Non-clinical Immunogenicity Risk Assessment (NCIRA)

Sebastian Spindeldreher

on behalf of the NCIRA working goup members

EIP Open Symposium

26th April 2022

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NCIRA

28 members from 21 companies

- Alyson Rust (Abzena)
- Amy Rosenberg (Epivax)
- Anja ten Brinke (Sanquin)
- Annelies Turksma (Sanquin)
- Åsa Marknell-Dewitt (Thermofisher)
- Axel Ducret (Roche)
- Bruno Nolasco (Generate Biomedicines)
- Campbell Bunce* (Abzena)
- Chloé Ackaert (immuneXperts)
- Diana Montgomery (MSD)
- Grzegorz Terszowski (Novartis)
- James Goggins (MSD)
- Karen Heyninck (Sanofi)
- Karolina Osterund (ThermoFisher)
- Kasper Lamberth (NovoNordisk)
- Lydia Michaut (TATAA)
- Mantas Malisauskas (Merck)
- Marie-Ange Buyse (Sanofi)
- Mark Kroenke (Amgen)
- Noel Smith (Lonza)
- Pedro Paz (Bayer)
- Piercesare Balestra (Merck)
- Samuel Pine (Sanofi)
- Sebastian Spindeldreher* (iBiologix)
- Sofie Pattijn (immunXperts)
- Sophie Tourdot (Pfizer)
- Tim Hickling (Roche)
- Vibha Jawa (BMS)

* Working Group leads

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Working group activities

Completed:

- Harmonization of antigenicity assays
  - Published December 2021, presented at several conferences
  - Will be presented in the context of new modalities at AAPS NBC – New and Unusual Modalities Track, May 10, 2022, in Anaheim, CA

Ongoing:

- Predicting Impact of Immunogenicity
  - Co-leads: Chloé, Tim and Samuel
- IRA for New Modalities
  - Co-leads: Lydia, Vibha and Noel

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Prediction of impact of immunogenicity

- What does impact mean?
  - Impact on exposure (PK), PD, efficacy or safety?
- What problem do we want to look at?
  - Do currently available tools meet the needs?
- What should we be trying to predict?
  - Impact as incidence isn't sufficiently valuable

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Actions

- Establish data set for assessing predictive approaches
  - Public data
    - 20 most recent monoclonals (approved during last 5-6 years)
  - Unpublished data from EIP members
    - 4 companies agreed, ongoing discussion with 2-3 further companies
    - Goal: 20 molecules that are approved or in development with clinical and non-clinical data
- Looking for additional companies to join initiative: Contact Chloé, Tim or Samuel
- Investigate available predictive approaches
  - Literature and EIP members' approaches
  - Modeling and simulation
  - Statistical modeling
- Goal: Publish current state, including areas for further work

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Expanding into collaborations

- EIP recognized that similar efforts were ongoing in North America
- Daniel Leventhal and collaborators were working on an immunogenicity database to collate public data to facilitate deeper analysis and access
- EIP decided to support collaborative approach:
  - EIP will contribute with public data from impact database
  - EIP effort focused on prediction of impact EIP on select no. compounds
- First database version is built with public data only
- Add ABIRISK database, if possible

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Immunogenicity Database Collaborative (IDC)

ImmunXperts
a Q² Solutions Company

Lilly

BIOTECH SQUARE

Pfizer

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SANOFI

DTU
Technical University of Denmark

Generate:Biomedicines
A Flagship Pioneering Company

Genentech

IDC Members list:
Daniel Leventhal (Generate BM)
Bruno Nolasco (Generate BM)
Sofie Pattijn (ImmunXperts, EIP)
Sophie Tourdot (Pfizer, EIP)
Morten Nielsen (DTU)
Richard Higgs (Eli Lilly)
Amin Osmani (Biotech Squared)
Stephen Kottmann (Generate BM)
Saketh Saxena (Generate BM)
EIP NCIRA subteam:
Tim, Chloé and Samuel

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Establishing a publicly available database cataloging the immunogenicity of therapeutic proteins

What is the IDC?

The IDC is a global, cross-industry (pharma, biotech, and academia) consortium established with the purpose of creating an open-access, uniform and curated database encompassing clinical and pre-clinical immunogenicity information for protein-based therapeutics. It is a grass-roots initiative led by volunteer members and contributors and holds no formal association to any single organization or industry working group.

Mission

To establish a shared and easily accessible database cataloging descriptors and relevant data associated with the immunogenicity of biotherapeutics.

