RSV 2018

11TH INTERNATIONAL RESPIRATORY SYNCYTIAL VIRUS SYMPOSIUM

OCT 31 - NOV 4, 2018
ASHEVILLE, NC, USA

FINAL PROGRAM
WE WOULD LIKE TO THANK OUR SPONSORS

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Oral Presenter and Poster Abstract Awards

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RSV2018 Symposium Awards

Travel Fellowship Awards

The RSV2018 Committee is pleased to announce that the Bill & Melinda Gates Foundation has supported fellows from economically disadvantaged countries to attend this conference.

<table>
<thead>
<tr>
<th>Name</th>
<th>Country</th>
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</thead>
<tbody>
<tr>
<td>Damian Alvarez-Paggi</td>
<td>ARGENTINA</td>
</tr>
<tr>
<td>Mani Bhargava</td>
<td>INDIA</td>
</tr>
<tr>
<td>Mauricio Caballero</td>
<td>ARGENTINA</td>
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<tr>
<td>Juan Gutman</td>
<td>ARGENTINA</td>
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<tr>
<td>Nusrat Homaira</td>
<td>BANGLADESH</td>
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<tr>
<td>Anna Aba Kafintu-Kwashie</td>
<td>GHANA</td>
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<tr>
<td>Moses Chapa Kiti</td>
<td>KENYA</td>
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<tr>
<td>Sofia Laudanno</td>
<td>ARGENTINA</td>
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<tr>
<td>Lilian Mayieka</td>
<td>KENYA</td>
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<tr>
<td>Adamu Tayachew Mekonnen</td>
<td>ETHIOPIA</td>
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<tr>
<td>Norosoa Razanjatovo</td>
<td>MADAGASCAR</td>
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<tr>
<td>Inés Sananez</td>
<td>ARGENTINA</td>
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<tr>
<td>Bishnu Upadhyay</td>
<td>NEPAL</td>
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<tr>
<td>Ziyaad Valley-Omar</td>
<td>SOUTH AFRICA</td>
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The RSV2018 Committee is pleased to announce that PATH has supported fellows from economically disadvantaged countries to attend this conference.

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<tbody>
<tr>
<td>Jefferson Buendia</td>
<td>COLUMBIA</td>
<td>Maduja Divarthna</td>
<td>SRI LANKA</td>
<td>Lien Anh Ha Do</td>
<td>VIETNAM</td>
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<tr>
<td>Temitayo Famoroti</td>
<td>SOUTH AFRICA</td>
<td>Stephanie Goya</td>
<td>ARGENTINA</td>
<td>Maria del Valle Juarez</td>
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<tr>
<td>Everlyn Kamau</td>
<td>KENYA</td>
<td>Romina Libster</td>
<td>ARGENTINA</td>
<td>Jonjee Morin</td>
<td>PHILIPPINES</td>
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<tr>
<td>Joyce Nyiro</td>
<td>KENYA</td>
<td>Elijah Kolawole Olapido</td>
<td>NIGERIA</td>
<td>James Otieno</td>
<td>KENYA</td>
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<tr>
<td>Irum Perveen</td>
<td>PAKISTAN</td>
<td>Ana Souza</td>
<td>BRAZIL</td>
<td>Irene Adema Wangwa</td>
<td>KENYA</td>
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RSV2018 Committee Awards

Young Investigator Best Oral Abstract Awards

Cameron Griffiths  University of Alberta, Canada
Jie (Jae) Yang  University of Wisconsin-Madison, USA

The RSV2018 Committee also granted awards to the following young investigators who achieved top scores in oral and poster abstracts:

Emanuele Andreano  University of Siena, Italy
Stephanie Ascough  Imperial College London, UK
Jonathon Coey  Queens University Belfast, UK
Shari Cho  University of Washington, USA
Farah Elawar  University of Alberta, Canada
Helen Groves  Queens University Belfast, UK
Tiffany Jenkins  Nationwide Children’s Hospital Research Institute, USA
Annenfleur Langedijk  UMC Utrecht, Netherlands
You Li  University of Edinburgh, UK
Megan Schmidt  University of Iowa, USA
Ting Shi  University of Edinburgh, UK
Mathilde Turfkruyer-Husson  Uniformed Services University of the Health Sciences, USA
Xunyan Ye  Baylor College of Medicine, USA
## PROGRAM

### DAY 1  Wednesday October 31

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<th>Time</th>
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<tr>
<td>1400-1830</td>
<td>Registration &amp; Poster Setup</td>
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<tr>
<td>1830-1845</td>
<td>Opening Address – Chair <strong>Martin Moore</strong> Emory University</td>
</tr>
<tr>
<td></td>
<td>Introduction to Keynote Speaker – Co-Chair <strong>Chris Stobart</strong> Butler University, USA</td>
</tr>
<tr>
<td>1845-1930</td>
<td><strong>Keynote Address</strong></td>
</tr>
<tr>
<td></td>
<td>Recent Insights into the Structure, Function, and Antigenicity of the F and G Glycoproteins</td>
</tr>
<tr>
<td></td>
<td><strong>Jason McLellan</strong> University of Texas at Austin, USA</td>
</tr>
<tr>
<td>1930-1945</td>
<td><strong>In Memoriam: José Melero</strong></td>
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<tr>
<td>1945-2115</td>
<td><strong>Welcome Reception</strong></td>
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</tbody>
</table>

**End of Day 1**

### DAY 2  Thursday November 1

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<tr>
<th>Time</th>
<th>Event</th>
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<tbody>
<tr>
<td>0630-0800</td>
<td>Breakfast</td>
</tr>
<tr>
<td>0700-1000</td>
<td>Registration &amp; Poster Setup</td>
</tr>
<tr>
<td>0800-0930</td>
<td><strong>SESSION 1  Clinical Impact and Epidemiology of RSV</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Moderators:</strong> <strong>Susan Gerber</strong> Centers for Disease Control and Prevention (CDC), USA</td>
</tr>
<tr>
<td></td>
<td><strong>Gayle Langley</strong> Centers for Disease Control and Prevention (CDC), USA</td>
</tr>
<tr>
<td>0800-0830</td>
<td><strong>Plenary I</strong></td>
</tr>
<tr>
<td></td>
<td>Strengthening Global RSV Surveillance: A Roadmap for the Future</td>
</tr>
<tr>
<td></td>
<td><strong>Susan Gerber</strong> Centers for Disease Control and Prevention (CDC), USA</td>
</tr>
<tr>
<td>0830-0845</td>
<td><strong>O1</strong> Incidence and Evaluation of the Change in Functional Status Associated with Respiratory Syncytial Virus Infection in Hospitalized Older Adults</td>
</tr>
<tr>
<td></td>
<td><strong>Angela Branche</strong> University of Rochester, USA</td>
</tr>
<tr>
<td>0845-0900</td>
<td><strong>O2</strong> Viral-bacterial interactions in infants with Respiratory Syncytial Virus Infection: Impact on clinical outcomes</td>
</tr>
<tr>
<td></td>
<td><strong>Asuncion Mejias</strong> The Research Institute at Nationwide Children's Hospital, USA</td>
</tr>
<tr>
<td>0900-0915</td>
<td><strong>O3</strong> Evaluating the diagnostic performance of various case definitions in detecting respiratory syncytial virus infections among pediatric admissions to a referral hospital, coastal Kenya</td>
</tr>
<tr>
<td></td>
<td><strong>Patrick Munywoki</strong> Centers for Disease Control and Prevention (CDC), Kenya</td>
</tr>
<tr>
<td>0915-0930</td>
<td><strong>O4</strong> Association of age at first severe RSV diseases with subsequent risk of asthma: a population-based cohort study</td>
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<tr>
<td></td>
<td><strong>Nusrat Homaira</strong> School of Women’s and Children’s Health, UNSW Medicine, Australia</td>
</tr>
<tr>
<td>0930-1000</td>
<td>Coffee break</td>
</tr>
</tbody>
</table>
### SESSION 2  Recent Developments in RSV Virology

**Moderators:**
- Gaya Amarasinghe *Washington University, USA*
- Lindsay Broadbent *Queen’s University Belfast, UK*

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<tr>
<th>Time</th>
<th>Session</th>
<th>Speaker</th>
<th>Affiliation</th>
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</table>
| **1000 - 1030** | **Plenary 2**  
**Immune evasion mechanisms of RSV non-structural proteins**  
Gaya Amarasinghe *Washington University, St. Louis, USA* |                                |                               |
| **1030 - 1045** | **O5**  
Respiratory Syncytial Virus Binds to a Signaling Coreceptor which Induces Recruitment of its Receptor, Nucleolin, to the Cell Surface during Entry  
Cameron Griffiths *University of Alberta, Canada* |                                |                               |
| **1045 - 1100** | **O6**  
Palladin mediates the association of RSV M protein with microfilaments in infected cells  
Shadi Shahriari *University of Canberra, Australia* |                                |                               |
| **1100 - 1115** | **O7**  
Airway epithelial and immune cell responses to RSV G protein interaction with fractalkine receptor CX3CR1  
Larry Anderson *Emory University, USA* |                                |                               |
| **1115 - 1130** | **O8**  
Ultrastructural Studies of RSV Assembly by Cellular Cryo-Electron Microscopy  
Jie (Jae) Yang *University of Wisconsin-Madison, USA* |                                |                               |

### Poster Session 1

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<thead>
<tr>
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<th>Session</th>
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<tr>
<td><strong>1230 - 1330</strong></td>
<td><strong>Poster Session 1</strong></td>
<td></td>
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</table>
| **1330 - 1500** | **SESSION 3**  
**Immune Response to RSV**  
**Moderators:**  
Steven Varga *University of Iowa, USA*  
Tracy Ruckwardt *NIH/NIAID/VRC, USA* |                                |                               |
| **1330 - 1400** | **Plenary 3**  
Inflammasome Activation is Influenced by RSV Strain Differences  
Steven Varga *University of Iowa, USA* |                                |                               |
| **1400 - 1415** | **O9**  
Attenuation of human airway epithelial cell innate immune responses to respiratory syncytial virus (RSV) in newborn infants compared to older infants  
Helen Groves *Queen's University Belfast, UK* |                                |                               |
| **1415 - 1430** | **O10**  
Unraveling the respiratory syncytial virus (RSV) antibody functional repertoire in adult healthy donors  
Emanuele Andreano *University of Siena, Italy* |                                |                               |
| **1430 - 1445** | **O11**  
RSV infection in early life is associated with defective tissue resident memory T cell differentiation  
Mathilde Turfkruyer-Hussor *Uniformed Services University of the Health Sciences, USA* |                                |                               |
| **1445 - 1500** | **O12**  
Identification of novel factors associated with severe RSV disease in infants  
Ultan Power *Queen’s University Belfast, UK* |                                |                               |

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<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Speaker</th>
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<tbody>
<tr>
<td><strong>1500 - 1530</strong></td>
<td><strong>Coffee Break</strong></td>
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</tbody>
</table>
| **1530 - 1630** | **SESSION 4**  
**Novel RSV Monoclonal Antibodies**  
**Moderators:**  
James Crowe *Vanderbilt University Medical Center, USA*  
Natalie Thornburg *Centers for Disease Control and Prevention (CDC), USA* |                                |                               |
| **1530 - 1600** | **Plenary 4**  
Neutralizing Antibody Determinants on RSV Fusion Protein  
James Crowe *Vanderbilt University Medical Center, USA* |                                |                               |
| **1600 - 1615** | **O13**  
Discovery and in vitro characterization of a potent broadly neutralizing antibody isolated from human memory B-cells  
Zhifeng Chen *Merck & Co Inc.* |                                |                               |
### Session 5: Advancements in RSV Vaccines

**Moderators:** Ursula Buchholz (NIH/NIAID, USA)  
Michael Teng (University of South Florida, USA)

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<tr>
<th>Time</th>
<th>Title</th>
<th>Presenters</th>
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</table>
| 1645-1815 | **Plenary 5**  
Live Attenuated Pediatric RSV Vaccines  
**Ursula Buchholz**  
NIH | **Jacqueline McDonald**  
WHO 1st International Standard for Antiserum to RSV  
National Institute of Biological Standards and Control (NIBSC), UK |
| 1645-1800 | **O16**  
Intranasal RSV F bound to Lactococcal particles induces durable systemic immune responses in human volunteers  
**Stephanie Ascough**  
Imperial College London, UK |
| 1645-1800 | **O17**  
Magnitude and Durability of Anti-F IgG and Palivizumab-Competitive Antibody (PCA) Responses One Year Following Immunization with RSV F Nanoparticle Vaccine Adjuvanted with Aluminum Phosphate, or a Novel Adjuvant  
**Vivek Shinde**  
Novavax Inc. |
| 1645-1800 | **O18**  
WHO 1st International Standard for Antiserum to RSV  
**Jacqueline McDonald**  
National Institute of Biological Standards and Control (NIBSC), UK |
| 1645-1800 | **O19**  
RSV F and G sequence evolution over the past three RSV seasons (2015/16-2017/2018) in the United States and Puerto Rico and implications for mAb/vaccine development  
**Hong Jin**  
MedImmune/AstraZeneca |
| 1645-1800 | **O20**  
Characterization of Antigenic Site-Specific Competitive Antibody Responses to the Fusion Protein in RSV Infected Hematopoietic Cell Transplant Adults  
**Xunyan Ye**  
Baylor College of Medicine, USA |
| 1645-1800 | **O21**  
New Insights into RSV Entry: ATPase Sodium/Potassium-Transporting Subunit Alpha-1 (ATP1A1) is Important for Macropinocytic Entry of RSV  
**Matthias Lingemann**  
National Institute of Allergy and Infectious Diseases, USA |

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**End of Day 2**

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### Day 3: Friday November 2

