials and post-marketing surveillance have shown that with correct protocols, **antibody-based immune suppression does not inherently pose a major threat**, especially when compared to conventional immunosuppressive regimens.

In conclusion, antibodies offer a sophisticated means to **modulate the immune system**, addressing critical medical needs with increasing safety and specificity. Their role in diseases like NMOSD showcases how targeted suppression can lead to improved outcomes without broadly compromising immune defense.



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Session 3. Immuno-oncology and Tumor Imaging

sciforum-127701: Advances in Tumor Imaging to Effectively Optimize Immuno-oncology Strategies for Ensuring Appropriate Treatment and Patient Well-Being

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In the last decade, immuno-oncology has revolutionized cancer therapy by harnessing the body's immune system to target and eliminate tumor cells, offering durable responses particularly in malignancies previously considered treatment-resistant. This approach exploits immune checkpoints, monoclonal antibodies, *Chimeric Antigen Receptor* (CAR) T-cells, and innovative cancer vaccines to activate, promote, and enhance immune responses specific to tumor-associated antigens. However, the complexity of tumor-immune interactions necessitates advanced tumor imaging techniques to accurately diagnose, monitor, and tailor effective immunotherapy techniques. Tumor imaging plays a pivotal role in visualizing immune cell infiltration, tracking immune responses in real-time, and identifying immune-related adverse events. Recent innovations such as hybrid *Magnetic Resonance Imaging* (MRI), *Computed Tomography* (CT), and *Positron Emission Tomography* (PET) (PET/CT and MRI) combined with novel tracers—like radiolabeled antibodies targeting *Programmed Death-Ligand 1* (PD-L1)—allow precise quantification of immune activation within the tumor microenvironment. These modalities facilitate early assessment of therapeutic efficacy, guiding personalized treatment adjustments. Furthermore, multimodal imaging approaches integrating molecular and anatomical data improve the delineation of tumor boundaries, detect metastases, and evaluate emerging resistance mechanisms. As immuno-oncology moves toward personalized medicine, imaging biomarkers will be essential in stratifying patients most likely to benefit from immune-based therapies, predicting outcomes, and minimizing toxicity. Continued research in tumor imaging will enhance our understanding of immune dynamics, ultimately improving treatment precision and patient survival in cancer care. The main aim of this was to advance and develop the in-depth understanding and application of innovative tumor imaging techniques that accurately visualize and quantify immune responses within the tumor microenvironment. By enabling personalized immunotherapy strategies, improving personalized treatment and monitoring will significantly enhance patient therapeutic outcomes, as a result of appropriate treatment corresponding to effective and modern cancer care.



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sciforum-144959: Immuno-oncology and Tumor Imaging: Advancing Precision Medicine Through Novel Antibody-Based Therapeutic and Diagnostic Platforms

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Background

The convergence of immuno-oncology and tumor imaging represents a paradigmatic shift in cancer management, where therapeutic antibodies serve dual roles as both treatment modalities and diagnostic tools. This field has witnessed unprecedented growth, with bispecific antibodies, antibody-drug conjugates (ADCs), and radioimmunotherapy emerging as transformative approaches.

Methods

Recent advances encompass multiple innovative platforms addressing tumor heterogeneity and resistance mechanisms. Bispecific antibodies demonstrate remarkable versatility by simultaneously engaging immune effector cells and tumor-associated antigens, achieving tumor-specific cytotoxicity without MHC restriction. Next-generation ADCs incorporate dual-payload designs and novel linker technologies, enabling synergistic cytotoxic effects while minimizing off-target toxicity. Radioimmunotherapy has evolved with theranostic strategies utilizing single antibodies conjugated to different radioisotopes for combined imaging and therapy.

Imaging Innovations

Molecular imaging modalities have revolutionized cancer detection through antibody-based approaches. Fluorescence-guided surgery utilizes tumor-specific antibodies conjugated to near-infrared fluorophores, enabling real-time intraoperative tumor visualization. Immuno-PET/SPECT combines nanomolar sensitivity with antibody specificity, enabling the assessment of whole-body biomarker distribution and the prediction of treatment response. These platforms support precision medicine by enabling patient stratification and dynamic monitoring of antigen expression heterogeneity.

Clinical Impact

The integration of therapeutic and diagnostic antibodies has demonstrated clinical success, with over 200 marketed antibody therapeutics currently available. Checkpoint inhibitors targeting PD-1/PD-L1 pathways have established immunotherapy as a cornerstone of cancer treatment, while emerging targets, including LAG-3 and CD47, offer expanded therapeutic opportunities.

Conclusions

The synergistic integration of immuno-oncology and tumor imaging through antibody-based platforms represents a transformative approach to cancer care, enabling personalized treatment strategies based on real-time tumor characterization and overcoming current therapeutic limitations.