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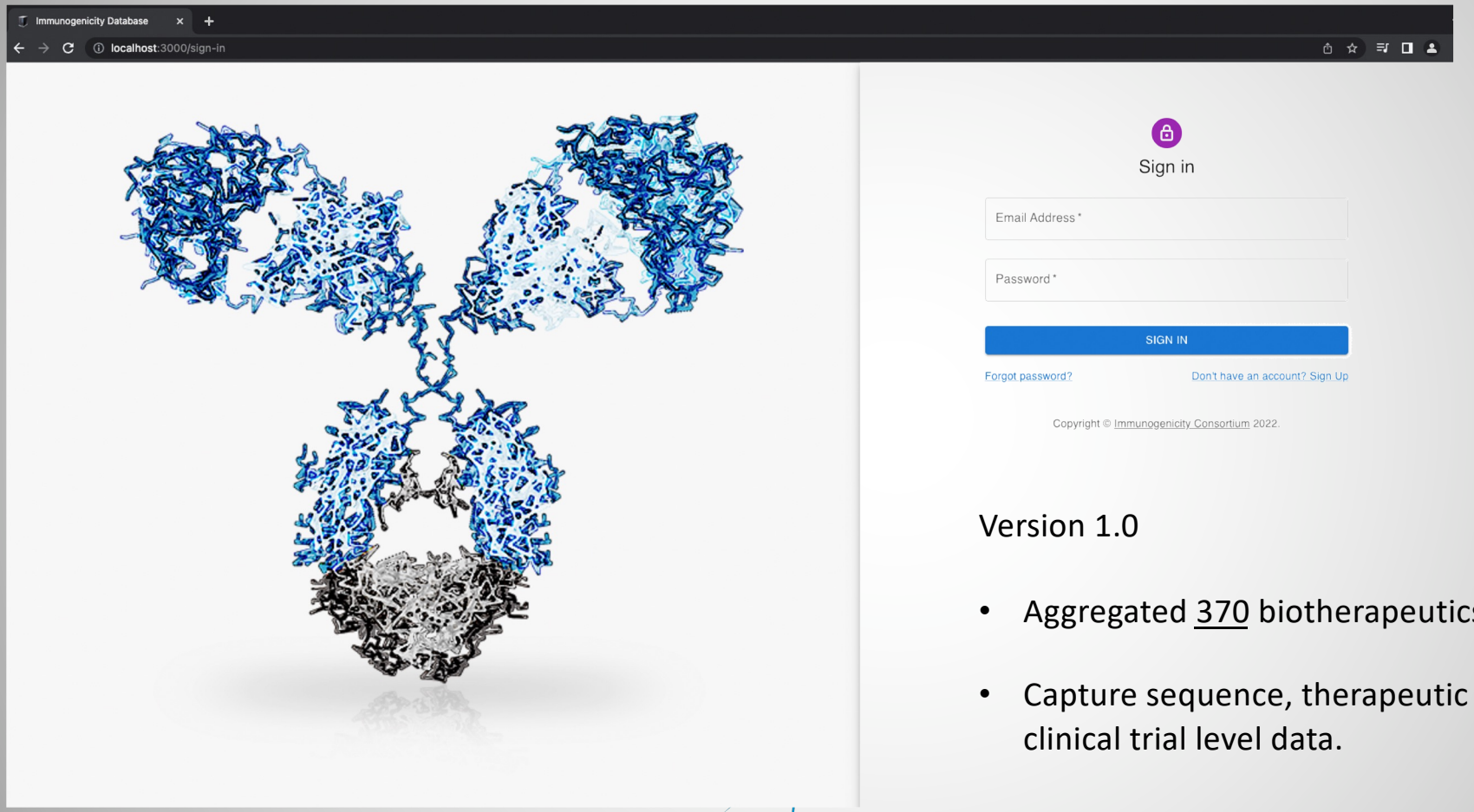
State of the database



Version 1.0

- Aggregated 370 biotherapeutics.
- Capture sequence, therapeutic and clinical trial level data.