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<tr>
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<tbody>
<tr>
<td>0630-0800</td>
<td><strong>Breakfast</strong></td>
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</tbody>
</table>
| 0800-0930 | **Session 6**  
RSV Protein Structure and Function  
**Moderators:** Barney Graham (NIH/VRC, USA)  
Annelies Leemans (University of Antwerp, Belgium) |
| 0800-0830 | **Plenary 6**  
RSV F Glycoprotein Structure Determines Vaccine Immunogenicity  
**Barney Graham**  
NIH | **Barney Graham**  
NIH/VRC, USA |
| 0830-0845 | **O19**  
RSV F and G sequence evolution over the past three RSV seasons (2015/16-2017/2018) in the United States and Puerto Rico and implications for mAb/vaccine development  
**Hong Jin**  
MedImmune/AstraZeneca |
| 0845-0900 | **O20**  
Characterization of Antigenic Site-Specific Competitive Antibody Responses to the Fusion Protein in RSV Infected Hematopoietic Cell Transplant Adults  
**Xunyan Ye**  
Baylor College of Medicine, USA |
| 0900-0915 | **O21**  
New Insights into RSV Entry: ATPase Sodium/Potassium-Transporting Subunit Alpha-1 (ATP1A1) is Important for Macropinocytic Entry of RSV  
**Matthias Lingemann**  
National Institute of Allergy and Infectious Diseases, USA |
<table>
<thead>
<tr>
<th>Time</th>
<th>Session/Activity</th>
<th>Speaker/y</th>
<th>Institution/Location</th>
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<tbody>
<tr>
<td>0915 - 0930</td>
<td>&quot;The Apical Loop of the Respiratory Syncytial Virus Fusion Protein F2 Subunit Is Critical for Fusion Activity&quot;&lt;br&gt;Mark Peeples&lt;br&gt;The Ohio State University, USA</td>
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<tr>
<td>0930 – 1000</td>
<td>Coffee Break</td>
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<tr>
<td>1000 - 1130</td>
<td><strong>SESSION 7</strong>&lt;br&gt;RSV Pathogenesis and Experimental Models&lt;br&gt;Moderators: Marina Boukhvalova&lt;br&gt;Sigmovir Biosystems, USA&lt;br&gt;Peter Wright&lt;br&gt;Geisel School of Medicine at Dartmouth, USA</td>
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<tr>
<td>1000 - 1030</td>
<td>Plenary 7&lt;br&gt;RSV Pathogenesis, Prevention, and Animal Models&lt;br&gt;Marina Boukhvalova&lt;br&gt;Sigmovir Biosystems, Maryland, USA</td>
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<tr>
<td>1030 - 1045</td>
<td>O23 Respiratory syncytial virus (RSV) infection increases neutrophil trans-epithelial migration and adherence resulting in increased damage to ciliated airway epithelial cells&lt;br&gt;Rosalind Smyth&lt;br&gt;UCL GOS Institute of Child Health London, UK</td>
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<tr>
<td>1045 - 1100</td>
<td>O24 Genetic determinants of severe respiratory syncytial virus infections in infants&lt;br&gt;Martin Wetzke&lt;br&gt;Medical School Hannover, Germany</td>
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<tr>
<td>1100 - 1115</td>
<td>O25 MUC5B is the predominant gel-forming mucin obstructing the distal airways during RSV bronchiolitis&lt;br&gt;Raymond Pickles&lt;br&gt;UNC-Chapel Hill, NC, USA</td>
<td></td>
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<tr>
<td>1115 - 1130</td>
<td>O26 <em>Streptococcus Pneumoniae</em> Infection in Respiratory Syncytial Virus Infected Neonatal Lambs&lt;br&gt;Sarhad Alnajjar&lt;br&gt;Iowa State University, Oregon State University, USA</td>
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<tr>
<td>1130 - 1200</td>
<td>Coffee Break</td>
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<tr>
<td>1200 - 0130</td>
<td><strong>SESSION 8</strong>&lt;br&gt;Anti-RSV Therapies&lt;br&gt;Moderators: Janet Englund&lt;br&gt;Seattle Children’s Hospital, USA&lt;br&gt;John DeVincenzo&lt;br&gt;University of Tennessee, USA</td>
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<tr>
<td>1200 - 1230</td>
<td>Plenary 8&lt;br&gt;Challenges for RSV Antivirals&lt;br&gt;Janet Englund&lt;br&gt;Seattle Children’s Hospital, University of Washington</td>
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<tr>
<td>1230 - 1245</td>
<td>O27 Efficacy of the non-fusion human respiratory syncytial virus (hRSV) replication inhibitor JNJ-64166037 in hRSV infected lamb model&lt;br&gt;Panchan Sitticharoenchai&lt;br&gt;Iowa State University, USA</td>
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<tr>
<td>1245 - 1300</td>
<td>O28 EDP-938, a Novel Non-Fusion Replication Inhibitor of RSV, Displays a High Barrier to Resistance In Vitro&lt;br&gt;Michael Rhodin&lt;br&gt;Enanta Pharmaceuticals, USA</td>
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<tr>
<td>1300 - 1315</td>
<td>O29 Antiviral effects, pharmacokinetics (PK) and safety of the respiratory syncytial virus (RSV) fusion protein inhibitor, JNJ-53718678 (JNJ-8678), in RSV-infected infants with bronchiolitis, in the Phase 1b Study 53718678RSV1005&lt;br&gt;Marita Stevens&lt;br&gt;Janssen Infectious Diseases Bvba, Belgium</td>
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<tr>
<td>1315 - 1330</td>
<td>O30 Ziresovir (AK0529): Update on Clinical Development for the Treatment of Respiratory Syncytial Virus (RSV) Disease&lt;br&gt;Stephen Toovey&lt;br&gt;Ark Biosciences, Switzerland</td>
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<tr>
<td>1330 - 1900</td>
<td>Free Afternoon - Optional Activities</td>
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<tr>
<td>1900 - 2030</td>
<td>Robert M. Chanock Lectures&lt;br&gt;introduced by Peter Openshaw, Imperial College London</td>
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<tr>
<td>1900 - 1945</td>
<td>From the Young to the Old and back again: A Journey Through the Varied World of RSV&lt;br&gt;Edward Walsh&lt;br&gt;University of Rochester Medical Center, USA</td>
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<tr>
<td>1945 - 2030</td>
<td>RSV, A Virus for All Ages&lt;br&gt;Ann Falsey&lt;br&gt;University of Rochester Medical Center, USA</td>
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<tr>
<td>Time</td>
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<tr>
<td>0630</td>
<td>Breakfast</td>
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<tr>
<td>0800</td>
<td>Keynote Address</td>
<td>The Road to RSV Vaccine Impact: ‘History doesn’t repeat itself, but it sure does rhyme’</td>
<td>Katherine O’Brien</td>
</tr>
<tr>
<td>0845</td>
<td>Short Break</td>
<td></td>
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</tr>
<tr>
<td>0855</td>
<td>SESSION 9</td>
<td>RSV Prophylaxis and Vaccines II</td>
<td>Moderators: Ruth Karron, Susan Bueno</td>
</tr>
<tr>
<td>0855</td>
<td>Plenary 9</td>
<td>The Interaction between Human Metapneumovirus and the Host Immune System</td>
<td>Bernadette van den Hoogen</td>
</tr>
<tr>
<td>0925</td>
<td>O31</td>
<td>Defining the Humoral and B Cell Response after Vaccination with a Stabilized Prefusion RSV F Subunit Vaccine</td>
<td>Emily Phung</td>
</tr>
<tr>
<td>0940</td>
<td>O32</td>
<td>Evaluation of Novel RSV Live Attenuated Vaccine in a Non-Human Primate Model</td>
<td>Tiffany Jenkins</td>
</tr>
<tr>
<td>0955</td>
<td>O33</td>
<td>Pfizer RSV Vaccine Program</td>
<td>Kena Swanson</td>
</tr>
<tr>
<td>1010</td>
<td>Coffee Break</td>
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</tr>
<tr>
<td>1030</td>
<td>SESSION 10</td>
<td>RSV’s Global Impact and Epidemiology</td>
<td>Moderators: James Nokes, Yasmeen Agosti</td>
</tr>
<tr>
<td>1030</td>
<td>Plenary 10</td>
<td>Global perspective on the RSV problem</td>
<td>D. James Nokes</td>
</tr>
<tr>
<td>1100</td>
<td>O33</td>
<td>Global and regional disease burden estimates of respiratory syncytial virus associated with acute respiratory infections in older adults in 2015: A systematic review and meta-analysis</td>
<td>Ting Shi</td>
</tr>
<tr>
<td>1115</td>
<td>O34</td>
<td>Global patterns in monthly activity of respiratory syncytial virus: a systematic review and modelling study</td>
<td>You Li</td>
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<tr>
<td>1130</td>
<td>O35</td>
<td>Prospective, epidemiological study of the incidence of respiratory syncytial virus (RSV) lower respiratory tract infections (LRTIs) from birth up to 2 years of age in diverse global settings</td>
<td>Joanne Langley</td>
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<tr>
<td>1145 - 1200</td>
<td>WHO Global RSV Surveillance based on GISRS – building evidence for policy</td>
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<td>Siddhivinayak Hirve, World Health Organisation</td>
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<td>1200 - 1300</td>
<td>Lunch Break</td>
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<td>1300 - 1430</td>
<td>SESSION 11 Global Perspective of the RSV Problem</td>
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<td>1300 - 1330</td>
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<td>RSV Prevention: How to Get from The Lab to The Village</td>
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<td>Daniel Feikin, World Health Organisation, Switzerland</td>
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<td>1330 - 1335</td>
<td>BMGF’s vision on RSV Community Mortality Studies</td>
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<td>Keith Klugman, Bill &amp; Melinda Gates Foundation, USA</td>
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<td>1335 - 1342</td>
<td>RSV Gold</td>
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<td>Natalie Mazur, University Medical Center Utrecht</td>
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<td>1342 - 1349</td>
<td>Argentina Site</td>
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<td>Fernando Polack, Fundación Infant, Buenos Aires, Argentina</td>
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<td>RSV Burden from the CHAMPS Study</td>
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<td>Dianna Blau, CDC, USA</td>
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<td>1356 - 1403</td>
<td>RSV Burden from the ZPRIME Study</td>
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<td>Christopher Gill, Boston University School of Public Health, USA</td>
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<td>1403 - 1430</td>
<td>Executing on the vision (process, academic-community partnership, hurdles, and lessons learned) – 3 community mortality sites</td>
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<td>Wilson: India - Eric Simoes The Children’s Hospital, Colorado, USA &amp; Ashish Satav, MAHAN Trust; Argentina – Mauricio Caballero, Fundación INFANT, Argentina; Zambia – Christopher Gill, Boston University, USA; Lawrence Mwananyanda, Right to Care-EQUIP</td>
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<td>1430 - 1500</td>
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<td>1500 - 1630</td>
<td>SESSION 12 Maternal Immunity and Maternal Vaccination</td>
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<td></td>
<td>Maternal Immunity and Vaccination</td>
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<td>Helen Chu, University of Washington, USA</td>
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<td>1530 - 1545</td>
<td>O36 Transplacental Respiratory Syncytial Virus and Influenza Antibody Transfer in Alaska-Native Mother-Infant Pairs</td>
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<td>Helen Chu, University of Washington, USA</td>
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<td>1545 - 1600</td>
<td>O37 Efficacy of RSV Maternal Immunization Varies with the Version of the Prefusion F Antigen in Virus-like Particle Vaccine Candidates</td>
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<td>Trudy Morrison, University of Massachusetts Medical School, USA</td>
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<td>1600 - 1615</td>
<td>O38 Progress Toward a Vaccine for Maternal Immunization to Prevent Respiratory Syncytial Virus Lower Respiratory Tract Illness (RSV LRTI) in Infants</td>
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<td>Louis Fries, Novavax, Inc.</td>
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<td>1615 - 1630</td>
<td>O39 Advancing Maternal Immunization and the RSV MI Roadmap</td>
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<td>Deborah Higgins, PATH, USA</td>
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### End of Day 4

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<td>1800-2200</td>
<td>Ticketed SOCIAL EVENT – Conference Dinner at the Biltmore</td>
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<td>Shuttles will depart at 6pm from the Vanderbilt Wing Lobby, Grove Park Level 7</td>
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### DAY 5  
**Sunday November 4 - Departures**

- **Young Investigator Best Abstract Award**
Background
Respiratory Syncytial Virus (RSV) causes severe respiratory illnesses in infants and older adults. Mortality disproportionately affects the elderly, can exacerbate chronic cardiopulmonary conditions and may result in loss of function. The purpose of this study was to determine the incidence of RSV infection in hospitalized adults and evaluate functional changes associated with RSV hospitalization in older adults >60 years.

Methods
Adults >18 years of age admitted with an acute respiratory infection (ARI) or exacerbation of chronic cardiopulmonary disease (e.g. CHF, COPD, asthma) preceded by an ARI within 14 days were screened. Subjects were included if hospitalized for > 24 hours with laboratory confirmed RSV and residing in two catchment areas (Rochester, NY and New York, NY). Illness history, comorbidities and demographic characteristics were collected at enrollment. Enrolled subjects >60 years underwent functional status evaluation retrospectively 2 weeks prior to hospitalization, at enrollment, discharge and 2 months using the Lawton-Brody Instrumental Activity of Daily Living (IADL) Scale (0-8), Barthel (ADL) Index (0-100), MRC Breathlessness score (1-5) and Mini-Cog instrument.

Results
From October 2017 to March 2018, 2883 adults hospitalized with ARI were tested and 322 (11%) positive for RSV. Seventy-two adults >60 years underwent functional assessment. Mean age was 75 years, 53% were female and 58% demonstrated impaired cognition on admission. Five subjects died during hospitalization and one prior to 2-month follow-up. Interim analysis of 2-month functional assessment was available for 39 subjects. RSV illness resulted in acute functional loss in almost all patients. Although there were no statistically significant differences between mean pre-hospitalization and 2-month functional scores, IADL (6.7 vs. 6.0, p=0.27), ADL (90.4 vs. 88.5, p=0.67) and MRC (2.96 vs. 2.7, p=0.57), 23% of subjects required a higher level of care at discharge. Additionally, RSV hospitalization resulted in decreased ADL scores in 36% of subjects and worsening respiratory function in 18% assessed at 2 months (Figure).

Conclusions
Older adults hospitalized with RSV infection demonstrate acute functional decline which may result in prolonged loss of function in some patients.
O2

VIRAL-BACTERIAL INTERACTIONS IN INFANTS WITH RESPIRATORY SYNCYTIAL VIRUS INFECTION: IMPACT ON CLINICAL OUTCOMES

ASUNCION MEJIAS 1, Octavio Ramilo 1, Sara Mertz 1, Jeffrey Naples 2, Alejandro Diaz 1, Eleonora Bunsow 1, Alexis Juergensen 1, Cristina Garcia-Maurino 1,

1 Center for Vaccines and Immunity, The Research Institute at Nationwide Children’s Hospital
2 Pediatric Critical Care Medicine, Nationwide Children's Hospital

Background

Previous studies suggest that RSV increases NP bacterial colonization. However, the role of NP colonization with potentially pathogenic bacteria (PPB) in the pathogenesis and clinical manifestations of RSV bronchiolitis is not well understood. We sought to determine the frequency, type and density of NP PPB detection in infants with RSV infection compared with healthy controls (HC) and its association with clinical outcomes.

Methods

Single-center, prospective study of previously healthy infants with RSV infection and age-matched HC. Inpatients (IP) were enrolled within 24h of hospitalization, outpatients (OP) at the ED or primary clinics and HC at well-child visits. RSV infection and the following PPB: [S. pneumoniae (Spn), M. catarrhalis (Mc), H. influenzae (Hi) and S. aureus (Sa)] were detected and quantified by PCR. We compared demographic, clinical characteristics and outcomes of care according to NP PPB detection.

Results

From 2010 to 2018, we enrolled 815 infants: 664 with RSV infection [IP, 560; OP, 104] and 151 HC. RSV+ OP (6.1 [3.7-10.7] mo) and HC (6.9 [3.8-10.8] mo) were older than IP (2.5 [1.4-5.4] mo; p<0.001). Identification of ≥1 PPB was 89% in RSV+ infants [IP, 88%; OP, 90%] vs. 63% of HC (p<0.0001). While Hi or >1 PPB detection was higher in RSV infection (p<0.001), SA detection predominated in HC (p<0.05; Fig 1). Frequency of Spn detection was comparable between groups; however, Spn loads were one log higher in RSV+ infants vs. HC (p=0.001) adjusted for antibiotic use. Differences in colonization rates remained different in RSV+ infants vs. HC across age ranges (<3, 3-6, >6-12 and >12-24 mo). Last, RSV patients (both IP & OP) with Spn or Hi detection had fever more frequently (70%-74% vs. 25%-47%; p<0.0001), higher clinical disease severity scores (p=0.01), and higher blood neutrophil counts (34%-36% vs. 16%-19%; p<0.001), vs. those with Mc, SA detection or PCR negative. In addition, NP detection of Hi in RSV children was associated with higher frequency of atelectasis/consolidation by chest X-ray (p<0.005).

Conclusions

These data suggest that NP colonization with PPB is high in infants with RSV infection independent of age, and that specific bacteria, namely Spn and Hi, are associated with enhanced clinical disease severity.

O3

EVALUATING THE DIAGNOSTIC PERFORMANCE OF VARIOUS CASE DEFINITIONS IN DETECTING RESPIRATORY SYNCYTIAL VIRUS INFECTIONS AMONG PEDIATRIC ADMISSIONS TO A REFERRAL HOSPITAL, COASTAL KENYA

PATRICK MUNYWOKI 1, Noel Joseph 2, Greiven Otieno 2, Mwanajuma Ngama 2, James Nokes 2,3

1 CDC-Kenya 2 KEMRI-Wellcome Trust Research Programme, Kilifi, Kenya 3 School of Life Sciences and Zeeman Institute for Systems Biology & Infectious Disease Epidemiology Research (SBIDER), University of Warwick, Coventry, United Kingdom

Background

A range of non-uniform case definitions have been used in various respiratory syncytial virus (RSV) disease burden studies. Clinical definitions proposed by the World Health Organization (WHO) target impact evaluation in RSV vaccine trials and improved RSV surveillance for hospitalized children aged <6 months. Quantifying the diagnostic performance of these definitions is critical in improving RSV surveillance for disease burden estimation beyond the first 6 months of life.
Methods
We used data from a long-term inpatient surveillance of children aged <5 years admitted with a respiratory illness to Kilifi County Hospital from 2002 to 2017. Collected nasopharyngeal specimens (NPS) were screened for RSV by Immunofluorescence antibody test (IFAT) from 2002, and also by real-time multiplex polymerase chain reaction (RT-PCR) from 2007. Sensitivity and specificity of various case definitions used in detecting RSV infection were calculated. The impact of the case definitions on burden estimation of RSV-associated hospitalization will be assessed by determination of average annual incidence rates.

Results
Over the 16 years of surveillance, 12,808 children were enrolled and tested, of which 2,655 (20.7%) were RSV positive. Most (79.8%) RSV positive cases were <1 year of age. A modified (fever not a requirement) severe acute respiratory infection (SARI) case definition for children <6 months had the highest sensitivity 92.1% (95% CI; 90.6 – 93.4%) with a corresponding specificity of 40.6% (39.1 – 42.1%). For case definitions targeting all under-fives age category, SARI case definition had the highest sensitivity of 81.6% (80.1 – 83.1%) with a specificity of 48.6% (47.7 – 49.6%). Age, comorbidities, presence of other pathogens and inclusion of fever were found to influence the diagnostic performance of various case definitions. The sensitivity and specificity of the WHO clinical endpoint for severe RSV disease among children between 6-59 months was 76.7% (74.1 – 79.2%) and 32.0% (30.7 – 33.1%), respectively. Case definitions targeting detection of severe RSV-associated disease for specific age groups yielded high burden estimates compared to those targeting the overall under-five age bracket.

Conclusions
Our results suggest the modified and standard SARI case definitions are the most suitable for RSV surveillance with the highest sensitivity for children <6 months and 6-59 months, respectively. These findings indicate that modified case definitions based on study aims, target age group among other factors might be required to improve RSV case detection in surveillance.

ASSOCIATION OF AGE AT FIRST SEVERE RSV DISEASES WITH SUBSEQUENT RISK OF ASThma: A POPULATION-BASED COHORT STUDY

NUSRAT HOMAIRA 1, Ju-Lee Oei 2,3, Nancy Briggs 4, Lisa Hilder 2,5, Barbara Bajuk 6, Adam Jaffe 2,7, Saad B. Omer 8

Background
The burden of respiratory syncytial virus (RSV) disease is highest in the first three months of life and linked to an increased risk of asthma. A maternal RSV vaccine is in development to protect against infant infection but it is unclear if this will also be protective against childhood asthma.

Methods
We conducted a retrospective cohort study using population-based linked administrative data for all children born in New South Wales, Australia, between 2001-2010 to determine the association between age at first severe RSV disease and the risk of development of subsequent pediatric asthma. All children with a first episode of RSV-coded hospitalization at 0-3 months, 3-6 months, 6-12 months, and 12-24 months were followed. The primary outcome was any episode of asthma-coded hospitalization beyond the age of 2 years. Poisson estimation with robust standard errors was used to calculate adjusted incidence rates and rate ratios of asthma hospitalization in children with severe RSV diseases.

Results
In a cohort of 847,516 children; 21,641 children had their first RSV coded hospitalization within the first two years of life (29% at ages 0-3 months, 20% at 3-6 months, 25% at 6-12 months and 25.5% at 12-24 months), 1,805 (8%) of them were subsequently hospitalized for asthma after age 2 years. The incidence/1000 child-years (95% CI) of first asthma hospitalization in children who had their first RSV episode at 0-3 months was 0.5 (0.3-0.7), 3-6 months was 1.1 (0.7-1.5), 6-12 months was 1.8 (1.4-2.2) and 12-24 months was 2.5 (1.9-3.2).
The rate ratios compared to children aged 0-3 months were 2.0 (1.3-3.3) for children aged 3-6 months, 3.5 (2.2-5.2) for aged 6-12 months and 4.8 (3.1-7.5) for aged 12-24 months.

Conclusions

Compared to young infants, children with RSV infection in the 2nd year of life are at increased risk of hospitalization for asthma. Maternal immunization might not be sufficient for reducing burden of RSV-associated childhood asthma hospitalizations.

SESSION 2    RECENT DEVELOPMENTS IN RSV VIROLOGY

O5 RESPIRATORY SYNCTIAL VIRUS BINDS TO A SIGNALING CORECEPTOR WHICH INDUCES RECRUITMENT OF ITS RECEPTOR, NUCLEOLIN, TO THE CELL SURFACE DURING ENTRY

CAMERON GRIFFITHS 1, Leanne Bilawchuk 1, Kyla Jamieson 2, Lionel Jensen 1, Farah Elawar 3, Wenming Duan 3, Bernard Thienpont 4, Bart Vanaudenaerde 5, John McDonough 5, David Proud 2, Theo Moraes 6, David Marchant 1

1 Li Ka Shing Institute of Virology, Department of Medical Microbiology and Immunology, University of Alberta, Edmonton, Alberta, Canada
2 Snyder Institute for Chronic Diseases, Department of Physiology and Pharmacology, University of Calgary, Calgary, Alberta, Canada
3 Program of Translational Medicine, Hospital for Sick Children Research Institute, Toronto, Ontario, Canada
4 Laboratory for Functional Epigenetics, Department of Human Genetics, KU Leuven, Leuven, Belgium
5 Department of Chronic Diseases, Metabolism, and Ageing, KU Leuven, Leuven, Belgium
6 Program of Translational Medicine, Hospital for Sick Children Research Institute, Toronto, Ontario, Canada; Departments of Paediatrics and Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Ontario, Canada

Background

To enter host cells, respiratory syncytial virus (RSV) binds to nucleolin (NCL) on the cell surface. However, bronchial epithelial cells express low levels of cell surface NCL, which is unexpected as they are the primary target of RSV infection. Using live cell imaging, we observed that NCL actively redistributed from the nucleus to the cell surface. At the surface, NCL formed patches around bound RSV particles during viral fusion. Furthermore, RSV activates multiple cellular kinases prior to entry that mediate cell surface NCL trafficking. This led us to hypothesize that RSV initially binds to an abundant cell surface “signaling coreceptor”, which utilizes the host cell signaling network to recruit NCL from the nucleus to trigger the fusion of viral particles waiting at the cell surface.

Methods

Purified RSV was used to infect 1HAEo bronchial epithelial cells in the presence of specific inhibitors targeting candidate RSV signaling coreceptors and the downstream kinases activated before RSV entry. RSV infectivity was measured using a modified immuno-plaque assay. Imaging flow cytometry and confocal microscopy quantified the interaction of RSV with NCL during virus entry after treatment with receptor/kinase inhibitors in 1HAEo cells and normal human bronchial epithelial cells grown in air-liquid interface culture. The roles of novel signaling coreceptors were supported by co-immunoprecipitation with RSV, microscopy, and kinase activity assays. The expression of coreceptor and kinase factors that are important for RSV infection of ciliated bronchial epithelial cells is supported by single cell RNA-SEQ of a human lung.

