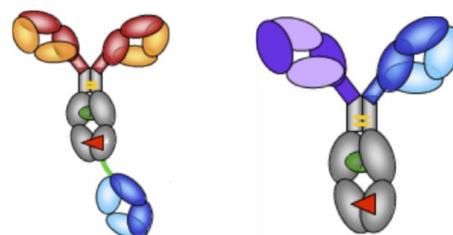# HELM for Antibody Registration

Roche's Pharmaceutical Research and Early Development (pRED) informatics team has adopted the Pistoia Alliance's Hierarchical Editing Language for Macromolecules (HELM) as a fundamental building block of their antibody registration tool. As a result, the HELM notation and the HELM Antibody Editor (HAbE) are being rolled out throughout Roche's bio-therapeutics group ("Large Molecule Research") to improve the speed, accuracy and effectiveness of antibody research.

Advanced Notation Solution

As recently as two years ago, simple antibody formats were described just by their sequences, with PowerPoint slides used to illustrate more complex formats. This worked well for standard antibodies but less so for non-standard ones. Today, the former non-standard antibody designs have become the new de-facto standard, representing up to 90% of the current portfolio. As the volume of antibody designs rapidly increased, there became a clear need for a more advanced solution.

Protein domains are the building blocks for antibody analysis, annotation, handling, and visualization. Modern antibody designs have highly complex formats with large numbers of protein domains featuring ADCs, coupled proteins, bi/tri-specifics, cross-Mab technology, and scFv/scFab modules connected to the termini. New formats continue to appear almost every week. The pRED informatics department together with scientists from Roche Large Molecule Research identified the need for a solution that could accurately represent all possible formats for registration, visualisation, and data analysis.


Examples of PowerPoint-based antibody format descriptions that pre-date the development of HELM.

"The Penzberg pRED division numbers about 400 people supported by a 20-strong informatics group. The antibody registration tool with HELM at the core is a central part of Roche's pRED informatics strategy and is the highest prioritized project in the Penzberg research informatics group for the year 2015."

Margret Assfalg, Global Head of Discovery Workflows for Pharma Research & Early Development Informatics,Roche

Maximise Compatiblity

At the time, other standards could not handle large molecules properly and offered no simple way to extend them. Roche decided to do the work itself, in partnership with quattro research GmbH (Martinsried), by extending an existing public domain solution. HELM's independence from vendors, open source approach and zero licensing costs made it the preferred option.

Roche selected HELM to form the backbone of its antibody registration tool in order to standardize and thereby optimize the data flow between CROs, third party developers, and HELM-enabled data sources such as ChEMBL. They anticipated that HELM would become a widespread standard for accessing data sources of the future.