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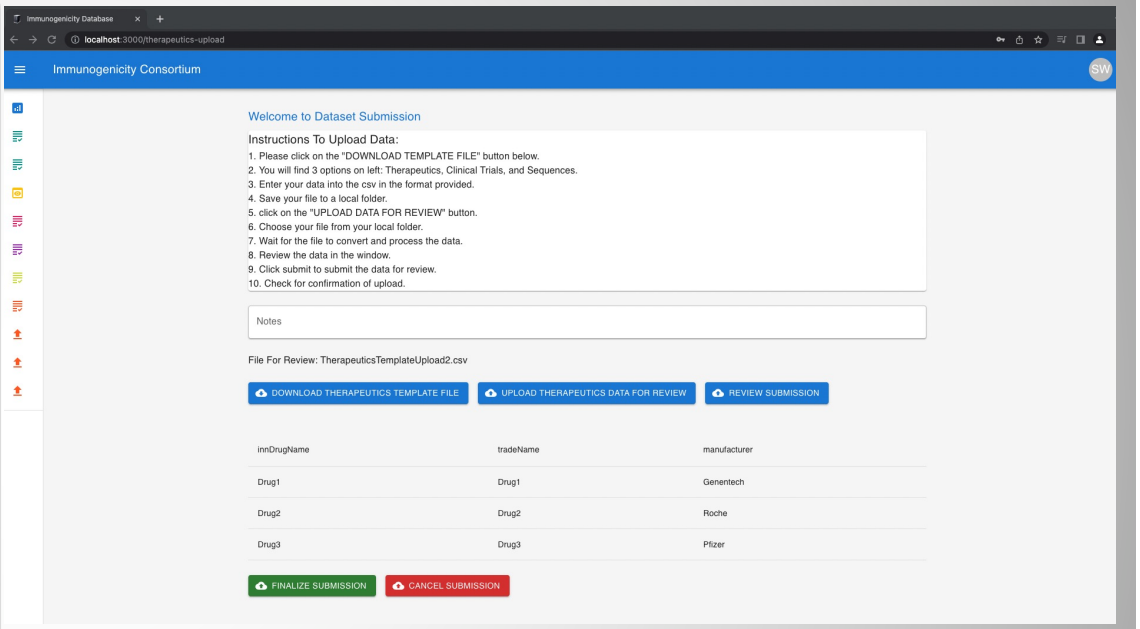
*pre-alfa version, subject to change

Immunogenicity Database Collaborative (IDC)

New therapeutic submission capabilities



Curated **open-access** resource

Full database **download** option

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Immunogenicity Risk Assessment for Novel Modalities

- Concept
  - Collect and discuss available knowledge and practices on the IRA of novel modalities
  - Provide EIP members with a learning platform for exchange of experiences and discussion of questions
- Mode
  - One topic of interest per session by inviting speakers (EIP members or external) to provide their visions and experiences in the field
  - The following session is dedicated to Q&A and discussion
- In scope
  - All novel modalities: CAR-Ts and other cell therapies (TILs, T-regs, NK…); nucleic acid therapies (ASOs, siRNAs…); AAV- and LNP-based in vivo gene therapies; in vivo and ex-vivo CRISPR-Cas9 edits
  - Prediction and confirmation of immunogenicity risk
  - Technical and logistical aspects and challenges
- Deliverables
  - Build a knowledge and learning platform
  - Template documents to support IND using preclinical risk assessment tools
  - Workshop or training course at EIP Symposium

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13 members from 11 companies

- Campbell Bunce (Abzena)
- Vibha Jawa* (BMS)
- Amy Rosenberg (Epivax)
- Arno Kromminga (Immunogenicity Integrated)
- Sebastian Spindeldreher (iBiologix)
- Lydia Michaut*& (iBiologix)
- Noel Smith* (Lonza)
- Shuli Zhang (Merck)
- Grzegorz Terszowski (Novartis)
- Christian Joffroy (Novartis)
- Henrik Toft-Hansen (Novo)
- Olle Björkdahl (Novo)
- Boris Gorovits (Sana)
- Melody Janssen (SciPot)

* Subgroup leads

& Currently not associated with a member company

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Progress

- Internal talks and discussion sessions
  1. Vibha Jawa
     Risk based Bioanalytical Strategies for CART based therapies
  2. Paul Chamberlain
     Immunogenicity Risk Assessment: Points to consider for an Anti-Sense Oligonucleotide
  3. Amy Rosenberg
     Risk assessment and mitigation approaches

- Implementing a risk assessment document to support IND using preclinical risk assessment tools for the CART therapy related risks

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Do you want to join the NCIRA working group or a subgroup?

- NCIRA in general:
  - Campbell Bunce (campbell.bunce@abzena.com)
  - Sebastian Spindeldreher (sebastian.spindeldreher@ibiologix.com)

- Prediction of Impact:
  - Chloé Ackaert (chloe.ackaert@immunxperts.com)
  - Tim Hickling (timothy.hickling@roche.com)
  - Samuel Pine (samuel.pine@sanofi.com)

- Risk assessment for new modalities:
  - Vibha Jawa (vibha.jawa@bms.com)
  - Noel Smith (noel.smith@lonza.com)

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Session 1: Prediction of Immunogenicity

10:15 **COVID influence on in-vitro prediction assays**
Chloé Ackaert, ImmunXperts

10:45 **Computational Directed Improvements in Antibody Immunogenicity**
Bruno Gonzalez-Nolasco, Generate Biomedicines Inc

11:15 **Coffee Break**

11:45 **HLA-DQA1*05 allele – increased rate of immunogenicity**
Aleksejs Sazonovs, The Sanger Institute

12:15 **Lunch Break**

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