Results

We discovered an abundantly expressed cell surface protein and a downstream cellular kinase that mediate a signaling cascade to permit RSV entry. The signaling coreceptor co-localizes with bound RSV particles on the cell surface and its activity prior to RSV entry is important for viral entry. Inhibiting the downstream cellular kinase prevents NCL surface trafficking in response to RSV, thereby preventing viral entry. The signaling coreceptor and kinase that are central to this cascade are uniquely and highly expressed on ciliated human bronchial epithelial cells in the human lung.

Conclusions

Binding of RSV to its signaling coreceptor, that is abundantly expressed on human airway epithelial cells, induces a cellular signaling cascade. The cascade then results in the recruitment of NCL to RSV particles on the plasma membrane, where NCL mediates the entry of viral particles. This research examines the novel biological process of NCL cell surface trafficking to interact with RSV and yields potential therapeutic targets to inhibit the RSV entry process.
PALLADIN MEDIATES THE ASSOCIATION OF RSV M PROTEIN WITH MICROFILAMENTS IN INFECTED CELLS

SHADI SHAHRIARI 1, Reena Ghildyal 2

1 University of Canberra
2 Centre for Research in Therapeutic Solutions, Faculty of Science and Technology, University of Canberra, Canberra ACT, 2617, Australia

Background
The respiratory syncytial virus (RSV) matrix (M) protein interacts with the actin cytoskeleton in viral assembly and budding. The M-actin interaction may facilitate the transportation of the ribonucleoprotein complexes (RNPs) of RSV to viral assembly and budding sites. In this study we have investigated the M-actin interaction and the possible role of AKT.

The serine/threonine-specific protein kinase AKT has been shown to be required for RSV infection and plays a role in the organisation of the actin cytoskeleton. Actin organisation by AKT is made possible through its substrate palladin, an actin binding protein involved in actin remodelling that binds to proteins that bind actin.

Methods
Purified wildtype RSV M protein was used in an in vitro actin binding assay, followed by visualisation by SDS-PAGE. Vero cells were transfected to express full length M (1-256) protein as GFP-tagged proteins, followed by treatment with cytochalasin D and visualisation by live cell confocal microscopy.

AKT kinase assays were used to determine AKT activity in RSV infection. In addition, the effect of AKT inhibitors on RSV viral titres was investigated. Finally, the interaction of palladin and RSV M was determined through co-immunoprecipitation.

Results
M was found to bind directly to polymerised actin upon successful actin polymerisation and to monomeric actin in the absence of actin polymerisation.

RSV M also interacts with polymerised actin in a transfected cell system. De-stabilisation of the microfilament network by cytochalasin D resulted in mis-localisation of M from mostly cytoplasmic to diffused across both cytoplasm and nucleus; clearly, M is retained in the cytoplasm partly by its interaction with microfilaments.

We next investigated the possible role of AKT and its substrate, palladin, in the M-actin interaction. Through AKT kinase activity assays and inhibitor studies, we show that AKT is induced in RSV infection and that inhibition of AKT activity leads to reduced virus titres. Clearly, AKT activity is important for RSV replication and/or assembly. Palladin was co-immunoprecipitated with M from RSV infected cells.

Results
In conclusion, we show that RSV M is an actin binding protein and that palladin binds to M in infected cells. Further investigations are focused on determining whether M binds to phosphorylated or non-phosphorylated palladin and how the M-palladin interaction contributes to RSV assembly.

AIRWAY EPITHELIAL AND IMMUNE CELL RESPONSES TO RSV G PROTEIN INTERACTION WITH FRACTALKINE RECEPTOR CX3CR1

TATIANA CHIRKOVA 1, Christopher Anderson 2, Binh Ha 1, Bassam Rimawi 1, Antonius Oomens 3, Thomas Mariani 2, Larry Anderson 1

1 Emory University 2 University of Rochester 3 Oklahoma State University

Background
Respiratory syncytial virus (RSV) constitutes a significant burden for infant and young children’s health. Severe pneumonia and bronchiolitis induced by RSV result in high hospitalization rates and mortality each year in children <5 years of age. RSV is also
associated with the development of asthma later in life. Despite much research, no vaccine or highly effective anti-viral drug is yet available. The two RSV surface proteins, F and G, are key to the biology of infection and induction of protective immune responses. Both proteins bind to the cell surface through heparin binding domains, G protein also has a CX3C motif and can bind to the fractalkine receptor CX3CR1. CX3CR1 is expressed in various cell types, including immune cells and primary human airway epithelial cells. Studying the role of the G-CX3CR1 interaction in infection and host response in HAEC and immune cells is important to understanding human RSV disease pathogenesis.

Methods
Cellular responses to RSV G-CX3CR1 interaction were evaluated in human primary airway epithelial cells (HAEC) and monocyte derived dendritic cells (moDC). HAEC were infected with RSV strains containing wild-type G (Gwt) or mutated G that does not bind to CX3CR1 (Gmut). Cytokine/chemokine responses in infected HAEC were determined using Luminex and qPCR assays. moDC from PBMC and CBMC specimens were stimulated with virus-like particles (VLP) containing Gwt or Gmut. moDC responses were evaluated by flow cytometry measuring the expression of surface activation markers (HLA-DR, CD40L, Jagged-1, CD86) and intracellular cytokines (IL-12, IFN-a). and assessing moDC-induced T cell activation after co-culture with allogenic CD4 naive T cells.

Results
RSV G-CX3CR1 interaction induced differential expression of cytokines in RSV-infected HAEC. Particularly, HAEC infected with Gwt-RSV had significantly lower IFN-a production compared to Gmut strains suggesting that RSV-CX3CR1 interaction alters the efficiency of anti-viral responses. In human moDC G-CX3CR1 interaction skewed innate immune cell responses towards Th2-directing phenotype. Human moDCs stimulated with Gwt-VLP showed higher expression of OX40L and Jagged-1 compared to Gmut-VLP stimulated samples. The following co-culture of VLP-stimulated moDC with allogenic naive CD4 T cells confirmed these observations. T cells exposed to Gwt-VLP stimulated moDC developed less Th1- and more Th2 functional phenotype presented by decreased levels of IFN-γ and increased production of IL-13.

Conclusions
RSV G protein interaction with CX3CR1 adversely affects protective anti-viral host responses in human primary airway epithelial and induces aberrant innate immune responses.

ULTRASTRUCTURAL STUDIES OF RSV ASSEMBLY BY CELLULAR CRYO-ELECTRON MICROSCOPY

JIE (JAE) YANG 1, Zunlong Ke 2,3, Rebecca Dillard 2, Tatiana Chirkova 2, Christopher Stobart 2, Cheri Hampton 2, Joshua Strauss 2, Martin Moore 2, Larry Anderson 2, Elizabeth Wright 2,4

1 Department of Biochemistry, University of Wisconsin-Madison 2 Division of Pediatric Infectious Diseases, Emory University School of Medicine, Children’s Healthcare of Atlanta, Atlanta 3 School of Biological Sciences, Georgia Institute of Technology, Atlanta 4 Robert P. Apkarian Integrated Electron Microscopy Core, Emory University, Atlanta

Background
RSV is an enveloped RNA virus that may display both filamentous and spherical morphologies. Virus assembly, budding, and release are critical steps for RSV egress. The surface glycoproteins, in particular F, are important for coordinating with the matrix protein M to drive the formation and elongation of mature RSV particles. Despite great advances in the understanding of the RSV budding process, many of the steps and associated macromolecular structures remain unclear. Using combinatorial structural and functional approaches, we defined some of these structures and proposed a model that defines several stages of RSV assembly.

Methods
We used cryo-electron microscopy (cryo-EM), cryo-electron tomography (cryo-ET), and conventional transmission electron microscopy to examine the structures of several RSV strains propagated in non-polarized cell lines and polarized airway epithelial cells. Functional assays including flow cytometry, viral titers, RNA quantification of RSV-infected cells were conducted. Whole-cell cryo-ET of RSV-infected cells combined with sub-volume averaging was used to determine the structures of complexes associated with the major stages of viral assembly. To preserve the integrity of macromolecular and cellular architecture, native-immunolabeling approaches of cryo-preserved RSV and infected cells was developed. This provided greater clarity into the three-dimensional structures and localization of RSV macromolecules at virus assembly sites.
Results
We reported that RSV is filamentous when newly released from both transformed non-polarized cell lines and polarized airway epithelial cells. RSV structure is independent of virus strain and cell type. Imaged RSV particles were infectious. The conclusion is further supported by the result that the majority of RSV F is in pre-fusion conformation at sites of assembly and on filamentous virus particles, while F is in the post-fusion state on spherical particles. Furthermore, the structural analysis resolved interactions retained between F and M. This approach captured the range of steps associated with RSV assembly at high, macromolecular-level resolution.

Conclusions
Here, we proposed an RSV assembly model where RSV assembly starts with the accumulation of viral proteins and genomic RNAs at the plasma membrane. During the active assembly state, coordinated viral and host cell components drive the protrusion and elongation of RSV filaments from the membrane. The narrowing of the cell proximal end of the RSV filaments signals the scission and subsequent release of RSV particles. This study is important because it provides direct structural evidence of processes associated with RSV assembly and budding.

SESSION 3 IMMUNE RESPONSE TO RSV

O9 ATTENUATION OF HUMAN AIRWAY EPITHELIAL CELL INNATE IMMUNE RESPONSES TO RESPIRATORY SYNCYTIAL VIRUS (RSV) IN NEWBORN INFANTS COMPARED TO OLDER INFANTS.

HELEN GROVES 1, Lindsay Broadbent 1, Hong Guo-Parke 1, Mike Shields 1, Ultan Power 1

1 Centre for Experimental Medicine, School of Medicine, Dentistry and Biomedical Sciences, Queen’s University Belfast, Northern Ireland

Background
RSV is a major respiratory pathogen in infants. Newborn infants, born at term or prematurely, are at greater risk of severe RSV-related disease compared to older infants. Reasons for this increased risk are poorly understood. RSV infection targets airway epithelial cells (AECs) and subsequent AEC innate immune responses represent an important first line of defence. Attenuated newborn RSV-induced type 1 interferon responses have been described in blood mononuclear cells. However, age-related changes in AEC immune responses to RSV infection have not been studied.

Methods
We generated three-dimensional well differentiated cultures of nasal AECs (designated WD-PNECs) from term and preterm infants at birth and from the same infants at one-year old. We exploited these cultures to determine RSV growth kinetics, cytopathology and innate immune response kinetics in the respective cohorts.

Results
We describe the first report of successful generation of WD-PNEC cultures derived from term and preterm newborn infants. Newborn term and preterm WD-PNECs displayed similar ciliated and goblet cell proportions. There was a trend towards increased RSV titres released from newborn term versus preterm WD-PNECs following infection. We observed significantly higher proportions of goblet cells in newborn-derived WD-PNECs compared to WD-PNECs derived from repeat samples at one-year old. RSV growth kinetics were similar in newborn and one-year cohorts. Importantly, RSV-induced secretion of interferon lambda-1, a key RSV-induced type 3 interferon in AECs, was significantly increased in one-year-derived WD-PNECs compared to newborn-derived WD-PNECs (p=0.0034). Furthermore, significantly higher secretion of chemokines IP-10 (CXCL-10) (p<0.05) and RANTES (CCL-5) (p<0.05) were detected following RSV infection of WD-PNECs derived from one-year-old infants compared to newborn infants.

Conclusions
This is the first description of age-related distinctions in AEC innate immune responses. These exciting results suggest AECs from older infants express greater levels of type III interferons and pro-inflammatory chemokines compared to AECs from newborn infants. These findings imply innate immune responses of AECs are less robust in early life, which may contribute to the increased susceptibility of very young infants to severe RSV disease.
O10
UNRAVELING THE RESPIRATORY Syncytial VIRUS (RSV) ANTIBODY FUNCTIONAL REPERTOIRE IN ADULT HEALTHY DONORS

EMANUELE ANDREANO 1,2, Ida Paciello 2, Monia Bardelli 2, Simona Tavarini 2, Chiara Sammicheli 2, Elisabetta Frigimelica 2, Silvia Guidotti 2, Giulia Torricelli 2, Ugo D’Oro 2, Rino Rappuoli 2, Oretta Finco 2, Francesca Buricchi 2

1 University of Siena, Department of Life Sciences, Italy 2 GSK, Siena, Italy

Background
Human RSV is a pneumovirus against which no vaccine is currently available and passive immunization is the only preventive strategy in high risk populations. RSV is responsible for over 33 million cases of acute low respiratory tract infection leading to up to 199.000 deaths annually. Among the 11 proteins encoded by this virus, the fusion protein in its prefusion state (preF) is considered the most immunogenic antigen, capable of eliciting highly neutralizing antibodies (nAbs). While infants and older adults are the populations at highest risk of acute RSV infection, healthy adults present the strongest and most mature immune system capable of naturally resolving infection by this pathogen. Therefore, deep characterization of preF antibody functional repertoire in adult healthy donors is a must do to better understand the effective natural response against this main viral antigen.

Methods
In order to unravel the preF-induced antibody functional repertoire, the methodology named by Rappuoli and coworkers as reverse vaccinology 2.0 was applied. This allowed to single cell sort over 1200 IgG+ preF-binder memory B cells isolated from four adult healthy donors. Following isolation, cell supernatants were tested by ELISA, to check the presence of IgG; by Gyrolab, to assess their binding specificity against the F-protein; and by plaque reduction neutralization assay (PRNA), to test their neutralization activity in vitro. In addition, the heavy and light chain sequences of retrieved nAbs were analysed in order to gain insight on the antibody preF-specific functional repertoire. Finally, most interesting nAbs will be expressed for structural analysis (Fig. 1).

Results
This workflow allowed us to retrieve over 200 naturally produced nAbs and to identify the predominant RSV F-protein specific gene rearrangement (IGHV1-18;IGHJ4-1 and IGKV2-30) which was shared by almost 15% of nAbs. This rearrangement is associated to a high binding capability towards the preF and recognition of a specific epitope region. Furthermore, up to 20 nAbs identified were selected and expressed as full length IgG for in-depth functional characterization and will be also expressed as Fab for structural analysis of predominant rearrangement derived-nAbs.

Conclusions
This approach meticulously defines the RSV preF functional repertoire elicited by natural infection and could help driving the design of novel vaccine antigens against this pathogen.

O11
RSV INFECTION IN EARLY LIFE IS ASSOCIATED WITH DEFECTIVE TISSUE RESIDENT MEMORY T CELL DIFFERENTIATION

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Background
Respiratory syncytial virus (RSV) disproportionately affects young infants, yet despite the high frequency of infection in early life, repeated infections occur throughout adulthood. These observations suggest that priming, when it occurs in early life, may recruit cells with lesser ability to respond to infection and differentiate into effective memory cells. Differentiation of RSV-specific tissue-resident memory T cells has been demonstrated in both human and murine adult models; however, whether a comparable population develops in the neonatal lung has not been shown.
Methods
Using a murine CB6F1/J hybrid model of RSV infection, we infected neonatal and adult mice and analyzed the phenotype of RSV-specific CD8 T cells 7 days post infection (primary response), 11 and 15 days after infection (during the acquisition of memory), and 6 weeks after infection (once memory is established).

Results
We found that 7 days post infection, adult mice had an abundant percentage and number of RSV-specific CD8 T cells in the lung tissue and airway. By comparison, in neonates, the majority of RSV-specific T cells were found within the blood and lung tissue and were notably absent from the infected airway. These striking differences indicate a neonatal deficiency in the migration of RSV-specific CD8 T cells to the site of viral infection. Adult CD8 T cells expressed high levels of CD69, a membrane molecule essential for the retention of CD8 T cells in the tissue, while neonatal T cells lacked this expression. At 11, 15 and 40 days after the primary infection, an increasing proportion of adult RSV-specific CD69+ CD8 T cells also acquired the integrin, CD103, differentiating into tissue-resident memory CD8 T cells, while neonatal T cells were unable to achieve this differentiation.

Conclusions
In conclusion, we have found that following infection, RSV-specific neonatal CD8 T cells failed to upregulate significant expression of CD69 and did not mobilize to the infected mucosal surface. These findings were associated with reduced RSV-specific tissue resident memory T cells compared to adults. Age-dependent alterations in priming and differentiation of RSV-specific CD8 T cells during early life may contribute to disease severity and repeated infections throughout life.

O12
IDENTIFICATION OF NOVEL FACTORS ASSOCIATED WITH SEVERE RSV DISEASE IN INFANTS.

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Background
Almost all infants are infected with RSV by 2 years. One to 3% of RSV-infected infants are hospitalised with severe disease. Clinical features that predispose to severe disease include prematurity, bronchopulmonary dysplasia, and congenital heart disease. However, the majority of hospitalised infants do not have underlying conditions and the reasons for susceptibility to severe disease remain obscure. The aim of this study was, therefore, to identify a protein(s) that might explain such susceptibility, at least in part.

Methods
We generated well differentiated primary nasal epithelial cell (WD-PNEC) cultures from infants with histories of severe (n=14) or mild (n=19) RSV disease, in an ethically-approved study. The WD-PNECs were infected with RSV BT2a (low passage clinical isolate) and monitored for virus growth kinetics, cytopathogenesis, chemokine (e.g., IP-10/CXCL10, TRAIL, RANTES/CCL5) and interferon lambda responses. Differential gene expression was determined by microarray and confirmed by RT-qPCR. In an exciting development, 1 differentially expressed gene, ptn, encodes pleiotrophin (PTN), which interacts with nucleolin (NCL), a co-factor for RSV entry. The antiviral capacity of PTN against RSV was determined in BEAS-2B and WB-PBECs using recombinant PTN, anti-PTN antibodies, and ptn-specific siRNAs.

Results
There were no significant differences between the WD-PBECs derived from the severe and mild cohorts in terms of viral growth kinetics, cell tropism and selected chemokine responses, including IP-10/CXCL10, TRAIL and RANTES/CCL5. However, diminished apical cell sloughing was evident in severe WD-PBECs following infection, along with significantly lower IFNA1 secretion. Interestingly, when differential gene expression was evident, expression of the identified genes, including isg15 and ifi6, was generally lower in severe WD-PBECs. Of considerable interest, diminished endogenous ptn expression was evident in severe WD-PNECs, irrespective of RSV infection. Importantly, pre-treatment with PTN blocked RSV infection in both BEAS-2B cells and WD-
PBECs, while neutralisation of PTN with either antibodies or siRNAs resulted in increased RSV replication. Therefore, PTN is a novel anti-RSV factor secreted from airway epithelium.

**Conclusions**

RSV replication kinetics are unlikely to explain disease severity. Counter-intuitively, diminished apical cell sloughing and expression/secretion of IFNλ1 and specific interferon stimulated genes following infection were associated with severity. Importantly, PTN was identified as a novel RSV antiviral protein that is endogenously expressed in human airway epithelium. Its lower expression in WD-PNECs from severe individuals may explain, in part, increased susceptibility to severe disease.

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**SESSION 4  NOVEL RSV MONOCLONAL ANTIBODIES**

**O13 DISCOVERY AND IN VITRO CHARACTERIZATION OF A POTENT BROADLY NEUTRALIZING ANTIBODY ISOLATED FROM HUMAN MEMORY B-CELLS**

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**Background**

Respiratory syncytial virus (RSV) infection is a major public health burden for infants and the elderly worldwide. Currently there are no approved vaccines and only one marketed antibody (Palivizumab, Synagis ®) for the prevention of RSV infection in high risk infants with moderate efficacy. Sampling human antibody repertoire have led to the realization that Fusion (F) protein in its pre-fusion conformation is the preferred target for potent neutralizing antibodies and thus makes the protein an attractive candidate for vaccine development.