Figure 1: An accurate antibody registration tool enables researchers to check if their antibody design already exists (e.g. Cross-Mab), preventing duplication of work. Researchers are able to search for constructs by specificity and browse all projects and platforms for other constructs with components in common with their own design. This eases the analysis and performance comparison of distinct functional modules (e.g. scFv, scFab) used within or across projects.
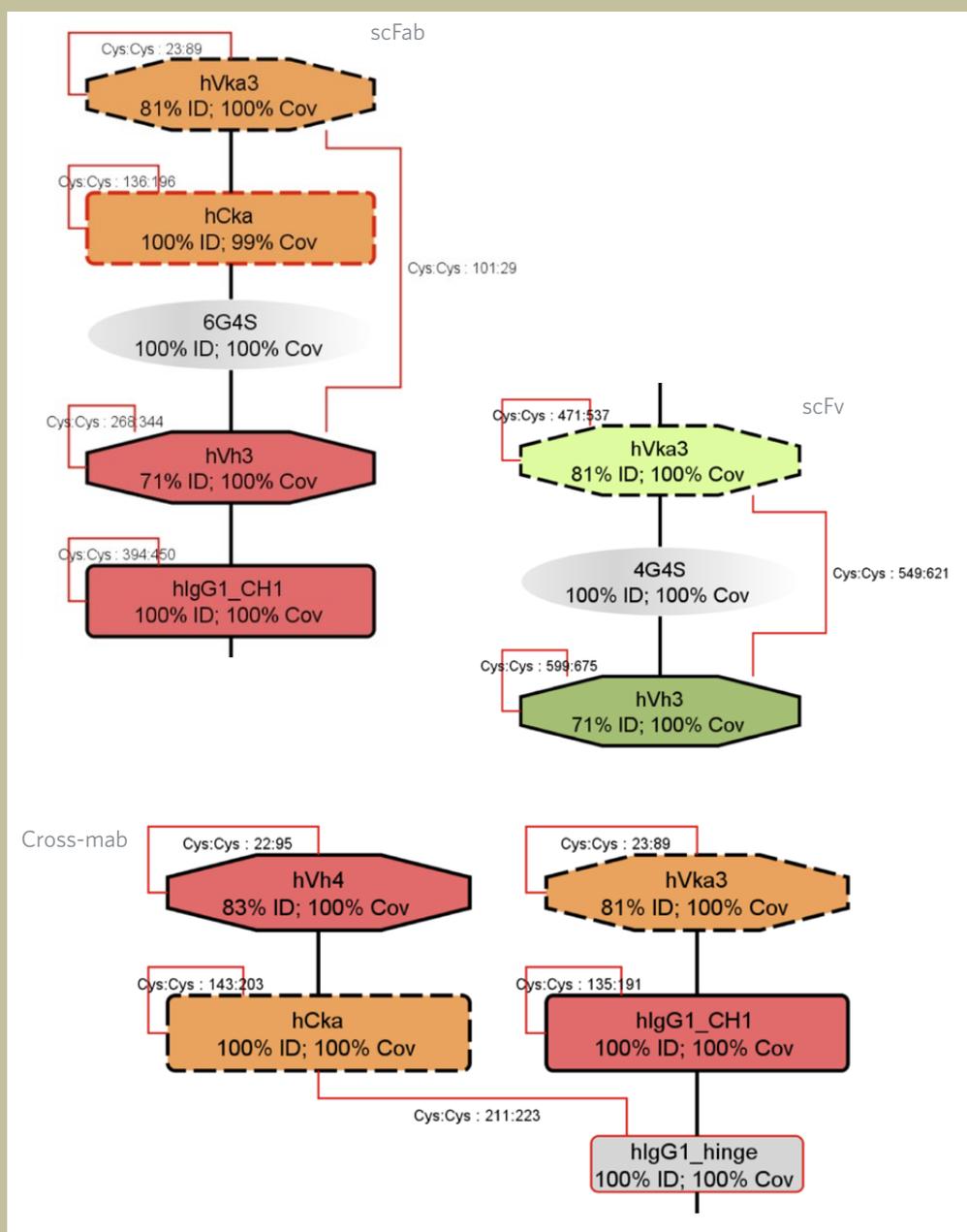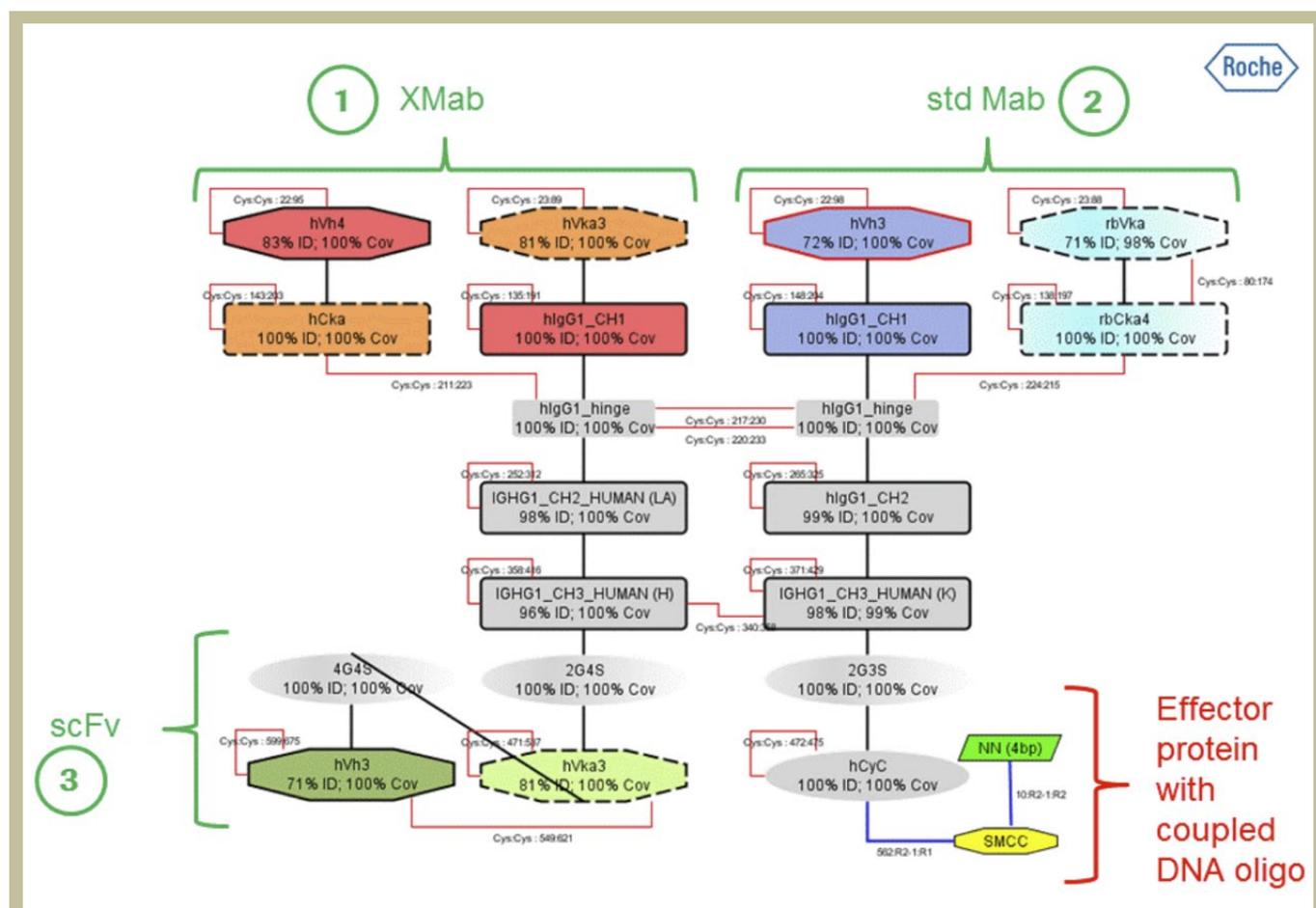
Figure 2: Based on the HELM format, Roche developed an antibody registration tool that allows the registration of all kinds of antibody-like constructs in an optimized way. The HELM Antibody Editor integrates smoothly with the open source HELM Editor.

