Support for Antiviral Drug Research in the Influenza Research Database (IRD) and Virus Pathogen Resource (ViPR)

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Overview

The Influenza Research Database (IRD, www.fludb.org) and Virus Pathogen Resource (ViPR, www.viprbrc.org) are publicly accessible repositories integrating biological data and analysis tools in support of research of Orthomyxoviridae, Bunyaviridae, Caliciviridae, Coronaviridae, Flaviviridae, Filoviridae, Hepeviridae, Herpesviridae, Paramyxoviridae, Picornaviridae, Poxviridae, Reoviridae, Rhabdoviridae, and Togaviridae. These resources are undergoing expansion to support antiviral research with the addition of a comprehensive infrastructure incorporating drug-target data, viral host factor data, and analysis tools facilitating investigation of these data.

Objectives

- Facilitate discovery of host pathways/proteins as potential drug targets to produce antiviral effects.
- Facilitate identification of promising candidates for repurposing among previously FDA approved drugs

Approach

Incorporate into ViPR and IRD:

- Comprehensive collection of antiviral drug and host factor data related to virus infection
- Infrastructure and toolset supporting access and integrated analysis incorporating all types of –omics data

Specific Aims

Specific Aim 1: (To be implemented in May, 2016)

- Compile known viral protein targets for all antiviral drugs
- Include specific interaction sites (if available)
- Compile antiviral resistance mutations for supported viruses
- Implement interface to support access and analysis

Specific Aim 2:

- Compile host factor data relevant to virus infection
- Implement interface to support access and analysis

Specific Aim 3:

- Semantic representation of all compiled data
- Interface supporting graph-based analysis of network models

Sources of Data (Specific Aim 1)

ATC: Direct Acting Antivirals
DrugBank: General Drug Information
Pharmacology Interacting Proteins
Protein Data Bank: Drug-Target Binding Sites
Resistance Databases / Literature: Antiviral Resistance Mutations

Figure 1. Included data was compiled from public resources. General drug data was compiled from Drugbank (http://www.drugbank.ca/). Drug binding data was compiled from Protein Data Bank (http://www.rcsb.org). Antiviral resistance data was compiled from databases and relevant literature.

Antiviral Data Access in ViPR / IRD

VIR / IRD

Figure 2. An antiviral search interface will be accessible from ViPR and IRD. Selecting a drug loads a webpage containing comprehensive drug data. Further target details (including drug binding sites and resistance mutations) can be accessed from this page.

Antiviral Binding Site Data in ViPR / IRD

Figure 3. ViPR representation of Idoxuridine binding in Human herpesvirus 1. ‘Known Binding Sites’ in ViPR is accessed from the ‘Drug Details’ page in ViPR and IRD. Specific drug binding site data (amino acid and location in a reference sequence) compiled from crystal structure experiments are available on this page.

Antiviral Resistance Data in ViPR / IRD

Figure 4. ViPR representation of amino acid changes in Hepatitis C virus associated with resistance to antivirals. This data is accessed from the ‘Drug Details’ page in ViPR and IRD. Specific virus amino acid changes (including location in reference sequence), resistance or sensitivity, and literature references are also available on this page.

Direct Acting Antiviral Drugs

Antiviral Drugs Selected for Inclusion:

‘Direct Acting Antivirals’; Anatomical Therapeutic Chemical (ATC) Code: J05A

Indicated Viruses for Direct Acting Antiviral Drugs

<table>
<thead>
<tr>
<th>Targeted Virus</th>
<th>ATC</th>
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<tbody>
<tr>
<td>Human Immunodeficiency virus</td>
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</tr>
<tr>
<td>Human herpesvirus 1, 2</td>
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<tr>
<td>Hepatitis C virus</td>
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<tr>
<td>Influenza A Virus</td>
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<td>Human herpesvirus 6</td>
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<td>Human T-lymphotropic virus 1</td>
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</tbody>
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Conclusion and Future Work

- Comprehensive antiviral drug data, including specific drug interaction sites, and antiviral resistance mutations available in May, 2016.
- Integration of host factor data in late 2016
- Analysis tools for analysis of semantic network models: late 2016, and continuing in 2017

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