**Methods**

Here we report the isolation of a potent and broad RSV neutralizing monoclonal antibody (mAb), which was discovered through molecular cloning of cultured RSV post-fusion Fusion (F) protein-baited single-sorted human memory B cells. In this report, the mAb was characterized for binding affinity and in vitro neutralization potency.

**Results**

The study revealed the antibody has picomolar affinity for both pre and post-fusion F as assessed by surface plasmon resonance, and is able to neutralize both RSV strain A Long and RSV strain B Washington with IC50 values of 4.4 ng/ml and 6.0 ng/ml respectively. The antibody binding site (IV) was analyzed for RSV clinical isolate sequence diversity. Sequence alignment showed that the mAb binding site was conserved in 1,264 clinical isolates (RSV A and B). We further tested the in vitro potency of the antibody against a panel of 46 clinical isolates from both RSV A and B subtypes. The panel was comprised of diverse F sequences isolated from different geographical locations and different years. The antibody was able to potently neutralize all 46 clinical isolates tested with equal potency against A and B subtypes.

**Conclusions**

Overall, the fully human mAb we have isolated binds to the conserved site IV and is broadly neutralizing with equal potency on RSV A and B viruses.
A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL EVALUATING THE EFFICACY AND SAFETY OF SUPTAVUMAB, FOR THE PREVENTION OF MEDICALLY ATTENDED RSV INFECTION IN PRETERM INFANTS

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Background
Regeneron developed a monoclonal antibody (suptavumab) against the F protein of RSV with a 10-30 fold higher neutralization activity than palivizumab designed to be administered once or twice during an RSV season.

After demonstrating efficacy against RSV A and RSV B subtypes in vitro and in vivo studies in mice and cotton rats; safety in healthy adults; and a scaled PK model in infants based on concentration-time data of suptavumab in healthy adults, a pivotal Phase 3 trial was conducted in preterm infants

Methods
A double-blind, randomized, placebo-controlled global trial of 30 mg/kg of suptavumab administered intramuscularly to preterm infants born at 29 through 36 weeks gestational age and not eligible to receive palivizumab, was conducted between 20 Nov 2015 and 26 Sep 2017 to assess its efficacy in preventing medically-attended RSV infections, defined as either RSV-confirmed hospitalizations or outpatient lower respiratory tract illness (LRTI). Subjects were randomized 1:1:1 to either one (1) or two (2) doses suptavumab, 8 weeks apart, or placebo.

Results
1154 preterm infants were randomized, 5 did not receive study drug, and 1149 (383 placebo group, 385 suptavumab 1-dose group and 381 suptavumab 2-dose group) were included in the analysis. Demographic and baseline characteristics were similar across groups. There were no significant differences in the primary outcome of RSV hospitalization or outpatient LRTI (8.1% placebo group, 9.3% 2-dose suptavumab group and 7.7% in the 1-dose suptavumab group) or in the secondary outcome of RSV hospitalization or outpatient upper or lower respiratory tract infections. Analysis by RSV subtype revealed 62.10% (95% CI - 4.981, 86.320) reduction in RSV A hospitalization or outpatient LRTI in the suptavumab 1-dose group and a similar 61.42% (-6.618, 86.038) reduction in the suptavumab 2 dose group, compared to placebo. However, for RSV B, compared to placebo, hospitalization or outpatient LRTI was -36.37% (-155.628, 27.250) for the 1-dose suptavumab group, versus -68.79% (-208.248, 7.579) for the 2-dose suptavumab group. Treatment-emergent adverse events (TEAE) reported in > 5% of subjects, conditions commonly observed in infants, were similar across groups. All predicted concentrations of suptavumab, in both 1-dose and 2-dose groups, were above EC 99 threshold for both RSV A and RSV B, at the time of first infection.

Conclusions
Suptavumab, administered as either one or two doses 8 weeks apart, was well tolerated, but did not reduce RSV hospitalizations or outpatient LRTI. A differential effect on RSV A and RSV B outcomes was observed.
THERAPEUTIC POTENTIAL OF ALX-0171 IN RSV-INFECTED PAEDIATRIC BRONCHIAL EPITHELIUM.

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Background
RSV causes severe lower respiratory tract infections in young infants worldwide. However, there are no effective RSV-specific treatments available. Ablynx nv is developing an anti-RSV nanobody, ALX-0171, that targets the RSV F site II epitope. It has potent in vitro neutralising activity against many RSV isolates (Detalle et al, Antimicrob Agents Chemother. 60:6-13, 2015), and is targeted for therapeutic use in infants. We previously reported a RSV infection model in well-differentiated primary paediatric bronchial epithelial cell (WD-PBEC) cultures that replicated hallmarks of RSV infection in infants, including virus replication, cell sloughing and chemokine responses (Villenave et al, PNAS 109:5040-45, 2012). Importantly, WD-PBECs remain intact for days post-infection (dpi), thereby facilitating use of our RSV/WD-PBEC model to study therapeutic interventions.

Methods
ALX-0171 therapeutic potential was studied in WD-PBECs (n=3 donors) infected with RSV BT2a (MOI~0.1), or mock infected. RSV-infected cultures were treated with High (1000 nM), Mid (100 nM) or Low (10 nM) ALX-0171 or palivizumab concentrations, or buffer. Virus growth kinetics, cytopathogenesis and chemokine secretions were measured. Virus growth kinetics and efficacy of ALX-0171 was also compared for two RSV clinical isolates: BT2a and Memphis 37.

Results
High and Mid ALX-0171 completely neutralised apically-released RSV following treatment initiation as late as 4 days post-infection (dpi). In contrast, Low ALX-0171 antiviral activity was limited. By comparison, only High dose palivizumab efficiently neutralised RSV. When measured by RT-qPCR, there was a trend towards reduced mean viral loads following High ALX-0171 or palivizumab treatment at 1 dpi, compared to buffer-treated cultures. ALX-0171 treatment resulted in a reduction in RSV+ ciliated cells in a dose-dependent manner.

The IC50 for ALX-0171 at 24 hpi was 346.9 nM and 363.6 nM for BT2a and Memphis 37, respectively, while for palivizumab, IC50 was 1048 nM and 1090 nM for BT2a and Memphis 37, respectively.

Conclusions
ALX-0171 demonstrated a strong, dose-dependent, capacity to neutralise RSV released from paediatric WD-PBECs, even when treatment was initiated at 4 dpi, a time when clinical symptoms are often well developed in infants. This strong neutralising capacity was evident for 2 clinical isolates of RSV, BT2a and Memphis 37, and was invariably superior to palivizumab under these experimental conditions. However, both ALX-0171 and palivizumab had limited effects on RSV replication in WD-PBECs, as measured by RT-qPCR. This study validates our RSV/WD-PBEC model for the pre-clinical evaluation of RSV antivirals.

SESSION 5  ADVANCEMENTS IN RSV VACCINES

WHO 1ST INTERNATIONAL STANDARD FOR ANTISERUM TO RSV

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Background
Respiratory Syncytial Virus (RSV), a leading cause of lower respiratory tract illness resulting in significant morbidity and mortality among infants, elderly, and immunocompromised individuals, has been a focus of vaccine development efforts in recent years. RSV neutralisation assays are useful for providing evidence of antibody function in the evaluation of immunogenicity of RSV vaccine candidates. Here we report a collaborative study (CS) that was conducted with the aim to establish the 1st International
Standard (IS) for antiserum to RSV, to enable the harmonisation of RSV neutralisation assay results across diverse assay formats.

Results
The results showed that inter-laboratory variability in neutralisation titres was reduced when values were expressed relative to those of either of the two candidate IS. Sera from both maternal and elderly clinical trials were included and both candidate IS were considered commutable for these sample types as well as for paediatric sera samples. Further studies will be needed to determine the usefulness of this standard against RSV B viruses, while different standards will be required for animal samples and monoclonal antibodies. Stability testing results for 16/284 and 16/322 showed them to be stable when stored at -20°C.

Conclusions
The WHO Expert Committee on Biological Standardisation reviewed the CS results and established 16/284 as the 1st International Standard for antiserum to RSV for harmonisation of RSV neutralisation assay output, with an assigned unitage of 1000 International Units (IU) of anti-RSV neutralising antibodies per vial. The IS 16/284 is available on NIBSC’s catalogue.

O17 INTRANASAL RSV F BOUND TO LACTOCOCCAL PARTICLES INDUCES DURABLE SYSTEMIC IMMUNE RESPONSES IN HUMAN VOLUNTEERS

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Background
Naturally acquired immunity to RSV infection is only partially and transiently protective against re-infection. SynGEM is a novel intranasal vaccine comprising RSV F protein coupled to immunostimulatory bacterium-like particles (BLPs) from Lactococcus lactis. Since it induces high levels of systemic and mucosal antibodies in cotton rats, we tested whether intranasal SynGEM could boost mucosal immunity and systemic virus-specific B and T cells in adult human volunteers.

Methods
As part of a first-in-human randomised controlled trial of SynGEM, 48 adult volunteers received either placebo or SynGEM at a low or high dose via intranasal spray at day 0 and day 28. Antigen-specific T cell and B cell responses were quantified by FluoroSpot and flow cytometry, contrasting with responses during the course of experimental infection with live RSV. Healthy adenotonsillar cells were cultured with SynGEM antigens; F-specific IgG, IgA and IgM, T cell associated cytokines and proliferative responses were measured.

Results
SynGEM induced F-specific mucosal IgA in most individuals, particularly in those with lower pre-existing IgA titres. Virus-specific nasal IgA responses were more heterogeneous than systemic IgG, with respect to both magnitude and timing of response following vaccination. Polyfunctional CD4+ T cells recognising conserved epitopes within the RSV F protein were detected in SynGEM vaccinees, along with post-F specific IgA+ B cells. Systemic IgG+ and IgA+ plasmablasts increased significantly following vaccination, but only IgG+ memory B cells (MBCs) increased significantly. In vitro culture of adenotonsillar cells showed dose-dependent IgG, IgA and IgM production and proliferation of both CD4+ and CD8+ T cells in response to SynGEM. Type 1 and T follicular helper cell-associated cytokine production was also observed in response to culture with the vaccine antigens.

Conclusions
SynGEM induces dose-dependent antibody responses associated with appropriate T-helper cytokine production and is the first non-replicating intranasal RSV subunit vaccine to induce persistent human antibody responses. The BLP platform represents a promising strategy for needle-free mucosal vaccination against RSV infection.  Attachment
O18
MAGNITUDE AND DURABILITY OF ANTI-F IgG AND PALIVIZUMAB-COMPETITIVE ANTIBODY (PCA) RESPONSES ONE YEAR FOLLOWING IMMUNIZATION WITH RSV F NANOPARTICLE VACCINE ADJUVANTED WITH ALUMINUM PHOSPHATE, OR A NOVEL ADJUVANT

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Background
Following the recent Phase 3 efficacy trial of a one-dose unadjuvanted RSV F vaccine in older adults which failed to meet its primary objectives, we undertook clinical evaluation of multiple adjuvanted formulations/regimens of RSV F nanoparticle vaccine in the same population to enhance the magnitude and durability of vaccine-specific antibody responses.

Methods
Formulation/regimen arms included (in 25 subjects/arm): placebo, one-dose 135µg RSV F unadjuvanted (as reference), one or two doses of 95µg or 120µg RSV F with 0.3mg or 0.4mg aluminum (Al) as phosphate salt, and one or two doses of 35µg, 65µg or 135µg RSV F with 50µg of Matrix-M1 adjuvant. Multiple vaccine-induced antibody specificities were evaluated: anti-F IgG, palivizumab-competitive antibodies (PCA), RSV neutralizing antibodies by two methods (CPE and ELISA based), and antibodies competitive with monoclonal antibodies against known pre- and post-fusion broadly neutralizing epitopes (BnE). Long-term anti-F IgG and PCA data were available at Day 385 following immunization. Cellular immunity was also measured. Safety assessments included solicited, unsolicited, medically-attended, and serious adverse events.

Results
All regimens were clinically tolerable with modestly higher transient reactogenicity in Matrix-M1-containing arms. Four formulations/regimens induced the best post-vaccination peak antibody responses: one and two-dose regimens of 120µg RSV F with 0.4mg Al, and one and two-dose regimens of 135µg RSV F with 50µg Matrix-M1. Among these, the two-dose Matrix-M1-adjuvanted regimen induced superior peak and long-term immunogenicity as compared to all other regimens, including: significantly higher polyfunctional CD4+ T cell responses, > 12-fold and 8-fold peak increases over baseline in anti-F IgG and PCA, and ~100% and 70% peak increases over the unadjuvanted formulation in anti-F IgG and PCA, respectively; 68% and 72% higher anti-F and PCA, respectively, as compared to the reference unadjuvanted formulation at Day 385, and >2.5–3.4 fold increases over baseline by CPE and ELISA-based MN methods, respectively. Antibodies competitive with monoclonal antibodies against known pre- and post-fusion epitopes were also induced and enhanced by adjuvants.

Conclusions
Administration of a two-dose regimen adjuvanted with Matri-M1, significantly improved peak and long-term antibody responses to RSV F vaccine, while demonstrating an acceptable safety profile.

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SESSION 6  RSV PROTEIN STRUCTURE AND FUNCTION

O19

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Background
In support of the clinical development of MEDI8897, a potent anti-RSV F mAb with an extended half-life for prevention of RSV disease in all infants, we are conducting multi-year global RSV surveillance programs. The [Observational US Targeted Study of Monoclonal Antibody Resistance and Testing of RSV (OUTSMART-RSV)] is the first prospectively designed, systematic RSV molecular epidemiology study covering patients of all age groups across the US census regions as well as Puerto Rico.
Methods

More than 2000 RSV positive respiratory samples have been analyzed by Sanger sequencing (1st season, 2015-16) and high throughput next generation sequencing methods (2nd and 3rd seasons, 2016-17, 2017-18). The RSV F (MEDI8897 target) and the second hypervariable region of G (for subtyping) genes were sequenced directly from clinical specimens to understand RSV molecular epidemiology, viral evolution and the impact of F protein sequence variations on the susceptibility of different RSV isolates to MEDI8897 neutralization.

Results

RSV A and RSV B co-circulated in these three seasons with RSV A dominance in 2015-16 (59%) that shifted to RSV B dominance in 2016-17 (54%) and 2017-18 (~70%). Most RSV A and RSV B isolates clustered into the ON1 and BA9 genotypes, respectively. The second hypervariable region of the RSV G protein had sequence diversity in the duplicated regions for both RSV A and B strains. RSV B G proteins had an additional 7 amino acid C-terminal extensions in ~22% of the isolates from 2016-17 and ~13% from 2017-18. The C-terminal of G proteins from 2015-16 were not analyzed due to incomplete sequences. The F protein from the first two seasons showed a few distinct amino acid substitutions (natural polymorphism) in different antigenic regions. Substitutions of L172Q/S173L in antigenic site V in RSV B were present at a frequency of 89% in the first season and continued to be dominant in the second (99%) and the third season. Substitutions of I206M/Q209R in site Ф emerged in the second season with a frequency of ~19% and continued to persist into the third season. Several other polymorphisms in the MEDI8897 binding site (AA62-69, 196-212) were identified at residues 65, 68 and 206 for RSV A F and residues 66, 209, and 210 for RSV B F at a very low frequency (0.2-2.1%). All the MEDI8897-binding site variants identified were susceptible to MEDI8897 neutralization in vitro. The polymorphisms in the F protein antigenic sites and other sequence variations in the F protein from the third RSV season are currently being evaluated and will be presented.

Conclusions

This study, as a part of our ongoing global surveillance study towards understanding RSV epidemiology and viral evolution, provides strong support for clinical development RSV antivirals and vaccines.

O20 CHARACTERIZATION OF ANTIGENIC SITE-SPECIFIC COMPETITIVE ANTIBODY RESPONSES TO THE FUSION PROTEIN IN RSV INFECTED HEMATOPOIETIC CELL TRANSPLANT ADULTS

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Background

Recent studies of human sera showed that the majority of the respiratory syncytial virus (RSV) neutralizing antibodies are directed against prefusion F of RSV and revealed the importance of prefusion antigenic site Ø specific antibodies. However, detailed analysis of multiple antigenic site-specific competitive antibody responses to RSV fusion protein and their contribution to virus clearance in humans have been lacking so far.

Methods

We prospectively enrolled a cohort of RSV infected adult hematopoietic transplant (HCT) recipients (n=40). Serum samples (n=80) were collected at enrollment (acute) and 14 to 60 days post-enrollment (convalescent). Antigenic site-specific F protein antibodies were measured against pre-fusion site Ø, post-fusion site I, and antigenic sites II and IV present in both the pre-fusion and post-fusion F protein conformations utilizing four different competitive antibody assays developed with biotinylated monoclonal antibodies (mAb) D2S, 131-2A, palivizumab, and 101F, respectively. The lower limit of detection were 30 μg/mL, 0.5 μg/mL, 1 μg/mL, and 0.5 μg/mL for the competitive antibody assays that measured sites Ø, I, II and IV antigenic site-specific responses, respectively. Neutralizing antibody (Nt Ab) titers to RSV/A and B subgroups was determined by microneutralization assays.

Results

The overall findings in HCT RSV infected adults revealed: 1) significantly increased concentration in antigenic site-specific competitive antibodies in convalescent sera (all p<0.01); 2) comparable concentrations in the convalescent serum samples of
antigenic site-specific competitive antibodies between RSV/A and RSV/B infected HCT adults (all p>0.05); 3) significantly increased concentrations of competitive antibodies targeting sites II, IV, and I in HCT adults who shed RSV <14 days compared to HCT infected adults who shed RSV >14 days (all p<0.01); and 4) statistically significant correlation between the concentration of the antigenic site-specific competitive antibodies and neutralizing antibody titers against RSV/A and RSV/B (r ranged from 0.35 - 0.83 for acute sera, and 0.53 - 0.88 for convalescent sera; all correlations with p<0.05).

Conclusions
In HCT adults infected with RSV, antigenic site-specific antibody responses occurred in sites found in both the prefusion and postfusion F conformations, and were associated with viral clearance and neutralizing antibody titers.

O21
NEW INSIGHTS INTO RSV ENTRY: ATPASE SODIUM/POTASSIUM-TRANSPORTING SUBUNIT ALPHA-1 (ATP1A1) IS IMPORTANT FOR MACROPINOCYTIC ENTRY OF RSV.

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Background
The involvement of cellular proteins in respiratory syncytial virus (RSV) infection is not well understood, including the process of viral entry.

Methods
We performed a genome-wide siRNA screen in which the expression of ~21,600 genes was individually knocked down in human airway epithelial A549 cells (3 siRNAs per gene, evaluated separately), followed by infection with RSV expressing GFP. Reduction in GFP expression was putative identification of a host protein important for efficient RSV infection. Off-target effects were minimized by seed sequence analysis. Target genes identified by the high throughput screen were validated manually (3 different siRNAs per gene, evaluated separately). Knock-down of cellular ATP1A1 resulted in one of the greatest reductions in GFP expression. We examined the role of ATP1A1 during RSV entry and infection, including validation in primary human airway epithelial cells.