The diagram shows a hypothetical tri-specific antibody based on **Cross-Mab technology** with conjugated effector protein automatically registered from 4 raw sequences by HAbE. An oligo has been manually attached to effector protein by HELM Editor.

"This kind of cross-company work is only possible with an organization such as the Pistoia Alliance to lead and co-ordinate it and it is pivotal to the success of Roche's adoption of HELM."

Bryn Roberts, Global Head of Operations for Pharma Research & Early Development, Roche

Pistoia Alliance Pivotal To Success

The original HELM standard was developed as an internal project at Pfizer. It was contributed to the public domain with the assistance and support of the Pistoia Alliance, who played a fundamental role in accelerating the open source release of Pfizer's technology. Without the ability to build upon the HELM Editor's features for attaching oligos and other chemical compounds, Roche would have had to spend much more time and effort to build a HAbE solution from scratch.

The ability to work with other HELM users as part of the Pistoia Alliance HELM project team is highly appreciated by the Roche pRED informatics team. Participation in lively discussions, the amazing variety of ideas and requirements presented, and the ability of the team to reach consensus even on contested topics is what makes the Pistoia Alliance valuable to its members.

"The HAbE brings together the best of both worlds: The fully automatic processing of antibody sequences to a detailed domain model of the final compound and the full flexibility of the HELM Editor to modify and extend the antibody by all means of chemistry."

Stefan Klostermann,
Expert Scientist,
Pharma Research & Early
Development Informatics,
Roche

Reception And Adoption

After presenting their work on the HELM Antibody Editor at the Bio-IT World Expo conference in 2014, at which the HELM project itself also won a Bio-IT Best Practices award, Roche has been approached by a number of other major pharmaceutical companies, who are mostly also Pistoia Alliance members, to provide demonstrations of their HELM-based antibody tools. By working together with Roche through the Pistoia Alliance these companies will make significant savings by building on existing, open, well-supported collaborative efforts, rather than going it alone to build their own.
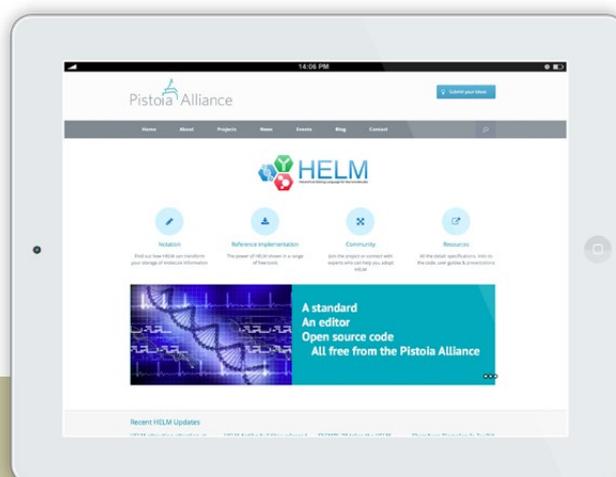
More information

info@pistoiaalliance.org
http://www.pistoiaalliance.org/

The HELM project website can be found at:
http://www.openhelm.org/
The HELM project team can be contacted by emailing:
info@openhelm.org/

Pistoia Alliance: Lowering barriers to R&D innovation

The Pistoia Alliance is a global, not-for-profit alliance of life science companies, vendors, publishers, and academic groups that work together to lower barriers to innovation in R&D.

Our members collaborate as equals on open projects that generate significant value for the worldwide life sciences community.