Assessing Coronavirus threats

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Human and Civet SARS-CoV nestle phylogenetically within Bat SL-CoV cluster

Li et al. Science 2005
Human SARS CoV Tor2
Human SARS CoV BJ01
Human SARS CoV GZ02
Civet SARS CoV SZ3
Bat SL-CoV Rs_4087-1
Bat SL-CoV Rs_4110
Bat SL-CoV Rs_4090
Bat SL-CoV Rs_4079
Bat SL-CoV Rs_3367
Bat SL-CoV Rs_4105
Bat SL-CoV Rs_SHC014
Bat SL-CoV Rs_4084
Bat SL-CoV Rs_3267-1
Bat SL-CoV Rs_3262-1
Bat SL-CoV Rs_3369
Bat SL-CoV Rf1
Bat SL-CoV Rs_4075
Bat SL-CoV Rs_4092
Bat SL-CoV Rs_4085
Bat SL-CoV Rs_3262-2
Bat SL-CoV Rs_3267-2
Bat SL-CoV HKU3-1
Bat SL-CoV Rm1
Bat SL-CoV Rp3
Bat SL-CoV Rs_4108
Bat SL-CoV Rs672
Bat SL-CoV Rs_4081
Bat SL-CoV Rs_4096
Bat SL-CoV Rs_4087-2
Bat SL-CoV Rs_4097
Bat SL-CoV Rs_4080
Bat SARS-related CoV BM48
Bat CoV HKU9-1

Ge et al. (2013) Nature
New isolate from bats (2015), even closer to SARS-CoV

<table>
<thead>
<tr>
<th></th>
<th>Bat SL-CoV WIV16</th>
<th>Human SARS CoV Tor2</th>
<th>Human SARS CoV BJ01</th>
<th>Human SARS CoV GZ02</th>
<th>Civet SARS CoV SZ3</th>
<th>Bat SL-CoV WIV1</th>
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<td>Bat SL-CoV WIV16</td>
<td>----</td>
<td>96</td>
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<td>97</td>
<td>93</td>
</tr>
<tr>
<td>Human SARS CoV Tor2</td>
<td>96</td>
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<td>99</td>
<td>99</td>
<td>98</td>
<td>92</td>
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<td>Civet SARS CoV SZ3</td>
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</tbody>
</table>

Spike protein gene homology, Bat SARS-Like CoVs vs. Human, Civet SARS-CoV
Memish et al. 2013 EID
Ecological Niche Models to identify MERS “EpiZone”

- Modeled distribution of MERS-CoV bats
- Camel production (FAO)
- Modeled risk of MERS spillover (horn of Africa)
New Coronavirus from bats in Mexico

Anthony et. al. 2013 *J. Gen Virol.*
• ~58 unknown viruses in *Pteropus giganteus*
• ~320,000 unknown viruses in all mammals; ~72,152 in the 1,244 known bat species
• One-off cost to identify 100% = $6.8 Billion
• One-off cost to identify 85% = $1.4 Billion
• Cost of SARS = $10-50 Billion
• ~250 bat viruses in last 5 years, 530 total = 7% of the estimated #

Anthony et al. *mBio* 2013
Global emerging disease ‘hotspots’

Jones et al. Nature 2008
Follow up Genetic and Experimental studies (post-PREDICT) to Further Assess Spillover Potential

- Virus isolation
- Sequence whole genome
- With temporally sampled viruses, measure mutation rates and phylodynamics
- Sequence receptor binding domain, if known
- Structural comparison with human receptors (e.g. 3D models, In silico)
- Cell line infection experiments (in vitro)
- Humanized mice and other animal experiments

With each step, increased risk possible
Ranking risk for zoonotic potential of novel viruses

VIRUS-INDEPENDENT TRAITS + VIRUS-SPECIFIC TRAITS = RISK OF SPILLOVER

GEOGRAPHIC HOTSPOTS FOR EMERGENCE

HOST SPECIES TRAITS, GEOGRAPHIC RANGE, RELATEDNESS

HOST ABUNDANCE

VIRAL PREVALENCE IN HOST

GEOGRAPHICAL/HOST CONTACT INTERFACE

HOST BREADTH/PLASTICITY

PROPORTION KNOWN ZOONOSES IN VIRUS FAMILY

PHYLOGENETIC RELATEDNESS TO KNOWN ZOONOSES

OTHER VIRUS-SPECIFIC TRAITS

KNOWN ZOONOSES IN VIRUS FAMILY

PHYLOGENETIC RELATEDNESS TO KNOWN ZOONOSES

EPIDEMIOLOGICAL/CONTACT INTERFACE
<table>
<thead>
<tr>
<th>MODEL/FACTOR</th>
<th>Increased Risk</th>
<th>Decreased Risk</th>
<th>Data Used/Needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Hotspots v2</td>
<td>Hotspot</td>
<td>Coldspot</td>
<td><strong>EHA</strong> - Human pop density, mammal diversity, environmental drivers, landuse</td>
</tr>
<tr>
<td>2. Geographic viral range</td>
<td>More sites (=large viral spatial range)</td>
<td>Few sites</td>
<td><strong>GAINS</strong> – lat/long <strong>HP3</strong> - sum of host ranges</td>
</tr>
<tr>
<td>3. Interfaces</td>
<td>High risk interface</td>
<td>Low risk activity</td>
<td><strong>GAINS</strong> data and (<strong>CKJ</strong>’s lit review model)</td>
</tr>
<tr>
<td>4. Viral prev. in host</td>
<td>High</td>
<td>Low</td>
<td><strong>GAINS</strong> test data, need denominator</td>
</tr>
<tr>
<td>5. Host abundance</td>
<td>High</td>
<td>Low</td>
<td><strong>GAINS</strong> surveillance data; need effort</td>
</tr>
<tr>
<td>6a. Host Taxa</td>
<td>Rodents, bats, primates</td>
<td>Other mammals</td>
<td><strong>HP3</strong> and <strong>CKJ</strong> - Use if only have Order or Family level info.</td>
</tr>
<tr>
<td>6b. Host Species Traits and Phylog</td>
<td>High predicted number shared</td>
<td>Low predicted viruses shared</td>
<td><strong>HP3</strong> - Use if host Species or Genus info. Categorize continuous model output</td>
</tr>
<tr>
<td>7. Viral Family – Host Phylog Breadth</td>
<td>Large breadth and decent dataset</td>
<td>Small breadth</td>
<td><strong>HP3</strong> - Mean/median host phylogenetic range per viral family or genus. <strong>GAINS</strong> data on hosts if new virus.</td>
</tr>
<tr>
<td>8. Viral Family – % zoonotic</td>
<td>&gt;50% of viruses known to be human</td>
<td>&lt;50%</td>
<td><strong>HP3</strong> - Based on known zoonoses/viral diversity for each viral family. Factor in # viruses too, not just %.</td>
</tr>
<tr>
<td>10. Cophylogeny</td>
<td>Disrupted cophy</td>
<td>Concordant cophy</td>
<td><strong>GAINS</strong> and <strong>Genbank</strong> - need host and viral seq data. Categorize # events/virus.</td>
</tr>
</tbody>
</table>
Collaborators

- UC Davis, Metabiota, WCS, Smithsonian
- Univ. Wyoming (David Finnoff)
- Columbia Univ. (Ian Lipkin, Simon Anthony)
- 100+ partners in 24 countries
- Wuhan Institute of Virology, Yunnan CDC
- Universiti Malaysia Sabah, Sabah Wildlife Dept.

Funders