Results
Knock-down of ATP1A1 expression caused significant reductions in viral GFP expression and the production of infectious RSV (Fig. A and B) with minimal effect on cell viability. A reduction was not observed with vesicular stomatitis virus (VSV) expressing GFP (Fig. A), indicating the effect was RSV-specific. A number of different approaches failed to detect binding of RSV surface proteins to ATP1A1, suggesting the lack of a direct role in viral attachment. In the absence of ATP1A1 knock-down, confocal microscopy of RSV-infected A549 cells detected a clustering of ATP1A1 and RSV proteins very early in RSV infection that was independent of virus replication and thus involved RSV proteins in the input inoculum (Fig. C). Numerous lines of evidence indicated that the attachment of RSV to the host cell induced ATP1A1 signaling leading to the activation of cellular Src non-receptor tyrosine kinase and epidermal growth factor receptor (EGFR). This further led to the formation of macropinosomes containing RSV and ATP1A1, thus resulting in RSV entry. ATP1A1-mediated viral uptake could be inhibited by ATP1A1-specific chemical compounds, which might serve as a foundation for antiviral drug development.

Conclusions
ATP1A1 is an important factor for RSV entry that acts by mediating intracellular signaling leading to macropinocytic uptake of RSV.
THE APICAL LOOP OF THE RESPIRATORY SYNCYTIAL VIRUS FUSION PROTEIN F2 SUBUNIT IS CRITICAL FOR FUSION ACTIVITY

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Background
The respiratory syncytial virus (RSV) fusion (F) protein is a trimeric, membrane-anchored glycoprotein capable of mediating both viral to target-cell membrane fusion to initiate infection and cell to cell fusion, even in the absence of the attachment (G) glycoprotein. The F protein is initially expressed in a precursor form, whose functional capabilities are activated by proteolysis at two sites between the F1 and F2 subunits. This cleavage results in an F protein with a metastable, high-energy prefusion (pre-F) conformation.

Methods
To mediate fusion, the pre-F protein is triggered by an unknown stimulus, causing much of the F1 subunit to refold dramatically while F2 changes minimally. We hypothesized that contact with a molecule on the target cell membrane triggers this conformational change, and the most likely site for interaction with a target-cell component would be at the apex of the protein. We determined the importance of the residues in the apical loop of F2 by alanine scanning mutagenesis of 14 amino acids in this F2 loop. Each mutant was expressed in HEK 293A cells and its presence on the cell surface, in the pre-F form, and as a trimer, all determined by monoclonal antibody binding. A luciferase fusion assay was used to quantify the ability of each mutant to cause cell-cell fusion. We also developed a method to force pre-F to trigger by lowering the ionic strength of the medium and used it to determine if mutations prevent pre-F protein triggering or refolding.

Results
Alanine replacement of each of the four lysines and one isoleucine in the apical F2 loop completely disrupted the fusion function demonstrating that they are essential, two are of intermediate importance, and five are not important. Alanine replacement did not result in the loss of the pre-F trimer conformation for any of these mutants. Each of the four lysines required its specific charge for fusion.

Conclusions
Alanine replacement of three essential lysines on the ascent to the apex prevented fusion even after low ionic strength forced fusion, suggesting they are involved in refolding but not triggering. However, an alanine replacing Ile64, also on the ascent to the apex, or Lys75 at the apex, prevented fusion, but was reversible with low ionic strength forced triggering, suggesting they are involved in the natural triggering of the F protein, not its refolding. The essential residues identified in the apical domain of F2 are adjacent to the apical loop of F1 which, upon triggering, refolds into the long heptad repeat A (HRA) with the fusion peptide at its N-terminus. These residues are likely involved in triggering and/or refolding the F protein and as such may be ideal targets for antiviral drug development.
O23
RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION INCREASES NEUTROPHIL TRANS-EPITHELIAL MIGRATION AND ADHERENCE RESULTING IN INCREASED DAMAGE TO CILIATED AIRWAY EPITHELIAL CELLS.

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Background
RSV targets ciliated epithelial cells for infection but results in mild cytopathology in vitro. Severe RSV bronchiolitis is associated with massive neutrophil infiltration into the lungs. The immunological role of these neutrophils remains largely unknown. To determine whether neutrophil migration contributes to epithelial damage during severe RSV infection, we have developed an in vitro neutrophil migration model using differentiated primary cells.

Methods
Primary human nasal AECs were cultured at air liquid interface (ALI) on the underside of a transwell insert (3 µm pore) for 28 days. Cells were infected with GFP RSV (MOI 5) for 72h. Purified venous neutrophils were stained using a fluorescent dye and added to the top (basolateral) chamber of the transwell for up to 24 hours. Migrating neutrophils and ciliated epithelial cells were directly observed using an inverted microscope equipped with a high speed video camera to assess ciliary beat frequency (CBF). Transwells were removed and stained to assess neutrophil attachment. Apical supernatants were collected to measure markers of cell damage.

Results
RSV infection increases the attachment of migrating neutrophils to the apical surface of ciliated airway epithelial cells (Figure 1). This was associated with an increase in AEC damage and decrease in CBF, which was not observed in the mock infected controls (Figure 2).

Conclusions
This study shows for the first time that neutrophils remained attached to AEC following trans-epithelial migration and that this contributes to airway damage in RSV infection. Future work with this model could reveal important mechanisms behind the development of severe RSV bronchiolitis.

O24
GENETIC DETERMINANTS OF SEVERE RESPIRATORY SYNCYTIAL VIRUS INFECTIONS IN INFANTS

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Background
Respiratory syncytial virus (RSV) is the most common cause of lower respiratory tract infections in infants. Disease severity varies widely among children and ranges from mild upper respiratory symptoms to severe bronchiolitis. Severe infections affect approximately 1% of young children, causing 50,000 to 200,000 deaths annually. Genetic factors governing disease severity are incompletely defined. Detailed knowledge of such genetic determinants and their impact on the pathogenesis will facilitate the
development of diagnostic measures for risk assessment, new therapeutic approaches for RSV infections and preventive strategies.

**Methods**

We established a cohort of pediatric patients suffering from severe RSV infection (IRIS cohort). From this cohort, 101 children aged between 0-2 years (mean age 7.2 month, 36 females/65 males) and suffering from severe acute RSV infections confirmed by PCR analysis were subjected to whole exome sequencing (WES). Severe infection was defined by oxygen saturation below 92 % and necessity of hospitalization.

**Results**

Since interferon-regulated immune responses are critical for the defense of RSV infections and the course of the disease, we focused on 5142 genes that either trigger expression of interferons, or contribute to interferon signaling or are controlled by interferons. In total 30,039 variants mapped to these genes. Heterozygosity and homozygosity counts in our cohort as well as in an ethnically matched sub-cohort of the Exome Aggregation Consortium (ExAC) were used to calculate the significance of association of variants with severe RSV infection. Collectively, 218 coding polymorphisms mapping to 84 genes were significantly associated with severe RSV infection. To identify polymorphisms directly influencing RSV infection, associated genes expressed in primary human airway epithelial cells were silenced and the impact on RSV infection was quantified. Moreover, their expression upon RSV infection of air-liquid interface cultures of human airway epithelial cells was quantified with single cell resolution. More than six novel viral restriction or dependency factors were identified including proteins involved in cellular ER-stress response and regulation of ER-associated protein degradation (ERAD), in inflammatory cytokine signaling and a protein kinase activated by double-stranded RNA which mediates the effects of interferon in response to viral infection.

**Conclusions**

This integrated approach combining clinical phenotyping, WES, variant calling/association and functional screening provides a new paradigm for discovery of genetic traits and protein functions affecting the course and outcome of infectious diseases.

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**O25**

MUC5B IS THE PREDOMINANT GEL-FORMING MUCIN OBSTRUCTING THE DISTAL AIRWAYS DURING RSV BRONCHIOLITIS.

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**Background**

RSV infection of the bronchiolar airways of infants results in clogging of the distal airways with cellular debris that causes airflow obstruction and decline of lung function. The obstructive cellular debris is largely composed of sloughed necrotic epithelial cells and neutrophil-rich inflammatory cell infiltrates. Mucus secretions, generally considered important in airway obstructive diseases, are rarely observed in the distal airways of infants with RSV bronchiolitis based on histochemical AB-PAS mucin staining. As the biochemical and biophysical properties of mucus secretions are important in the progression of chronic mucob-oblitive airway diseases, we applied more technically advanced methods to determine whether mucins contribute to distal airway obstruction during RSV bronchiolitis. Appreciating the contribution of mucins to the obstructive cellular debris may guide therapeutic strategies for alleviating distal airway obstruction caused by RSV infection.

**Methods**

To identify whether mucins are present in the lower airways of infants with RSV bronchiolitis, bronchoalveolar lavage was performed on infants intubated for RSV bronchiolitis or for non-pulmonary diseases.

**Results**

Proteomic analysis of airway lavages detected the secreted, gel-forming mucins, MUC5B and MUC5AC in all samples but MUC5B was 10-fold more abundant in infants with RSV bronchiolitis compared to controls. MUC5AC levels were not different between...
the groups. Slot blot assay of MUC5B and MUC5AC protein confirmed the increased concentrations of MUC5B, but not MUC5AC, in RSV-infected infants. MUC5B mRNA, but not MUC5AC mRNA, was increased in bronchial epithelial cell brushings from infants with RSV bronchiolitis but not controls, suggesting increased MUC5B production in RSV-infected infants could be attributed to increased secretion of MUC5B from the surface epithelium of the lower airways.

To test whether the distal bronchiolar airway epithelium can produce MUC5B during virus infection, we utilized a mouse model of severe virus bronchiolitis that recapitulates the distal airway obstruction observed in RSV-infected human infants. Like RSV infection in humans, murine parainfluenza virus robustly infected the bronchiolar airway epithelium of mice and increased the expression and secretion of Muc5b into the distal airway lumen contributing to the obstruction of the distal airways by mucocellular debris.”

Conclusions

We conclude that MUC5B production by the distal airways in response to virus infection contributes to the total mass of obstructive material in the distal airways. Therapeutic strategies aimed at reducing MUC5B in the distal airways during RSV bronchiolitis may be useful in alleviating the severity of distal airway disease during RSV infection.
O27

EFFICACY OF THE NON-FUSION HUMAN RESPIRATORY SYNCTIAL VIRUS (HRSV) REPLICATION INHIBITOR JNJ-64166037 IN HRSV INFECTED LAMB MODEL

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Background

This study was to evaluate the efficacy of non-fusion replication inhibitor (JNJ-64166037), for the therapeutic treatment of human respiratory syncytial virus (hRSV) by experimental trial on hRSV infected lamb model. In contrast to semi-permissive models, RSV replicates to a high extent in this juvenile species and causes a severe lung pathology that is similar to one occurring in human pediatric populations.

Methods

Neonatal lambs (1-3 days of age) were infected with the clinical isolate hRSV Memphis 37 via nebulization. Infected lambs were treated orally 1 hour after virus inoculation then once daily 24 hours after the first treatment with dose range of antiviral compound (2, 10 and 50 mg/kg). The animals were later euthanized at day 6 post-infection for the evaluation of virus titers in the lung and bronchoalveolar lavages. In addition, disease severity was assessed by evaluating the lung lesions, and detection of viral antigen by immunohistochemistry and qRT-PCR.

Results

JNJ-64166037 plasma levels were maintained above the protein-adjusted EC90 at the highest tested dose (50 mg/kg) with a lung-to-plasma ratio of 0.7 indicating that the compound distributes to the infected organ. A dose-dependent antiviral effect was associated to a potent reduction (>100 fold) of the detectable lung infectious virions at 50 mg/kg. In addition, the amount of hRSV RNA correlated the pronounced effect observed on the production of infectious virions. Similar observations were done in bronchoalveolar lavages. Consistently, the amount of viral antigen detected in the lung was significantly lower with 50 mg/kg and elevated with lower dosage of treatment Lack of macroscopic and microscopic lung lesions were seen with this dose regimen.

Conclusions

Oral administration of the non-fusion replication inhibitor JNJ-64166037 at the appropriate dose has potent antiviral effects in the lamb model of RSV infection by decreasing the level of hRSV in a dose-dependant manner. This mode of therapeutic intervention eliminated the hRSV-induced lung lesions assessed in the model. JNJ-64166037 might offer new opportunities of RSV bronchiolitis treatment in infants and children.

O28

EDP-938, A NOVEL NON-FUSION REPLICATION INHIBITOR OF RSV, DISPLAYS A HIGH BARRIER TO RESISTANCE IN VITRO

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Background

Respiratory Syncytial Virus (RSV) represents an important global health challenge with significant morbidity and mortality in infants, older adults, and immunocompromised populations. There currently exist no approved vaccines or therapeutics directly targeting the virus. EDP-938 is a novel non-fusion small molecule inhibitor of RSV currently in clinical development. It has potent in vitro activity against both RSV-A and -B laboratory strains and clinical isolates with a half-maximal effective concentration (EC50) <100 nM. EDP-938-treated African Green Monkeys infected with RSV demonstrated a 4-log reduction in viral load as compared to untreated animals. Here, we report on the genetic and phenotypic profiles of EDP-938-resistant RSV mutant variants generated by repeated EDP-938 dose escalation.
Methods

RSV-A Long and RSV-B Washington strains were serially passaged in the presence of increasing concentrations of EDP-938. Cultures were monitored for cytopathic effect and viral RNA levels which were used to determine when to increase the concentration of EDP-938. Surviving populations of virus were plaque purified and the clonal populations were sequenced. Drug resistant viral populations were analyzed for susceptibility to EDP-938, and viral fitness was analyzed by quantifying viral RNA production, cytopathic effect, and plaque forming unit production. A reverse-genetics system was employed to confirm resistance and quantify the contribution of individual mutations.

Conclusions

EDP-938 presents a high barrier to RSV resistance. Repeated attempts to generate resistance in both RSV-A and -B failed when initially exposed to a 4x EC50 of EDP-938. By comparison, RSV fusion inhibitors resulted in the rapid generation of viral populations with a > 40,000-fold reduction in sensitivity to those fusion inhibitors. A stepwise increase in concentration of EDP-938, starting with 1x EC50, eventually led to a series of mutations which mapped to the N protein of the virus. EC50 fold shifts were further confirmed and the roles of individual mutations were elucidated using the RSV reverse-genetics system. Increased resistance to EDP-938 was inversely correlated with viral fitness. The most potent mutation, N protein M109K, caused a 67-fold decrease in sensitivity to EDP-938 but also resulted in a 100-fold lower viral titer. In summary, EDP-938 exhibits an attractive preclinical resistance profile supporting its further development as a therapy for the treatment of RSV.

O29 ANTIVIRAL EFFECTS, PHARMACOKINETICS (PK) AND SAFETY OF THE RESPIRATORY SYNCYTIAL VIRUS (RSV) FUSION PROTEIN INHIBITOR, JNJ-53718678 (JNJ-8678), IN RSV-INFECTED INFANTS WITH BRONCHIOLITIS, IN THE PHASE 1B STUDY 53718678RSV1005

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Background

JNJ-8678 is a RSV-specific fusion inhibitor and a potential new treatment for respiratory infections caused by RSV. Data from a Phase 1b study of PK, safety and antiviral effects in hospitalised RSV-infected infants are presented.

Methods

37 and 7 patients, respectively, were randomised to JNJ-8678 (ascending doses, Table) or placebo (PBO) treatment once daily for 7 days. PK assessments were based on sparse sampling using a population PK model in adults scaled for pediatrics, accounting for allometric principles and maturation of drug clearance pathways. Safety was evaluated by AE reporting, lab and ECG assessments. Antiviral activity was assessed by measuring viral load (VL) using a quantitative RT-PCR assay for RSV RNA from nasal swabs.

Results

Sparse PK data are described by an integrated PK model (Table) and indicated PK parameters for different dose levels were similar across age groups. Treatment with JNJ-8678 appeared to reduce VL more rapidly than PBO (Fig). Median change in VL from baseline (BL) in JNJ-8678-treated patients (combined dose groups) vs PBO was -1.98 vs -0.32 log10 copies/mL at Day 3. Mean differences in change from BL (90% Cl) of JNJ-8678 (combined dose groups) vs PBO on Days 2 and 3 were estimated -1.33 (-2.26; -0.39) and -1.62 (-2.55; -0.69) log10 copies/mL, respectively (general linear model, adjusted for BL VL; p≤0.05). There was a clear separation between JNJ-8678 and PBO, but no evident exposure-response relationship. JNJ-8678 was generally well tolerated with no new safety signals compared to adults and no dose relationship with AEs or lab abnormalities were observed.

Conclusions

This dataset in RSV-infected infants showed a clear trend for an early antiviral effect of JNJ-8678, which was similar across dose groups. JNJ-8678 treatment was generally well tolerated.
O30
ZIRESOVIR (AK0529): UPDATE ON CLINICAL DEVELOPMENT FOR THE TREATMENT OF RESPIRATORY SYNCYTIAL VIRUS (RSV) DISEASE
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Background
RSV disease occurs throughout life, and is particularly problematic in infants and older adults, especially those with comorbidities. A distinct mortality is associated with disease caused by RSV. There is currently no effective antiviral available for the treatment of RSV infection and an unmet medical need exists for a safe, and easily deployable treatment. Early intervention with RSV suppression may provide long-term health and pharmaco-economic benefit through reduction of post-infection wheezing.

Methods
Review of the clinical development status of Ziresovir (previously AK0529).

Results
Ziresovir is an orally administered small molecule RSV F-protein inhibitor of unique structure with activity against both RSV-A and RSV-B. Ziresovir is under development for the treatment of RSV disease in both children and adults. F-protein inhibition prevents viral entry and inhibits RSV-induced formation of the syncytium, which is pathognomonic of RSV infection. Pharmacologic F-protein inhibition has been validated in a human RSV-challenge model. Ziresovir has completed three adult studies, while a fourth is to shortly commence; an international multicenter study in infants hospitalized with RSV disease remains ongoing and includes clinical and virological endpoints, with evidence of viral load knockdown and preliminary examination compatible with clinical benefit. Pharmacokinetic data from adult and infant studies demonstrates predictable behavior with good bioavailability and ready attainment of the target concentration. There have been no SAEs in any Ziresovir study and analysis of safety data shows no particular pattern of AEs; severity of AEs is generally mild, with no severe AEs having been reported. Overall, Ziresovir has demonstrated good safety and tolerability in both adults and infants.

Conclusions
Ziresovir displays good safety and PK and development continues for treatment of RSV infection in adults and infants.

SESSION 9  RSV PROPHYLAXIS AND VACCINES II

O31
DEFINING THE HUMORAL AND B CELL RESPONSE AFTER VACCINATION WITH A STABILIZED PREFUSION RSV F SUBUNIT VACCINE (DS-CAV1)

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Background
Respiratory syncytial virus (RSV) causes substantial morbidity in children and the elderly, and no vaccine is currently available. An effective vaccine will require the induction of neutralizing antibodies, which can be elicited to several antigenic sites on the pre-fusion (pre-F) and post-fusion (post-F) conformations of the RSV fusion (RSV F) protein. The recent stabilization of the pre-F conformation revealed that surfaces unique to the pre-F conformation (such as antigenic sites 0 and V) are targets for highly neutralizing antibodies. A stabilized form of the pre-F protein (DS-Cav1) is currently in a phase I clinical trial (VRC 317), where participants receive two immunizations with DS-Cav1 with or without alum adjuvant.

Methods
We have optimized three monoclonal antibody competition assays by using antibodies that target site 0 (D25) or a shared surface (palivizumab, site II) to measure changes in D25 and palivizumab-competing antibodies following DS-Cav1 vaccination. Each assay
was independently optimized for antigen coating and competing antibody concentrations. To complement our serological studies, RSV pre-F and post-F proteins were used as tetramerized probes to identify and measure RSV-F specific B cells before and after DS-Cav1 vaccination using a 17-color flow cytometry panel.

**Results**

Using competitive binding assays on both pre-F and post-F antigens, we demonstrate a significant increase in both D25 and palivizumab-competing antibodies 4 weeks following DS-Cav1 vaccination. Using a subset of trial participants, we measured RSV-F specific B cells at weeks 0 and 2 and show an increase in both IgG+ and IgA+ antigen-specific memory B cells targeting pre-F and shared surfaces.