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sciforum-133729: Targeting the Tumor Microenvironment with Radiolabeled Antibodies: Bridging Immunotherapy and Molecular Imaging

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Advances in immuno-oncology have significantly transformed the therapeutic landscape of cancer treatment. However, evaluating the spatial and temporal dynamics of therapeutic antibodies within the tumor microenvironment (TME) remains a major challenge. Molecular imaging using radiolabeled antibodies has emerged as a powerful strategy to visualize and quantify antibody distribution, target engagement, and immune activation in real time. In this study, we describe the design and application of radiolabeled monoclonal antibodies that selectively bind to immune checkpoints and tumor-associated antigens. Employing imaging modalities such as positron emission tomography (PET) and single-photon emission computed tomography (SPECT), we demonstrate high specificity in detecting tumors, immune cell infiltration, and antigen heterogeneity in preclinical models. Radiolabeled antibody imaging enables longitudinal monitoring of therapeutic responses, allowing real-time assessment of treatment efficacy and adaptive changes in the TME. Importantly, this approach provides a non-invasive method for guiding patient selection, optimizing therapeutic dosing, and identifying mechanisms of resistance. By integrating diagnostic imaging with therapeutic antibodies, our work contributes to the advancement of antibody-based theranostics and precision oncology. The convergence of immunotherapy and imaging technologies paves the way for a more personalized and effective approach to cancer care, improving both clinical decision-making and patient outcomes. This innovative strategy holds significant potential to enhance the design and clinical translation of next-generation antibody therapeutics.



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Session 4. Humoral Immunity

sciforum-144718: A broad-spectrum SARS-CoV-2 immunization strategy targeting the highly conserved MPER of the Spike protein

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SARS-CoV-2 remains in circulation 5 years after the first cases of COVID-19 were reported, during which time several variants have been selected with mutations accumulating especially in the more accessible S1 subunit of the Spike protein (S). Consequently, current vaccine platforms have been updated to ensure effectiveness against the Omicron XBB.1.5 variant, highlighting the need for ongoing surveillance and updates of the antigens included in the immunization strategies. To overcome this limitation, we analyzed in a SARS-CoV-2-infected human cohort the immunogenicity of the highly conserved membrane-proximal external region (MPER) of the S2 subunit of the Spike, which is conserved across the Orthocoronavirinae subfamily. A portion of the patients, even if weakly, did elicit antibodies against the MPER. Additionally, we characterized its structure in a low-polarity environment and in lipid membranes, as well as showing its fusogenic potential, confirming its active involvement in the viral infection process. Therefore, we report the suitability of the MPER as a target for vaccination. Considering the impact that lipid membranes may have on the structure of this region, we assessed its expression in the membranes of eukaryotic cells. For that, we designed wild-type and modified S2-derived DNA sequences including the MPER. The results obtained support the feasibility of designing vaccines focused on the conserved MPER region.



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Session 5. Computational Antibody Engineering

sciforum-129009: "Next-Generation Antibody Design: Computational Approaches for De Novo Engineering, Affinity Maturation, and Personalized Therapeutics"

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Novel and developed computational approaches in the field of antibody engineering have revolutionized and leveraged advanced algorithms through machine learning and detailed structural modeling in order to deeply facilitate the de novo design of new, effective therapeutic agents based on antibodies, affinity maturation, and stability optimization, significantly enhancing and accelerating the drug development processes. The main purpose of this paper is to clearly illustrate how advanced computational antibody design techniques, such as de novo engineering, affinity maturation, and personalized modeling, can deeply affect modern and precision therapeutics by enabling the rapid development of highly specific and potent monoclonal antibodies tailored to specific critical diseases. We observed the rapid development of highly specific and potent monoclonal antibodies tailored for some specific critical diseases—particularly cancers; for example, *Human Epidermal Growth Factor Receptor 2* (HER2) or *Receptor Tyrosine-Protein Kinase erbB-2*- positive breast cancer or colorectal cancer. For autoimmune disorders such as *Rheumatoid Arthritis (RA)*, *Antikeratin*, *anticitrullinated peptides*, *anti-RA33*, *anti-Sa*, and *anti-p68 autoantibodies* have been shown to have >90% specificity for RA. Regarding infectious diseases, the immunoglobulins Ig M, Ig A, and Ig G are the key players in the response and the fight against COVID-19. The ultimate essential goal consists is to improve therapeutic efficacy, reduce off-target effects, and facilitate specific personalized treatment strategies that effectively address individual patients' molecular profiles. Machine learning algorithms like DeepMind's AlphaFold have dramatically improved the accuracy of antibody-antigen structure prediction, facilitating the rapid identification of high-affinity binders. In one instance, a computational redesign of an *anti-PD-1 (Immune checkpoint inhibitor)* antibody enhanced its binding affinity and stability, leading to a more potent immune checkpoint inhibitor for cancer therapy. Moreover, the de novo design of bispecific antibodies has enabled simultaneous targeting of multiple tumor antigens, such as *Cluster of Differentiation 3* (CD3) and *Epidermal Growth Factor Receptor* (EGFR), boosting immune activation in resistant cancers.



