HIResist: A Database of HIV-1 Resistance to Broadly Neutralizing Antibodies

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BACKGROUND

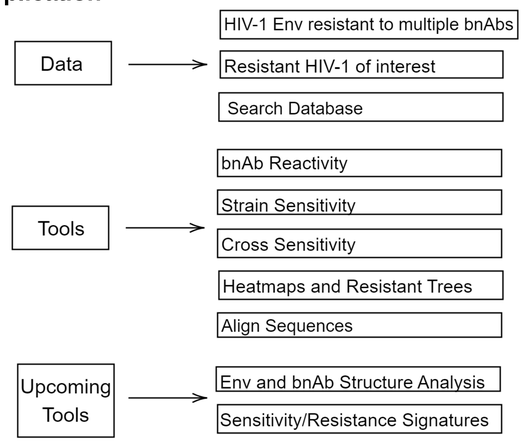
- HIV-1 envelope glycoproteins (Envs) mediate viral entry and are the sole target of neutralizing antibodies.
- The major determinant of Env functional and conformational state is the specific amino acid sequence.
- Sequence analysis is important to understand the pathways of HIV-1 resistance to bnAbs and is beneficial for future robust application of bnAbs for medical interventions.

Here, we introduce HIResist (HIV-1 Resistance to bnAbs), to analyze patterns of HIV-1 resistance to different bnAbs. HIResist is freely available online and is a comprehensive online resource with analysis and visualization tools designed to support the HIV-1 research community and the public.

DESIGN AND IMPLEMENTATION

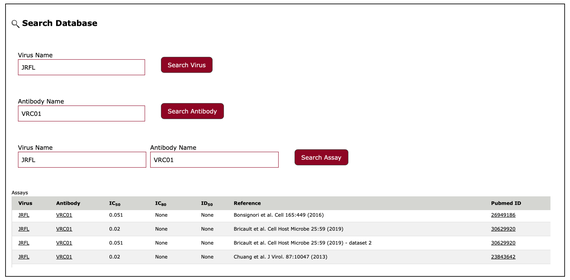
- HIResist is a Flask web application with Gunicorn production server and Apache reverse proxy.
- The application is written in Python (50%) and HTML/CSS/JavaScript (50%).
- Data is retrieved from the CATNAP database and stored in a periodically updated SQLite database.

Fig 1: The current and upcoming options on the web application

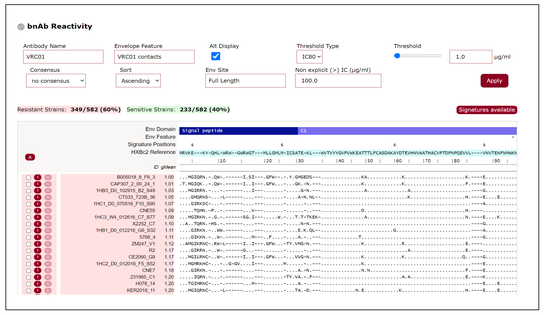


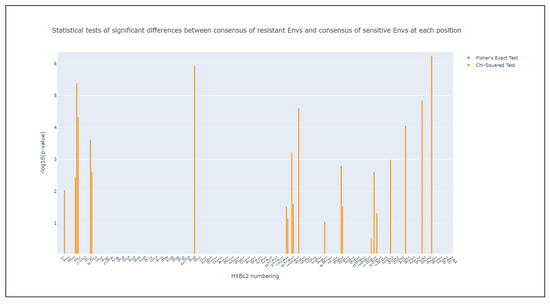
FEATURES

Search Database



bnAb Reactivity





Align Sequences

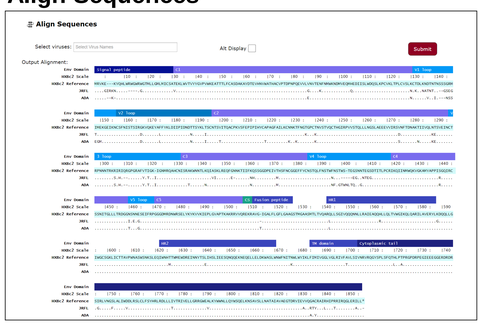


Fig 2: Search Database lists all assays in the database that are related to HIV-1 strain and/or specific antibody/Env ligands

Fig 3: bnAb Reactivity compares resistant (red) and sensitive (green) Envs at user-specified threshold

Fig 4: bnAb Reactivity generates statistical tests for significance of each consensus amino acid at each position of resistant and sensitive Envs

Fig 5: Strain Sensitivity identifies and displays neutralizing and non-neutralizing bnAbs/Env ligands for a user-selected HIV-1 Envs

FEATURES

Cross Sensitivity



Fig 6: Cross – Sensitivity generates plots of the sensitivity of all Envs to a pair of user-selected antibody/ligands.

CONCLUSIONS

- HIResist is an easy-to-use tool developed to encourage engagement and exploration within the scientific community to analyze relevant data without the need to have computational expertise.
- We are continuing to develop new tools to allow robust analysis of resistance/sensitivity of HIV-1 strains.

ACKNOWLEDGEMENT

This work was supported by the Avenir Award 1DP2DA049479=01 (NIH Director's New Innovator Award) from NIH/NIDA as well as the U01 grant 1U01AI169587 and R01 1R014AI167653, both from the National Institute of Allergy and Infectious Diseases. We would like to acknowledge the University of Minnesota Health Service Technology for supporting the server hosting the web application.

REFERENCE

Milind Misra, Jeffy Jeffy, Charis Liao, Stephanie Pickthorn, Kshitij Wagh, Alom Herschhorn, HIReist: A Database of HIV-1 Resistance to Broadly Neutralizing Antibodies. Accepted In Bioinformatics.

All images are adapted from the article