**Conclusions**

Quantifying antibody responses to the apex and the side of the pre-F protein will provide insight into the site-specificity of antibodies elicited by DS-Cav1 vaccination. These serological analyses will be complemented by phenotypic profiling of probe-binding RSV F-specific B cells before and after vaccination to provide further insight into B cell responses to vaccination.

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**O32 EVALUATION OF NOVEL RSV LIVE ATTENUATED VACCINE IN A NON-HUMAN PRIMATE MODEL**

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**Background**

Respiratory syncytial virus (RSV) is the most significant viral cause of lower respiratory tract disease in pediatric patients globally, but no vaccine is currently available. We have developed a series of live RSV vaccine candidates with attenuating mutations in their polymerase (L) protein and yield-enhancing mutations in their attachment (G) glycoprotein.

**Methods**

We compared one of our live attenuated vaccine candidates, RSV G(L208A)/L(G1875A), with the parental strain A2 RSV in a total of 3 rhesus macaques (Macaca mulatta). Rhesus macaques were immunized with either 10^6 pfu of the vaccine candidate, parental virus, or buffer lacking any virus, and macaques were challenged with 10^6 pfu RSV A2 virus at 30 days post-immunization. Bronchoalveolar lavage and nasal rinses were performed on alternating days following immunization and challenge, and virus was quantified from these samples. Blood and serum were collected from macaques every 7 days throughout the study to isolate PBMC's and quantify serum antibodies, respectively. PBMC's were isolated to assess the T cell response of each macaque to RSV by incubation with a library of RSV peptides in an ELISpot assay. The RSV peptide library is comprised of 13 groups of peptides that are overlapping 18-mers representing all of the RSV proteins, pooled into 13 groups.

**Results**

Immunization with the vaccine candidate resulted in no detectable virus production in the lungs or nasal cavity while the parental virus titers peaked at days 4 and 7 for the BAL and nasal wash, respectively. On day 30, both of these macaques, as well as an unimmunized macaque, were challenged with RSV A2 (10^6 pfu). No RSV was detected in the airways of the parental RSV-immunized macaque, while very low amounts of RSV were detected on days 2 and 5 in the nasal wash from the candidate vaccine macaque. 10-fold more RSV was produced by the unimmunized, challenged macaque. Significant antibody titers were generated against the post-F, pre-F and G proteins at 7 days post-challenge in the parental RSV-immunized and the candidate vaccine macaques, but antibodies were undetectable in the unimmunized macaque after RSV challenge. Four RSV peptide pools from the F, L, M, M2-1, and M2-2, NS1, and NS2 proteins elicited a strong T cell response in PBMC’s isolated from the macaques. The highest T cell responses were observed in the vaccine candidate and parental-RSV macaques at 7 days post-challenge, with the peptides from the M and M2-1 proteins generating the highest overall response.

**Conclusions**

RSV G(L208A)/L(G1875A) is an immunogenic and protective live attenuated RSV vaccine candidate in an in vivo NHP model.
Background
Respiratory syncytial virus associated acute respiratory infection (RSV-ARI) constitutes a substantial disease burden in (older) adults. We aimed to identify all studies investigating the disease burden of RSV-ARI in older adults aged 65 years old or more.

Methods
We estimated the incidence, hospital admission rate and in-hospital case fatality ratio (hCFR) of RSV-ARI in older adults aged ≥65 years stratified by region, with data from a systematic review of studies published between Jan 1996 and Apr 2018, and from 8 unpublished population-based studies. We applied these rate estimates to population estimates for 2015, to calculate the global and regional burden in older adults admitted with RSV-ARI in that year. We estimated the number of in-hospital RSV-ARI deaths by combining hCFR with hospital admission estimates from hospital-based studies.

Results
We estimated that in 2015, there were about 1.5 (95% CI 0.3-6.9) million episodes of RSV-ARI in older adults aged ≥65 years from industrialised countries (data missing in developing countries), and of these 214,000 (95% CI 100,000-459,000) (~14.5%) were admitted to hospitals. The global number of hospital admissions of RSV-ARI in older adults was estimated at 336,000 (UR 186,000-614,000). We further estimated about 14,000 (UR 5,000-50,000) in-hospital deaths related to RSV-ARI globally. Hospital admission rate and hCFR increased with advancing age.

Conclusions
The disease burden of RSV-ARI among older adults is substantial. Appropriate prevention and management strategies should be developed to accelerate the reduction in RSV-ARI disease burden in this population.
Methods
We conducted a systematic review of population-based studies supplemented by online data and unpublished research data reporting RSV seasonality. We calculated monthly annual average percentage (AAP) as the relative strength of activity. We calculated the duration of epidemics by the minimum number of months to account for 75% of annual positives, with each month being an epidemic month. We modelled monthly AAP of RSV using site-specific temperature (TEMP) and relative humidity (RH) for the prediction of local epidemic months. We assessed the model predictability by leave-one-out cross-validation. We also developed an online interactive tool for predicting the local RSV epidemic months (https://you-li.shinyapps.io/PredictionOfVirusEpidemics). Furthermore, we predicted the global RSV epidemic months on a 5-degree by 5-degree scale. The same methods stated above were also applied to influenza virus (IFV) for comparison.

Results
We included 183 sites reporting RSV seasonality. RSV epidemics started in late summer in the tropics of each hemisphere, reaching most temperate sites in winter months (Figure 1). RSV epidemic duration was longer than IFV in the temperate region but shorter than IFV in the tropics (Figure 2). Based on the association between TEMP, RH and monthly AAP presented in Figure 3, the model predicted RSV epidemic months with 81% sensitivity and 63% specificity; the predicted RSV onset month was 1.0 months [0.6-1.3] earlier than the observed onset. The predicted global RSV epidemics were presented in Figure 4. Figures 1-4 Attachment

Conclusions
This is the first review that provides global pictures of month-by-month activity of RSV. RSV seasonality is different from IFV, especially in the tropics. The seasonality information presented in this review has important implications for health services planning, the timing of RSV palivizumab and the strategy of future RSV vaccination.

O35 PROSPECTIVE, EPIDEMIOLOGICAL STUDY OF THE INCIDENCE OF RESPIRATORY SYNCYTIAL VIRUS (RSV) LOWER RESPIRATORY TRACT INFECTIONS (LRTIS) FROM BIRTH UP TO 2 YEARS OF AGE IN DIVERSE GLOBAL SETTINGS

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Background
Standardized RSV LRTI surveillance case definitions and methods that can be implemented across diverse global settings are essential for support and evaluation of emerging infant RSV prevention strategies. Current estimates of infant RSV disease morbidity and mortality vary widely [Shi, Lancet 2017], potentially due to pooling of studies with diverse methods and populations. Inter-country variation in disease burden estimates could be due to measurement error or true variation in incidence. This study (NCT01995175) aimed to measure the incidence of RSV LRTI using consistent methodology and World Health Organization (WHO) case definitions in a diverse population of infants from birth to 2 years of age.

Methods
Infants were enrolled and followed in 8 countries from 2013-2017. Children were monitored for LRTIs using active and passive surveillance from birth to 2 years of age. Nasal swabs were collected during symptom-directed examination visits for possible LRTI cases and tested for RSV using quantitative Reverse Transcription PCR. Incidence rates for first episodes of RSV LRTI were calculated using the 2005 WHO case definitions (LRTI and severe LRTI).
Results
In all, 2401 infants were followed, with 132 in Argentina, 100 in Bangladesh, 143 in Canada, 490 in Finland, 298 in Honduras, 585 in South Africa, 324 in Thailand, and 329 in the USA. In all, 206 (8.6%) infants had RSV LRTIs and 69 (2.9%) had severe RSV LRTIs. The overall RSV LRTI incidence at 0-5 months, 6-11 months and 12-23 months was 7.27, 5.60 and 2.87 per 100 child-years, respectively. The observed 0-5 month RSV LRTI incidence was the highest in Bangladesh and lowest in Finland. The highest 0-24 month RSV LRTI and severe LRTI incidence rates were seen in Honduras while lowest rates were observed in Finland [see table].

Conclusions
RSV LRTI was detected in all 8 settings with particularly high rates observed in Bangladesh, Honduras and Argentina. The substantial disparities in RSV incidence, despite the use of consistent methods, support true regional variations in disease burden. These results are particularly relevant in areas where RSV disease incidence data are scant. The pattern and incidence rates measured are consistent with global estimates reported from meta-analyses of RSV disease epidemiology. These data underscore the global relevance of RSV preventive strategies during infancy.

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SESSION 12 MATERNAL IMMUNITY AND MATERNAL VACCINATION

O36 TRANSPLACENTAL RESPIRATORY SYNCTIAL VIRUS AND INFLUENZA ANTIBODY TRANSFER IN ALASKA-NATIVE MOTHER-INFANT PAIRS

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Background
Respiratory syncytial virus (RSV) and influenza cause viral pneumonia in infants. Maternal immunization protects against severe disease in young infants through transplacental antibody transfer. Alaska Native infants are at risk for severe flu and RSV disease. An evaluation of RSV and influenza-specific antibody transfer in mother-infant pairs has not been performed in this population.

Methods
Serum samples collected during pregnancy and at birth from mother-infant pairs in Bethel, Alaska and Seattle, Washington were tested for RSV and influenza antibody using a microneutralization assay and hemagglutination inhibition assay (HAI), respectively, and compared across sites.

Results
Mean RSV antibody concentrations in pregnant women in Bethel, AK and Seattle, WA were similar (log2 RSV antibody 10.6 [SD:1.7] vs. 10.7 [SD: 1.6], P=0.86), but cord blood RSV antibody concentration was significantly lower in infants born to mothers in Alaska as compared to Seattle (log2 RSV antibody 11.0 [SD: 1.6] vs.12.2 [SD: 1.4], P<0.001). Mean cord:maternal RSV antibody transfer ratio was 1.15 [SD: 0.13] in mother-infant pairs in Seattle, WA (n=57) as compared to 1.04 [SD: 0.08] in Bethel, AK (n=75). Mean flu geometric mean titers for Seattle, WA were 47.28, 36.35, 78.11, 30.03 for pregnant women and 54.43, 40.62, 89.11, and 33.25 in cord blood for H1N1, H3N2, B/Yamagata, and B/Victoria, respectively. Mean cord blood: maternal antibody transfer ratio was 1.48 [SD: 0.41], 1.35 [SD: 0.11], 1.4 [SD: 0.10], and 1.45 [SD: 0.10] for H1N1, H3N2, B/Yamagata, and B/Victoria, respectively, in mother-infant pairs in Seattle, WA. HAI testing for Alaska pairs is pending.

Conclusions
Maternal to infant RSV transplacental antibody transfer was significantly lower in Alaska Native mother-infant pairs, which may be a potential contributor to higher rates of severe RSV disease in Alaska Native infants. Attachment
Efficacy of RSV Maternal Immunization Varies With the Version of the Prefusion F Antigen in Virus-Like Particle Vaccine Candidates

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Background
Respiratory syncytial virus (RSV) is a significant human pathogen severely impacting infants and young children, but no vaccine exists for this vulnerable population. Direct vaccination of infants is likely ineffective and potentially unsafe. Maternal vaccination is the best and safest approach to infant protection through the passive transfer of neutralizing antibodies (NA) in utero to the fetus or after birth through lactation. Using RSV primed, pregnant cotton rats as a surrogate human model, we showed that a single immunization with our novel RSV pre-fusion F protein (DS-Cav1 pre-F)-containing virus-like particles (VLPs) stimulated high titers of NA, protected their offspring from RSV challenge, and decreased pup lung pathology compared to that observed after RSV infection of offspring of mock-immunized dams (Nat. Commun. (2018)9:1904).

Methods
Several reports indicate that soluble DS-Cav1 pre-F is unstable. Thus, we prepared four new VLPs containing pre-F proteins different than DS-Cav1 and assessed their stability and immunogenicity in mice and cotton rats.

Results
We determined that VLP associated DS-Cav1 pre-F as well as the four new VLP associated pre-Fs were stable under a variety of conditions. The new pre-F VLPs bound, in ELISA, to pre-F specific monoclonal antibodies, AM14 and D25, at levels different from DS-Cav1 pre-F VLPs. Upon immunization of mice, two of these new pre-F VLPs stimulated serum NA titers 2 to 3-fold higher than the DS-Cav1 pre-F VLPs. These two-new pre-F VLPs were used as immunogens in RSV-primed, pregnant cotton rats to test their efficacy in protection of their 4-week-old pups from RSV challenge. The levels of NA induced in dams by the new VLPs as well as DS-Cav1 VLPs were similar. However, immunization of dams with the new pre-F VLPs reduced lung titers in the pups upon RSV challenge to lower levels than DS-Cav1 VLP immunization and immunization with one of these new pre-F VLPs reduced virus lung titers 10-fold over that detected after DS-Cav1 pre-F VLP dam immunization. Levels of serum NA and total anti-F antibodies in pups correlated with protection from challenge.

Conclusions
Different versions of pre-F protein containing VLPs varied significantly in binding pre-fusion F-specific monoclonal antibodies suggesting some variations in the pre-F protein conformation. Furthermore, one version of pre-F VLPs tested impacted the induction of NA titers in mice and, significantly, impacted the efficiency of transfer to pups and/or half-life of the NA received from immunized cotton rat dams.

Progress Toward a Vaccine for Maternal Immunization to Prevent Respiratory Syncytial Virus Lower Respiratory Tract Illness (RSV LRTI) in Infants

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Background
RSV is the leading cause of infant LRTI and hospitalization worldwide. The greatest burden of severe disease is in term infants <5 months old, hence the potential utility of maternal immunization for protection early in infancy. Novavax is developing an aluminum-adjuvanted RSV F nanoparticle vaccine for use in the 3rd trimester of pregnancy with the goal of preventing medically significant RSV LRTI in the first 3-6 months of life.
Methods
After dose-finding in 1,050 women of childbearing age, we evaluated safety and immunogenicity of the vaccine in a Phase 2 study in 50 healthy pregnant women (33 to 35 weeks gestation). Safety was assessed in mothers and infants, and RSV-specific antibodies in women at baseline, day 14, delivery, and days 35 and 180 post-partum, and in cord blood and infant sera on days 14, 35, 60 and 180 of life. We initiated a global observer-blind, randomized, placebo-controlled Phase 3 trial in up to 8,618 mother-infant pairs. Women receive one dose of RSV F vaccine or placebo between 28 and 36 weeks of gestation and are followed for safety, immunogenicity, and symptomatic RSV illness until 180 days post-partum. Infants are followed with active/passive surveillance for RSV LRTI for 180 days and for safety for 1 year. Infants are divided into 3 cohorts, each providing cord blood and two post-natal sera at different time points to characterize RSV antibody decay.

Results
In Phase 2, RSV F nanoparticle vaccine immunogenicity in pregnant women was similar to that in non-pregnant women, with no negative safety impacts. The vaccine induced anti-F IgG and neutralizing antibodies. Antibodies competitive with monoclonal antibodies to antigenic sites Ø, VIII, II, and IV on pre-F protein were detected by biolayer interferometry in maternal and infant sera. Transplacental transfer was more efficient (110 to 120%) in women immunized >30 days prior to delivery than those treated later; RSV antibody t1/2 ranged from 30 to 41 days in infants. The Phase 3 trial has enrolled >4,600 maternal-infant pairs in 11 countries over 7 RSV seasons. Periodic unblinded DSMB review has indicated no safety concerns. In November 2017, an informational analysis performed by an independent statistician, with Novavax remaining blinded, yielded a posterior probability of at least 90% that efficacy was > 0%.

Conclusions
RSV F nanoparticle vaccine is immunogenic in pregnancy, and antibodies are transferred transplacentally. The first formal analysis of the Phase 3 data addressing efficacy against medically-significant RSV LRTI is projected for Q1, 2019.

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ADVANCING MATERNAL IMMUNIZATION AND THE RSV MI ROADMAP

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Background
Respiratory syncytial virus (RSV) is the most common cause of lower respiratory tract infection in neonates and young infants. The risk of severe outcomes is highest in the first months of life and the vast majority of disease burden lies in low- and middle-income countries (LMICs). While vaccines are among the most cost-effective health interventions, no RSV vaccine has yet been registered. WHO’s 2017 RSV Vaccine Research and Development Technology Roadmap identified maternal immunization (MI) as a priority strategy for RSV vaccine development to address disease burden in young infants. Several maternal RSV vaccines are moving through clinical development, including a candidate in late-stage trials. Once licensed, successful implementation in LMICs will require well-informed, evidence-based decision making.

Methods
The Advancing Maternal Immunization (AMI) project, led by PATH in collaboration with WHO, aims to enable efficient, well-informed decisions around RSV MI introduction in LMICs. In 2017-18, AMI engaged experts to identify key questions across disease, product, health economics, and vaccine delivery topic areas for maternal RSV vaccines and compiled Advancing RSV maternal immunization: A Gap Analysis Report. This report identifies available evidence, work in progress, key remaining gaps and informed the development of a roadmap.

Results
The RSV MI Roadmap serves as a resource for RSV stakeholders, outlining priority activities and timeframes to meet remaining information needs. The roadmap activities are divided into disease burden, vaccine effect, safety surveillance, cost and financing, programmatic considerations, and implementation topic areas. Activities are staged according to vaccine development and implementation timelines to ensure evidence is available to enable global policy and financing decisions in the near term and country decisions over the longer term.
Conclusions

A strategy for RSV prevention in early life is urgently needed. The RSV MI Roadmap outlines priority activities to ensure meaningful vaccine impact where it is most needed in the shortest timeframe possible. The AMI project will facilitate collaboration among global MI stakeholders and support generation, tracking, and dissemination of evidence to enable timely and informed decision-making around RSV MI.

POSTER SESSIONS

POSTER SESSION 1
Virology (VIR)  Vaccines, Therapies & Treatments (VTT)

P1 DISTRIBUTION OF RESPIRATORY Syncytial Virus Subtypes A AND B AMONG CHILDREN PRESENTING WITH ACUTE RESPIRATORY TRACT INFECTION TO KEGALLA HOSPITAL, SRI LANKA.