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sciforum-144801: From Disorder to Defense: Intrinsically Disordered Region Based Antibody Engineering for Chandipura virus

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Chandipura virus (CHPV), a neurotropic member of the Rhabdoviridae family, has emerged as a significant public health concern in the Indian subcontinent due to its rapid progression to encephalitis and high fatality rates. Recent analysis of its dark proteome revealed a substantial presence of intrinsically disordered proteins (IDPs) and intrinsically disordered protein regions (IDPRs), particularly within the phosphoprotein (P), which exhibited the highest intrinsic disorder propensity among all CHPV proteins. IDPs are characterized by conformational flexibility, enabling them to mediate multiple and transient interactions with host factors, often via molecular recognition features (MoRFs). Such properties make them crucial for viral replication, immune evasion, and host machinery manipulation. In this study, we extend our findings toward an in silico pipeline for IDP-based antibody design targeting the CHPV P protein. Consensus IDR prediction, coupled with MoRF mapping, was integrated with epitope mapping algorithms to identify disordered yet immunogenic regions. Structural ensembles generated using AlphaFold2 and disorder-refined molecular dynamics simulations using Gromacs force field enabled the modeling of conformational variability for antibody docking. This approach facilitates the rational selection of epitope-rich, conformationally adaptable targets for monoclonal antibody engineering. Our findings highlight that targeting IDP regions traditionally overlooked in structure-based vaccine design, offers a novel paradigm for CHPV immunotherapeutics, potentially overcoming antigenic variability and functional plasticity.



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sciforum-137881: A Computational Workflow for The Prediction of Epitope/Paratope Regions and Antibody–Antigen Binding Poses

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Introduction

Predicting accurate binding poses in antibody–antigen complexes is challenging because some biological molecules might have more than one epitope. This study presents a computational workflow that integrates epitope/paratope prediction and protein–protein docking to predict accurate epitope and paratope residues, as well as antibody–antigen binding poses.

Methods

The computational workflow was applied to three different antibody–antigen systems: TNF- α , PD-L1, and IL-1 β . First, Essential Site Scanning Analysis (ESSA), a fast and effective elastic network model-based method, was used to determine essential residues for binding in the studied antigens and antibodies. ESSA-detected essential residues in antigens were then clustered to determine epitopes as well as central epitope residues and epitope-forming residues. Each epitope and ESSA-detected essential residues in antibodies were used to guide antibody–antigen docking calculations. The LightDock was used to perform docking calculations with/without the antibody mode option, and the top three poses with the highest docking score for each case were used for further analysis. Additionally, for a fair comparison, two blind docking runs were also performed on the studied systems.

Results

Our results showed that ESSA can successfully detect different epitope regions in the antigens, and these residues significantly improve the accuracy of antibody–antigen pose prediction compared to those of blind docking. Interestingly, we observe that the antibodies tend to bind to the incorrect epitope with high docking scores, despite the dockings being performed in antibody mode. On the other hand, without the antibody mode, ESSA-guided dockings alone generate more accurate binding poses with the highest docking scores compared to those of blind dockings.

Conclusions

These findings show that ESSA-detected essential residues improve antibody–antigen docking calculations and accurately pinpoint the correct epitope region for a specific antibody. This integrative workflow offers a powerful tool for computational epitope mapping, a critical step in rational antibody design.



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sciforum-137932: Computational Nanobody Design for Amyloid-Beta 42 Octamer in Alzheimer's Disease

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Introduction

Alzheimer's disease is the most common type of neurodegenerative disorder, and amyloid- β ($A\beta$) plaques are associated with this disorder. According to the amyloid cascade hypothesis, the accumulation of neurotoxic $A\beta_{42}$ generally plays a crucial role in the disease's progression. Emerging evidence shows that soluble oligomeric forms, especially tetramers and larger assemblies, are more neurotoxic than mature fibrils. Although several anti- $A\beta$ antibodies target different states of aggregation (from monomers to plaques), nanobody-based therapies do not exist yet. Here, we aim to identify nanobodies targeting the $A\beta_{42}$ octamer computationally.

Materials and Methods

A total of 40 nanobodies were modeled based on three enzymes known to interact with $A\beta_{42}$. Using three $A\beta_{42}$ -interacting enzymes as templates, we designed 40 nanobody sequences through Essential Site Scanning Analysis, Peptide Atlas, and AbNatiV, with structural modeling performed via SWISS-MODEL and AlphaFold3. Then, a site-specific docking approach using ClusPro was performed to evaluate nanobody- $A\beta_{42}$ binding, producing 120 nanobody- $A\beta_{42}$ octamer complexes. They were ranked based on docking scores, salt bridge formation, stable interface interactions, and solvent-accessible surface area, narrowing the candidates down to seven promising complexes. This pipeline prioritized seven high-affinity candidates, which were further evaluated by conventional molecular dynamics (MD) simulations to assess complex stability.

Results

Among all screened complexes, a single nanobody exhibited persistent binding to the $A\beta_{42}$ octamer, marked by prolonged interfacial contacts and minimal structural deviation. This candidate emerges as a potential diagnostic or therapeutic lead.

Conclusion

This study establishes an integrative computational framework for the systematic identification and evaluation of nanobodies targeting pathogenic amyloid aggregates, additionally offering a scalable strategy to prioritize high-affinity binders against disease targets.



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sciforum-144677: From Disorder to Design: Ensemble-Based Computational Antibody Discovery for IDP Targets in Zika Virus

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Zika virus (ZIKV), a mosquito-borne flavivirus, has emerged as a significant global health concern due to its association with severe neurological complications, including congenital microcephaly and Guillain-Barré syndrome. Despite recurring outbreaks across multiple continents, there are currently no licensed vaccines or specific antiviral therapies available. Previous intrinsic disorder profiling of the ZIKV proteome has revealed that several viral proteins harbour substantial intrinsically disordered regions (IDRs), with particularly high disorder propensity in the non-structural proteins NS4B and NS5, and in the C-terminal tail of the capsid protein. These flexible regions facilitate dynamic interactions with host factors, playing a pivotal role in viral replication, immune modulation, and evasion mechanisms. In this study, we present an open-access, end-to-end in silico antibody design pipeline specifically tailored to target these disordered viral proteins. Consensus IDR prediction was performed using IUPred3, fDPnn, PONDR, and IDPPred, enabling the identification of epitope-rich disordered segments. Structural ensembles for these regions were generated using AlphaFold2 modelling followed by FlexServ sampling to capture conformational heterogeneity. B-cell epitope profiling (BepiPred-3.0, ElliPro) was employed to identify accessible and potentially immunogenic regions, which were then docked to human germline antibody scaffolds sourced from SAbDab using HADDOCK 2.4 and ClusPro. Paratope optimisation was achieved with ABpredict2, while developability and manufacturability assessments were performed using Thera-P. Preliminary docking and scoring indicate that several candidate antibodies display predicted nanomolar-range affinities for the NS4B N-terminal disordered segment and the capsid tail epitopes, with favourable stability and developability profiles. This work demonstrates the feasibility of computational antibody engineering against naturally flexible ZIKV proteins, highlighting the potential of targeting the viral “dark proteome” to develop novel therapeutic interventions.



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sciforum-137456: Multi-Objective Active Learning for Nanobody Development

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Introduction

Nanobodies—compact, single-domain antibody fragments—are seeing increasing use in therapeutics and diagnostics due to their high specificity and stability. However, optimizing multiple properties such as expression yield and binding affinity remains experimentally costly. While machine learning can accelerate candidate selection, its effectiveness depends on the quality and diversity of labeled data. Standard active learning (AL) approaches address this by prioritizing informative samples, but typically ignore the practical constraints critical to nanobody development.

Methods

We present a multi-objective active learning (MOAL) framework tailored to nanobody discovery. This framework integrates predictive models for binding affinity and expression yield with uncertainty estimation from ensemble learning. Candidate selection is guided by three objectives: informativeness (model improvement), feasibility (predicted expression), and performance (binding affinity). To balance trade-offs among these objectives, we apply evolutionary multi-objective optimization algorithms, specifically NSGA-II and IBEA. This enables exploration of diverse, high-potential regions of nanobody sequence space.

Results

We evaluate our framework on a curated dataset of characterized nanobody sequences and a large-scale nanobody repertoire comprising over 10 million candidates. The curated data enable supervised learning, while the repertoire supports broad exploration. Our approach identifies nanobody candidates that are both experimentally viable and model-informative, improving generalization while reducing experimental costs. By avoiding redundant queries and favoring biologically diverse selections, this method supports efficient discovery.

Conclusions

Our domain-aware MOAL approach provides an effective strategy for guiding nanobody selection under multiple constraints. It enables iterative refinement of predictive models while maintaining experimental feasibility. Though it was developed for nanobody engineering, the framework generalizes to other biological domains requiring data-efficient, multi-objective decision-making.



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