JAAS JAYAWEERA 1, Faseeha Noordeen 2, Maduja Divarathna 2, Rukshan Rafeek 2, Adrian Morel 3

1 Teaching Hospital, Kandy  2 Faculty of Medicine, University of Peradeniya  3 Teaching Hospital, Kegalla

P2 PREVALENCE OF RESPIRATORY Syncytial Virus IN ACUTE RESPIRATORY TRACT INFECTIONS IN A SELECTED SAMPLE OF CHILDREN FROM SRI LANKA

MADUJA DIVARATHNA 1, Rukshan Rafeek 1, Adrian Morel 2, Faseeha Noordeen 1

1 Faculty of Medicine, University of Peradeniya  2 Teaching Hospital, Kegalla

P3 RSV GENE EXPRESSION PATTERNS DEPEND ON STRAIN & GENE START (GS) SIGNAL N-PHASE

FELIPE-ANDRES PIEDRA 1, Xueting Qiu 2, Vasanthi Avadhanula 3, Annette Machado 3, Do-Kyun Kim 4, James Hixson 4, Justin Bahl 2, Pedro Piedra 5

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P4
SURVEILLANCE OF RESPIRATORY VIRUSES IN THE OUTPATIENT SETTING IN RURAL COASTAL KENYA: BASELINE EPIDEMIOLOGICAL OBSERVATIONS

GRIEVEN OTIENO 1, Timothy Etyang 2, Alex Gichuki 2, Everlyn Kamau 2, Charles Agoti 3, Joyce Nyiro 1, Patrick Munywoki 3, James Nokes 4

1 Kemri-Wellcome Trust Research Programme  2 Kemri-Wellcome Trust Research Programme, Kilifi, Kenya  3 Kemri-wellcome Trust Research Programme, Kilifi, Kenya; Pwani University, Kilifi, Kenya  4 Kemri-wellcome Trust Research Programme, Kilifi, Kenya; School of Life Sciences and Zeeman Institute of Systems Biology and Infectious Disease Epidemiology Research (SBIDER), University of Warwick, Coventry, UK

P5
IN VITRO CHARACTERIZATION OF SUBGROUP A AND B RECOMBINANT HUMAN RESPIRATORY SYNCYTIAL VIRUSES BASED ON CLINICAL ISOLATES

PAUL W DUPREX 1, Rory D de Vries 2, Sham Nambulli 1, Linda J Rennick 1, Alwin de Jong 2, Laurine C Rijsbergen 2, Rik L de Swart 2

1 Boston University Medical School  2 Erasmus MC

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IN VIVO COMPARISON OF RECOMBINANT HUMAN RESPIRATORY SYNCYTIAL VIRUS STRAINS BASED ON CLINICAL ISOLATES IN COTTON RATS

LAURINE RIJSBERGEN 1, Rory de Vries 1, Linda Rennick 2, Sham Nambulli 2, Paul Duprex 2, Rik de Swart 1

1 Erasmus MC, dept. Viroscience  2 Boston University School of Medicine

P7
IMMUNOGOLD ELECTRON MICROSCOPY REVEALS THAT NUCLEOLIN (NCL) IS RECRUITED TO THE APICAL MEMBRANE OF HUMAN AIRWAY EPITHELIUM BY HUMAN RSV.

PETER MASTRANGELO 1, Gurpreet K Singhera 2, Delbert R. Dorscheid 2, Cameron A. Ackerley 3, Richard G. Hegele 3

1 University of Toronto  2 Centre of Heart Lung Innovation, St Paul’s Hospital and University of British Columbia, Vancouver, BC Canada  3 Laboratory Medicine and Pathobiology, University of Toronto, Toronto, ON Canada

P8
INTERACTION OF THE RSV MATRIX PROTEIN WITH THE VIRAL TRANSCRIPTASE.

SARAH CROFT 1, Elliot Atchison 1, Pete Strong 2, Garth Rapeport 2, Kazuhiro Ito 2, Reena Ghildyal 1

1 University of Canberra  2 Pulmocide Ltd UK
P9
MATHEMATICAL MODELING IDENTIFIES ADAPTIVE IMMUNITY AS A KEY CONTROLLER OF RESPIRATORY SYNCTIAL VIRUS (RSV) TITER IN COTTON RATS

DARREN WETHINGTON 1, Olivia Harder 2, Adrian Morel 2, Karthik Uppulury 1, William Stewart 3, Phylip Chen 4, Tiffany King 5, Mark Peeples 6, Stefan Niewiesk 2, Jayajit Das 7

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HUMAN METAPNEUMOVIRUS CELL-TO-CELL SPREAD IN RESPIRATORY CELL LINES AND 3D CULTURES

NICOLAS CIFUENTES 1, Santiago Restrepo 2, Rebecca Dutch 2

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DIFFERENCES IN RSV SUBTYPES: EXAMINATION OF FUSION AND EFFECTIVENESS OF FUSION PROTEIN SPECIFIC MONOCLONAL ANTIBODIES

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P12
ELUCIDATION OF THE ROLES OF IRF9 AND IFI6 IN RESPONSE TO RSV INFECTION

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STABILITY AND CONFORMATIONAL TRANSITIONS OF THE RSV NUCLEOCAPSID

DAMIÁN ALVAREZ-PAGGI, Sebastian Esperante, Mariano Salgueiro, Gonzalo Prat Gay

Instituto de Investigaciones Bioquimicas de Buenos Aires FIL-CONICET

P14
ROLE OF RSV POLYMERASE IN THE ANTIVIRAL EFFECT OF RIBAVIRIN

AMY FUNG, Jerome Deval

Alios Biopharma, Janssen
SECRETOME PROFILING OF AIRWAY EPITHELIAL CULTURES OF PAEDIATRIC ORIGIN INFECTED WITH HUMAN RESPIRATORY SYNCYTIAL VIRUS (HRSV)

OLIVIER TOUZELET 1, Lindsay Broadbent 2, Stuart Armstrong 3, Waleed Aljabr 4, Elaine Cloutman-Green 5, Ultan Power 2, Julian Hiscox 6

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RSV STRAIN-DEPENDENT GROWTH KINETICS, CYTOPATHOGENESIS AND INNATE IMMUNE RESPONSES FOLLOWING WD-PBEC INFECTION.

LINDSAY BROADBENT 1, Lyndsey Fergusson 1, Andrea Miller 1, Pedro Piedro 2, Michael Shields 3, Laurent Detalle 4, Ultan Power 1

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RSV ATTRIBUTABLE MORTALITY IN PORTUGAL BETWEEN 2014 AND 2018

ANA PAULA RODRIGUES 1, Susana Silva 1, Raquel Guiomar 2, Pedro Pechirra 2, Baltazar Nunes 1

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EPIDEMIOLOGY OF RESPIRATORY SYNCYTIAL VIRUS IN ANTANANARIVO, MADAGASCAR, 2011-2017: GENETIC DIVERSITY AND MECHANISM OF SEASONALITY.

NOROSOA RAZANAJATOVO 1, Tsiry Hasina Randriambolamanantsoa 1, Xenia Rybkina 2, Fanjasoa Rakotomanana 1, Joelinotahiana Rabarison 1, Jean-Michel Heraud 1

1 Institut Pasteur de Madagascar  2 McMaster University

MOLECULAR CHARACTERIZATION OF CIRCULATING RESPIRATORY SYNCYTIAL VIRUS (RSV) GENOTYPES IN A PAEDIATRIC CLINIC, ACCRA- GHANA

ANNA. ABA KAFINTU-KWASHIE

UNIVERSITY OF GHANA, SCHOOL OF BIOMEDICAL AND ALLIED HEALTH SCIENCES

MOLECULAR CHARACTERIZATION OF CIRCULATING RESPIRATORY SYNCYTIAL VIRUS (RSV) GENOTYPES IN A PAEDIATRIC CLINIC, ACCRA- GHANA

ANNA. ABA KAFINTU-KWASHIE 1, Theophilus Adiku 2, John Kofi Odoom 3, Evangeline Obodai 3, Elijah Paa Edu-Quansah 3

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A MATHEMATICAL MODEL TO PREDICT RESPIRATORY Syncytial VIRUS KINETICS IN INFANTS

AMBER SMITH 1, John DeVincenzo 1, Monica Brint 1, Sydney Busch 2

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DIFFERENTIAL PATHOGENESIS OF HUMAN METAPNEUMOVIRUS CLINICAL ISOLATES IN MOUSE MODELS

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HIGH-THROUGHPUT NEXT-GENERATION SEQUENCING OF HUMAN RESPIRATORY syncytial VIRUS SUBGROUPS A AND B

LIJUAN WANG 1, Terry Fei Fan Ng 2, Christina Castro 3, Rachel Marine 2, Laura Magaña 3, Natalie Thornburg 4, Teresa Peret 4

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INTERNATIONAL NETWORK FOR OPTIMAL RESISTANCE MONITORING OF RSV (INFORM RSV): AN INTERNATIONAL STUDY TO DETERMINE THE MOLECULAR HETEROGENEITY OF RSV IN CHILDREN (A RESVINET STUDY)

ANNEFLEUR LANGEDIJK 1, Marta Nunes 2, Terho Heikkinen 3, Mitsuaki Hosoya 4, Peter Richmond 5, Federico Montinon 6, Renato Stein 7, Anne Greenough 8, Joanne Wildenbeest 1, Robert Jan Lebbink 9, Frank Coenjaerts 10, Louis Bont 1

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EVALUATING THE ROLE OF PNEUMOCOCCOL CARRIAGE IN INFANT RSV AND INFLUENZA ILLNESS IN RURAL NEPAL

ALISTAIR MURRAY 1, Janet Englund 2, Jane Kupyers 3, James Tielsch 4, Joanne Katz 5, Laxman Shrestha 6, Subarna Khatry 5, Steven Leclerq 7, Mark Steinhoff 8, Helen Chu

1 The George Washington University School of Medicine & Health Sciences US 2 Seattle Children’s Hospital/University of Washington, Pediatrics, Seattle, WA/US 3 University of Washington, Department of Laboratory Medicine, Seattle,US 4 George Washington University Milken Institute School of Public Health, Global Health, Washington, DC/US 5 Johns Hopkins Bloomberg School of Public Health, International Health, Baltimore, MD/US 6 Nepal Institute of Medicine, Pediatrics and Child Health, Kathmandu/NP; Nepal Nutrition Intervention Project - Sarlahi (NNIPS), Kathmandu Nepal 7 Cincinnati Children’s , Global Health Center, Cincinnati, OH/US 8 University of Washington, Division of Allergy and Infectious Diseases, Seattle, US
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RSV INFECTION OF STAT2-/- GOLDEN SYRIAN HAMSTERS REPRODUCES THE PATHOLOGIC OUTCOMES OF RSV INFECTION OF HUMAN AIRWAYS.
RAYMOND PICKLES 1, Rong Li 2, Allison Boone 1, Megan Grant 1, Zhongde Wang 2
1 UNC-Chapel Hill NC 2 Utah State University, Logan, UT

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MOLECULAR CHARACTERISTICS AND SEASONALITY OF RESPIRATORY VIRUSES DETECTED FROM CHILDREN WITH INFLUENZA LIKE ILLNESS IN NEPAL
BISHNU PRASAD UPADHYAY 1, Megha Raj Banjara 2, Ram Krishna Shrestha 1, Masato Tashiro 3, Prakash Ghimire 2
1 National Public Health Laboratory, Department of Health Services, Kathmandu, Nepal 2 Central Department of Microbiology, Tribhuvan University, Kirtipur, Nepal 3 National Institute of Infectious Disease, Tokyo, Japan

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RSV INFECTION IN NORMAL HUMAN BRONCHIAL EPITHELIAL CELLS INDUCES FILOPODIA AND INCREASES CELL MIGRATION.
VERONICA KESSLER, Ken Ryan, Masfique Mehedi
University of North Dakota

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DETERMINANTS OF SURVIVAL TIME AMONG PATIENTS WHO WERE ADMITTED WITH RESPIRATORY INFECTION AND DIED IN A COUNTY REFERRAL HOSPITAL IN KENYA, 2016
LILIAN MAYIEKA 1, Samwel Mwalili 2, Geoffrey Arunga 3, Victor Omballa 4, Fred Otiato 4, Nancy Otieno 4
1 Ms 2 KEMRI/CDC 3 BroadReach Healthcare LLC 4 Kenya Medical Research Institute

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SEVERE RSV INFECTIONS IN CHILDREN AND ELDERLY DURING 2017/2018 WINTER SEASON
RAQUEL GUIOMAR 1, Ana Paula Rodrigues 2, Paula Cristóvão 3, Ines Costa 3, Pedro Pechirra 3, Patricia Conde 3, Baltazar Nunes 2, Hospital Network 4
1 INSTITUTO NACIONAL SAUDE DR RICARDO JORGE NIF501427511 2 Epidemiology Department, National Institute of Health Dr. Ricardo Jorge 3 National influenza and other respiratory virus reference laboratory. National Institute of Health Dr. Ricardo Jorge 4 Influenza Diagnosis Portuguese Hospitals

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RSV BINDS STREPTOCOCCUS PNEUMONIAE VIA PBP1A INCREASING ITS VIRULENCE AND ANTIBIOTIC SENSITIVITY
CLAIRE SMITH
UCL GOS Institute of Child Health
RESPIRATORY VIRUSES ASSOCIATED WITH SEVERE ACUTE RESPIRATORY INFECTION (SARI) AMONG CHILDREN UNDER FIVE YEARS OLD IN MOROCCO, DURING 2014-16 INFLUENZA SEASONS.

AMAL BARAKAT 1, Youssef Bakri 2, Samira Benkerroum 3, Zakia Regragui 3, Hassan Ihzmade 3, Fatima El Falaki Fatima 3, ABDERRAHMAN BIMOUHEN 1,2, Hicham Oumzil 3

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EVALUATION OF RESPIRATORY Syncytial Virus RESISTANT MUTANTS TO A POTENT HUMAN MONOCLONAL ANTIBODY TARGETING THE CONSERVED EPITOPE ON ANTIGENIC SITE IV OF RSV F PROTEIN

DAI WANG, Kalpit Vora, Arthur Fridman, Gwen Heidecker, Lan Zhang, Jennifer Galli, Kara Cox, Zhiyun We, Cheryl Callahan, Zhifeng Chen, Aimin Tang

Merck & Co. Inc.

A HUMAN BISPECIFIC ANTIBODY AGAINST RESPIRATORY Syncytial VIRUS REPRESENT A PROMISING ANTIVIRAL AGENT

LIANPAN DAI 1, Jinghua Yan 2

1 Beijing Institutes of Life Science, Chinese Academy of Sciences 2 Institute of Microbiology, Chinese Academy of Sciences

A NOVEL RSV VACCINE DESIGN AGAINST SUPPRESSION OF VACCINE ENHANCED DISEASE

BIN WANG

Key Laboratory of Medical Molecular Virology of MOH and MOE, Fudan University

RESPIRATORY Syncytial VIRUS (RSV) ENTRY IS INHIBITED BY SERINE PROTEASE INHIBITOR AEBSF WHEN PRESENT DURING EARLY STAGE INFECTION.

WINKE VAN DER GUCHT, Annelies Leemans, Guy Caljon, Louis Mae, Paul Cos, Peter Delputte

University of Antwerp

MRNA VACCINES EXPRESSING FORMS OF RSV-F PROTEIN ARE IMMUNOGENIC AND PROTECTIVE IN RODENT MODELS OF RESPIRATORY Syncytial VIRUS INFECTION

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1 Merck & Co. 2 Pfizer 3 IHRC INC 4 Centers for Disease Control and Prevention 5 Louisiana Department of Health
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AN MRNA BASED VACCINE EXPRESSING RSV F IS IMMUNOGENIC AND PROTECTIVE IN NON-HUMAN PRIMATE MODELS OF RESPIRATORYSYNCYTIAL VIRUS INFECTION
ANDREW BETT, Mike Citron, Dai Wang, Dan DiStefano, Cheryl Callahan, Pedro Cejas, Sinoeun Touch, Zhiyun Wen, Lan Zhang, Jessica Flynn, Hualin Li, Dan Freed
Merck Research Labs

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VRC/NIAID/NIH
LINGSHU WANG
NIAID/NIH

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EVALUATION OF ANTIBODY RESPONSE AND EFFICACY IN COTTON RATS INOCULATED WITH HISTORICAL RSV STRAINS AND CHALLENGED WITH CONTEMPORARY STRAINS
ANNETTE A MACHADO 1, David DeRubeis 1, Trevor J McBride 1, Miguel C Cantu 1, Letisha O Aideyan 1, Xunyan Ye 1, Anne M Hause 2, Vasanthi Avadhanula 1, Brian E Gilbert 1, Pedro A Piedra 3
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DEVELOPMENT OF LUMICITABINE AS AN EFFECTIVE REPLICATION INHIBITOR OF HUMAN METAPNEUMOVIRUS
JIA MENG
Alios/Janssen Pharmaceuticals

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CHARACTERIZATION OF POTENT RSV NEUTRALIZING MABS ISOLATED FROM HUMAN MEMORY B CELLS
XIAO XIAO 1, Kara Cox 1, Aimin Tang 1, Deborah Nahas 1, Jennifer Galli 1, Scott Cosmi 2, James Cook 1, Hua Su 1, Kerim Babaoglu 1, Stephen Soisson 1, Andrew Bett 1, Kalpit Vora 1
1 Merck & Co.  2 Merck & Co.; Eurofins Lancaster Laboratories Professional Scientific Services

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LABYRINTHOPEPTIN A1 AND A2 EFFICIENTLY INHIBIT CELL ENTRY OF HUMAN RESPIRATORY SYNCYTIAL VIRUS IN VITRO AND IN VIVO
SIBYLLIE HAID 1, Sebastian Blockus 1, Svenja M. Wiechert 1, Theresa Frenz 1, Martin Wetzke 2, Hans Prochnow 3, Ronald Dijkman 4, Bettina Wiegmann 5, Marc Stadler 6, Marie-Anne Rameix-Welti 7, Jean-Francois Eléouet 8, W. Paul Duprex 9, Suman R. Das 10
1 Institute for Experimental Virology, TWINCORE, Hannover, Germany  2 Department for Pediatric Pneumology, Allergy and Neonatology, Hannover Medical School, Hannover, Germany  3 Department of Chemical Biology, Helmholtz Centre for Infection Research, Braunschweig, Germany  4 Department of Infectious Disease and Pathobiology, Vetsuisse Faculty, University of Bern, Switzerland  5 Department of Cardiothoracic, Transplantation and Vascular Surgery, Hannover Medical School, Hannover, Germany  6 Institute for Micobial Drugs, Helmholtz Centre for Infection Research, Braunschweig, Germany  7 INSERM U1173 Infection-Inflammation, Université de Versailles Saint-Quentin, Montigny-le-Bretonneux, France  8 INRA Molecular Virology and Immunology, Université Paris-Saclay, Jouy-en-Josas, France  9 Boston University School of Medicine, Boston MA, United States  10 Department of Medicine, Vanderbilt University Medical Center
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MURINE PNEUMONIA VIRUS (MPV) EXPRESSING THE RESPIRATORY SYNCYTIAL VIRUS (RSV) FUSION F GLYCOPROTEIN FROM A SUPERNUMERARY GENE IS ATTENUATED AND IMMUNOGENIC IN RHESUS MACAQUES.

SHIRIN MUNIR
National Institute of Allergy and Infectious Diseases, NIH

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BO LIANG 1, Barbora Kabatova 2, Juraj Kabat 3, David Dorward 4, Xiang Liu 2, Sonja Surman 2, Xueqiao Liu 2, Annie Moseman 2, Ursula Buchholz 2, Peter Collins 2, Shirin Munir 2

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JENNIFER RAINHO
Sanofi Pasteur

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JONATHAN KINDER 1, Chelsea Barrett 2, Hong Jin 3, Nicole Kallewaard 3, Rebecca Dutch 4

1 University of Kentucky  2 Department of Molecular and Cellular Biochemistry, University of Kentucky  3 Employee of Medimmune  4 Professor, Chair of Molecular and Cellular Biochemistry, University of Kentucky

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FIONA FERNANDES, David Tabor, Li Yu, Hui Liu, Varsha Nair, Rebecca Halpin, Mark Esser, Hong Jin

Medimmune

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LESLIE VAN DER FITS 1, Eirikur Saeland 1, Renske Bolder 1, Marjolein van der Meer 1, Joke Drijver 1, Yolinda van Polanen 1, Marianke van Schie 1, Raphael Ho Tsong Fang 2, Vanessa Contreras 2, Nathalie Bosquet 2, Roger Le Grand 2, Hanneke Schuitemaker 1

1 Viral Vaccines, Janssen Vaccines & Prevention B.V., Leiden, The Netherlands  2 IDMIT, Fonenay-aux-Roses, France
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MAN CHEN, Azad Kumar, Syed M. Moin, Kaitlyn M. Morabito, Tracy J. Ruckwardt, Pamela J. Costner, LaSonji A. Holman, Somia P. Hickman, Grace Chen, Julie E. Ledgerwood, Michelle C. Crank, Barney S. Graham

Vaccine Research Center, National Institute of Allergy and Infectious Diseases, NIH

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ANN R FALSEY 1, Surender Khurana 2, Tsedale Getachew 3, Svitlana Kovtun 3, Tatiana Konstantinova 3, Aissatou Mbaye 3, Marina S. Boukhvalova 3, Kevin C Yim 3, Jorge CG Blanco 3

1 University of Rochester Medical Center. Rochester General Hospital 2 Division of Viral Products, Center for Biologics Evaluation and Research (CBER). Food and Drug Administration (FDA) 3 Sigmovir Biosystems, Inc

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ZHENGHUI LI 1, Paul Liberator 1, Lubomira Andrew 1, Vidia Roopchand 1, Young-In Kim 2, Lisa Harrison 2, Elizabeth Meals 2, Ryan Tomlinson 2, Irene Yurgelonis 1, Wei Chen 1, Lyndsey Martinez 1, Kyle Heim 1

1 Vaccine Research and Development, Pfizer Inc. 2 University of Tennessee Health Science Center and Molecular Diagnostics and Virology Laboratories, Le Bonheur Children’s Hospital,

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REBECCA LOOMIS 1, Man Chen 2, Azad Kumar 2, Assanatou Bamogo 2, Hua-Ren Cherng 3, Philip Johnson 4, Barney Graham 2

1 Vaccine Research Center, National Institutes of Health; Abramson Research Center, Children's Hospital of Philadelphia 2 Vaccine Research Center, National Institutes of Health 3 Abramson Research Center, Children’s Hospital of Philadelphia; University of Pennsylvania 4 Abramson Research Center, Children’s Hospital of Philadelphia

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JEEHYUN LEE, Laura Klenow, Elizabeth Coyle, Hana Golding, Surender Khurana

FDA

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KURT SWANSON

Sanofi
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PAULINE VERDIJK, Naomi van Vlies
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LAURENT DETALLE 1, Ultan Power 2, Michael Shields 2, Andrena Miller 2, Lyndsey Ferguson 2, Hong Guo Parke 2, Lindsay Broadbent 2
1 Ablynx NV, Belgium 2 Centre for Experimental Medicine, Queens University Belfast, N.Ireland

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LAURENT DETALLE 1, Ultan Power 2, Michael Shields 3, Andrena Miller 2, Lyndsey Ferguson 2, Lindsay Broadbent 2
1 Ablynx nv, Belgium 2 Centre for Experimental Medicine, Queens University Belfast, Northern Ireland 3 Centre for Experimental Medicine, Queens University Belfast, Northern Ireland; Royal Belfast Hospital for Sick Children, Belfast, Northern Ireland

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Pfizer Inc

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Rhiannon Penkert 1, Charles Russell 1, Allen Portner 1, Karen Slobod 2, Toru Takimoto 3, Bart Jones 1, Robert Sealy 1, Sherri Surman 1, John DeVincenzo 4, Geoffrey Neale 1, Robert Maul 5, Patricia Gearhart 5
1 St. Jude Children's Research Hospital 2 Cambridge Consulting 3 University of Rochester 4 Le Bonheur Children's Hospital 5 Institute on Aging, NIH

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HARALD ROUHA 1, Adriana Badarau 1, Georgios Tsouchnikas 1, Irina Mirkina 1, Lukas Stulik 1, Laura Walker 2, Ivana Dolezilкова 1, Eszter Nagy 3
1 Arsanis Inc 2 Adimab LLC 3 Independent Researcher
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MARIE GALLOUX 1, Vanessa Gaillard 2, Sébastien Brûlé 3, Bertrand Raynal 3, Origène Nyanguile 2, Jean-François Eléouët 4

1 INRA, 2 HES-SO Valais, Route du Rawyl 64, 1950 Sion, Switzerland, 3 Plate-forme de Biophysique des Macromolécules et de leurs Interactions, Institut Pasteur, Paris, France, 4 VIM, INRA, Université Paris-Saclay, Jouy-en-Josas, France.

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HUA SU, Lan Zhang, Sangita Patel, John Reid, Scott Cosmi, James Cook, Jennifer Galli, Andrew Bett, Aimin Tang, Zhifeng Chen, Kara Cox, Stephen Soisson

Merck & Co. Inc.

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RODERICK TANG 1, Barbara Schlingmann 1, Eduardo Lujan 1, Jorge Blanco 2, Marina Boukhvalova 2, Jason McLellan 3, Martin Moore 1

1 Meissa Vaccines Inc, 2 Sigmovir Biosystems Inc, 3 The University of Texas at Austin.

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ANNELIES LEEMANS 1, Marlies Boeren 1, Winke Van der Gucht 1, Isabel Pintelon 1, Kenny Roose 2, Bert Schepens 2, Xavier Saelens 2, Dalan Bailey 3, Wim Martinet 1, Guy Caljon 1, Louis Maes 1, Paul Cos 1

1 University of Antwerp, Belgium, 2 VIB; Ghent University, Belgium, 3 The Pirbright Institute, United Kingdom.

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MARIE-ANNE RAMEIX-WELTI 1, Ronan Le Goffic 2, Rolf Mueller 3, Zhaoguo Wang 4, Daniel Krug 3, Pan Xing 5, Yuzhen Gao 5, Long Wang 5, Xiaomei Zhang 5, Miaomiao Du 5, Jingjing CAO 6, Vincent Rincheval 1

1 UMR INSERM U1173 2I, UFR des Sciences de la Santé Simone Veil-UVSQ, 78180, Montigny-le-Bretonneux, France, 2 INRA, Unité de Virologie et Immunologie Moléculaires (UR892), Jouy-en-Josas, 78352, France, 3 Department of Microbial Natural Products, Helmholtz-Institute for Pharmaceutical Research Saarland (HIPS), Helmholtz Center for Infection Research (HZI) and Pharmaceutical Biotechnology, Saarland University, Campus C23, 66123 Saarbrücken, Germany, 4 Qingdao Municipal Center for Disease Control & Prevention, Qingdao, P.R. China, 5 Shandong University-Helmholtz Institute of Biotechnology, State Key Laboratory of Microbial Technology, College of Life Science, Shandong University, Jimo Binhailu 72, 266237 Qingdao, P.R. China, 6 Shandong University.

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MATTHEW SNAPE 1, Ilse Dieussaert 2, Antonio Gonzalez Lopez 2, Marta Picciolato 3, Wayne Woo 2, Thi Lien-Anh Nguyen 4, Paola Cicconi 1, Catherine de Lara 5, Paul Klenerman 5, Claire Jones 6, Esha Sarkar 6, Laura Silva-Reyes 6

1 Oxford Vaccine Group, Department of Paediatrics, University of Oxford, Oxford, UK; NIHR Oxford Biomedical Centre, Oxford, UK, 2 GSK, Rockville, USA, 3 GSK, Rixensart, Belgium, 4 GSK, Wavre, Belgium, 5 Experimental Medicine Division, Nuffield Department of Medicine, Peter Medawar Building, University of Oxford, Oxford, UK, 6 Oxford Vaccine Group, Department of Paediatrics, University of Oxford, Oxford, UK.
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PEDRO J CEJAS 1, Ryan Swoyer 1, Gregory O'Donnell 1, Mike Citron 1, Dan DiStefano 1, Cheryl Callahan 1, Lan Zhang 1, Jessica Flynn 1, Giuseppe Ciaramella 2, Christine Shaw 2, Amy Espe seth 1, Andy Bett 1, Amanda Leach 3, Shabir Madhi 4, Thanyawee Puthanakit 5, Peter Silas 6, Sonia Stoszek 3, Auchara Tangsathapornpong 7, Jama ree Teeratakulpisarn 8, Santiago Vidaurreta 9, Miia Virta 10, Khalequ Zaman 11

1 Merck & Co., Inc. 2 Moderna Therapeutics 3 GSK, Rockville, MD, USA 4 Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa 5 Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand 6 Wee Care Pediatrics, Syracuse, UT, USA 7 Faculty of Medicine, Thammasat University, Pathum Thani, Thailand 8 Khonkaen University, Khon Kaen, Thailand 9 Centro de Educación Médica e Investigaciones Clínicas Norberto Quirno, Buenos Aires, Argentina 10 Vaccine Research Centre, University of Tampere Medical School, Tampere, Finland 11 International Center for Diarrhoeal Disease Research, Dhaka, Bangladesh

P69 IN-DEPTH ANALYTICAL CHARACTERIZATION AND STRUCTURAL MODELING OF NOVAX RSV F NANOPARTICLE VACCINE

ERNEST MAYNARD 1, Daniel Scott 1, Oleg Borisov 1, Gale Smith 1, Joseph Curtis 2, Alexander Grishaev 2, Susan Krueger 2,

1 Novavax, Inc. 2 National Institute of Standards and Technology

P70 ANTIGENIC CHARACTERIZATION PREFUSOGENIC NANOPARTICLE VACCINE, PREFUSION, AND POSTFUSION F AGAINST A BROAD RANGE OF NEUTRALIZING MONOCLONAL ANTIBO DIES AND EPITOPE RESPONSES IN COTTON RATS

NITA PATEL 2, Jing-Hui Tian, Hanxin Lu, Mimi Guebre-Xabier, Gregory Glenn, Gale Smith

Novavax, Inc.

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QINGQING XIE 1, Qinghua Wang 1, Mimi Guebre-Xabier 2, Jing-Hui Tian 2, Michael Massare 2, Nita Patel 2, Gale Smith 2, Gregory Glenn 2

1 Baylor College of Medicine 2 Novavax, Inc

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TIMOTHY HAHN 1, Tim Kram 2, Yves Schwander 3, Stephan Gschwind 3, Eugene Wu 1, Eduard Orvisky 1, Kalpen Patel 1, Sarathi Boddapati 1, Roentgen Hau 1, Yen-Huei Lin 1

1 Novavax, Inc. 2 Rommelag USA Inc 3 Maropack AG
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HANXIN LU, Jing-Hui Tian, Mimi Guebre-Xabier, Nita Patel, Michael Massare, Gregory Glenn, Gale Smith  
Novavax, Inc.

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REBECCA DUBOIS¹, Ralph Tripp²  
¹ University of California Santa Cruz  ² University of Georgia

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ROBERT WELLIVER¹, Vadim Ivanov¹, James Papin², Alisha Preno², Rachel Staats¹, Kimberly McCormack², Abby Norris², Nicole Reuter²  
¹ University of Oklahoma Health Science Center  ² Oklahoma Baboon Research Reserve

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RINEKE DE JONG¹, Judith Bonsing¹, Haifeng Song², Badiaa Bouzya³, Kai-Fen Wang², Ilse Dieussaert², Ann-Muriel Steff²  
¹ Wageningen Bioveterinary Research, Houtriweg 39, 8221 RA, Lelystad, NL  ² GSK Vaccines USA, 14200 Shady Grove Road, Rockville, MD 20850, USA  ³ GSK Vaccines Belgium, 89, Rue de l’Institut, 1330 Rixensart, Belgium

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ARIN GHASPARIAN, Armando Zuniga, Oliver Rassek, Melissa Vrohlings  
Virometix AG

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MOSES KITI¹, Alessia Melegaro², Ciro Cattuto³, James Nokes⁴  
¹ KEMRI-Wellcome Trust Research Programme, Kenya  ² Bocconi University  ³ ISI Foundation  ⁴ KEMRI-Wellcome Trust Research Programme, Kenya; Warwick University, UK

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BINH HA¹, Samadhan Jadhao¹, Zunlong Ke², Elizabeth Wright³, Larry Anderson¹  
¹ Emory University  ² Cambridge University  ³ University of Wisconsin-Madison
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XUETING QIU, Justin Bahl
University of Georgia College of Veterinary Medicine, Dept. of Infectious Diseases

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ELIJAH KOLAWOLE OLAIDOPO, I.O Omomowo, J.K. Oloke, E. H.Awoyelu
Ladoke Akintola University of Technology,P.M.B. 4000, Ogbomoso, Nigeria

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MICHAEL TENG 1, Kim Tran 1, Olivia Harder 2, Stefan Niewiesk 2
1 Department of Internal Medicine, University of South Florida Morsani College of Medicine 2 Department of Veterinary Biosciences, The Ohio State University College of Veterinary Medicine

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JESSICA ATWELL, Robert Weatherholtz, Raymond Reid, Kamelia Kellywood, Mathuram Santosham, Katherine O’Brien, Laura Hammitt
Johns Hopkins Center for American Indian Health, Johns Hopkins Bloomberg School of Public Health, Baltimore MD; Center for Immunization Research, Johns Hopkins Bloomberg School of Public Health

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MIAOGE XUE 1, Rongzhang Wang 2, Mijia Lu 2, Olivia Harder 2, Phylip Chen 2, Anzhong Li 2, Xueya Liang 2, Mark Peeples 2, Stefan Niewiesk 2, Jianrong Li 2
1 THE OHIO STATE UNIVERSITY 2

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JUAN GUTMAN
Fundación Infant
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XIAO LI 1, Marina Antillon 1, Lander Willem 1, Joke Bilcke 1, Mark Jit 2, Philippe Beutels 3

1 Centre for Health Economics Research & Modelling Infectious Diseases, University of Antwerp, Belgium 2 Department of Infectious Disease Epidemiology, London school of Hygiene and Tropical Medicine, UK 3 Centre for Health Economics Research & Modelling Infectious Diseases, University of Antwerp, Belgium

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CYNTHIA MATHEW 1, Reena Ghildyal 2, Andrea Burgarcic 3

1 Respiratory Virology Group, Health Research Institute, University of Canberra, Canberra, 2617, Australia 2 University of Canberra, Australia 3 Endeavour College of Natural Health, Level 2, 269 Wickham St, Fortitude Valley, Queensland, 4006, Australia

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CHARACTERIZATION OF A WILD TYPE HRSV HUMAN CHALLENGE STOCK (RSV-NICA) IN COTTON RATS

ADRIAN WILDFIRE 1, Martha Murreddu 2, Kai Lipinski 3, Marion Hucke 3, Bruno Speder 1, Katrien Vermeiren 1, Rienk Jeeninga 4, Leon de Waal 4, Martin Schutten 4

1 SGS Life Sciences 2 Viroclinics Biosciences.com 3 Vibalogics GmbH 4 Viroclinics Biosciences B.V. 5 Clinical Virology And Diagnostics

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KATHRIN ENDT 1, Yvonne Wollmann 2, Jana Haug 2, Constanze Bernig 2, Markus Feigl 2, Markus Kalla 2, Sonia T. Wennier 2, Robin Steigerwald 2, Mark Suter 3, Paul Chaplin 2, Ariane Volkmann 2

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POSTER SESSION 2
Clinical Studies (CS) Evolution & Epidemiology (EE) Immunology (IMM)

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RSV MONOCLONAL ANTIBODY (MK-1654) PHASE 1 PHARMACOKINETICS (PK) IN HEALTHY ADULTS AND POPULATION PK MODELING FOR PREDICTIONS IN PEDIATRIC PATIENTS

LUZELENA CARO, Hua Ma, Dong Geng, Kalpit Vora, Ghassan Fayad, Dennis Wolford, Antonio Aliprantis, Brian Maas

Merck & Co., Inc., Kenilworth, NJ, USA
A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL TO ASSESS THE SAFETY AND TOLERABILITY OF A RESPIRATORY SYNCYTIAL VIRUS (RSV) NEUTRALIZING MONOCLONAL ANTIBODY (MK-1654) IN HEALTHY SUBJECTS

RADHA RAILKAR 1, Dong Geng 1, Kalpit Vora 1, Hua Ma 1, Brian Maas 1, Luzelena Caro 1, Dennis Wolford 1, Antonios Aliprantis 1, Andrew Lee 1, Laura Sterling 2, Eseng Lai 1

1 Merck & Co., Inc. 2 Celerion

THE P53 TUMOR SUPPRESSOR ENHANCES THE INNATE IMMUNE RESPONSE TO RSV VIA A TLR8 SNP

DANIEL MENENDEZ 1, Joyce Snipe 2, Jacqui Marzec 3, Cindy Innes 4, Fernando P Polack 5, Mauricio Caballero 5, Shepherd H.Schurman 4, Steven R. Kleeberger 2, Michael A.Resnick 2

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RESPIRATORY SYNCYTIAL VIRUS (RSV) AND INFLUENZA INFECTIONS IN CHILDREN UNDER 2 YEARS OF AGE IN ULAANBAATAR, MONGOLIA AND RELATION TO PNEUMOCOCCAL CARRIAGE.

LIEN ANH HA DO

Murdoch Children’s Research Institute

RSV-SPECIFIC T CELL RESPONSES IN THE PHASE I CLINICAL TRIAL OF THE STABILIZED PREFUSION RSV F SUBUNIT PROTEIN DS-CAV1

TRACY RUCKWARDT, Juliane Hill, Kaitlyn Morabito, Man Chen, Pamela Costner, LaSonji Holman, Somia Hickman, Michelle Crank, Grace Chen, Julie Ledgerwood, Barney Graham

NIH/NIAID/VRC

MOLECULAR DIAGNOSTIC AND SEROLOGICAL INVESTIGATION OF RSV IN PEDIATRIC LONG TERM CARE FACILITIES

MOHAMMED RASHEED 1, Mila Prill 2, Suvang Trivedi 1, Brett Whitaker 2, Becky Dahl 2, Gayle Langley 2, Susan I. Gerber 2, Lindsay Kim 2, Sibyl Wilmont 3, Lisa Saiman 3, Natalie J. Thornburg 2

1 IHRC Inc. , Atlanta GA 2 Centers for Disease Control and Prevention, National Center for Immunizations and Respiratory Diseases 3 Department of Pediatrics, Columbia University Irving Medical Center

THE IMPORTANCE OF RESPIRATORY SYNCYTIAL VIRUS IN THE YOUNG FEBRILE INFANT POPULATION

ERIN NICHOLSON 1, Vasanthi Avadhanula 2, Laura Ferlic-Stark 2, Kirtida Patel 2, Karen Gincoo 2, Pedro Piedra 1

1 Baylor College of Medicine Department of Molecular Virology and Microbiology; Baylor College of Medicine Department of Pediatrics-Infectious Disease 2 Baylor College of Medicine Department of Molecular Virology and Microbiology
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DIGITAL BIOMARKERS TO DETECT RESPIRATORY SICKNESS BY MEASURING; ACTIVITY, VOICE, AND AUDIBLE RESPIRATORY SYMPTOMS

PAUL WACNIK 1, Hao Zhang 1, Adan Rivas 1, Shyamal Patel 1, Dimitrios Psaltos 1, Mar Santamaria 1, Jon Bruno 1, Rachel Chasse 1, Armando Cortez 1, Dmitri Volfson 1, Greg Schiurring 2, Anne O’Brien 2

1 Digital Medicine & Translational Imaging, Early Clinical Development R&D, Pfizer Inc., Cambridge, MA 2 Department of Physical Medicine & Rehabilitation, Spaulding Rehabilitation Hospital, Harvard Medical School

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KEMRI-Wellcome Trust Research Programme

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ANGELA GENTILE, Maria Florencia Lucion, Maria Soledad Areso, Julia Bakir, Mariana Viegas, Alicia Mistchenko, Agustina Maria Rainelli, Lucia Paglieri, Maria del Valle Juarez

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US Centers for Disease Control and Prevention

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IRUM PERVEEN
Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad, Pakistan

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