Transcriptional effects of enterovirus D68 infection

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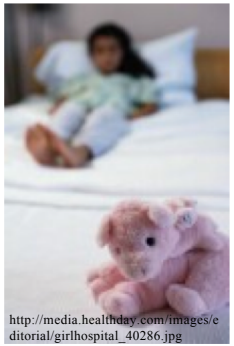
2014 Outbreak of Acute Flaccid Myelitis (AFM)

Mid-August 2014 – mid-January 2015:

- 120 cases of acute flaccid myelitis/paralysis (AFM) in the US with unknown etiology (Ayscue 2014, Messacar 2015, Van Haren 2015, Greninger 2015)



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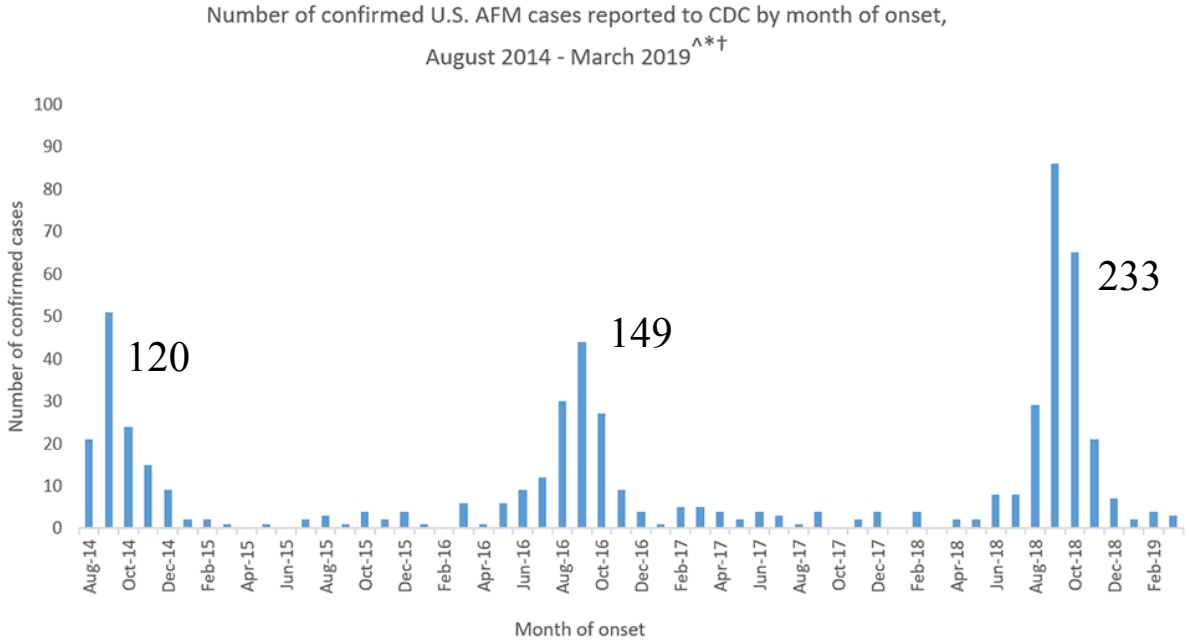
Acute flaccid myelitis outbreak



* The data shown from August 2014 to July 2015 are based on the AFM investigation case definition: onset of acute limb weakness on or after August 1, 2014, and a magnetic resonance image (MRI) showing a spinal cord lesion largely restricted to gray matter in a patient age ≤21 years.

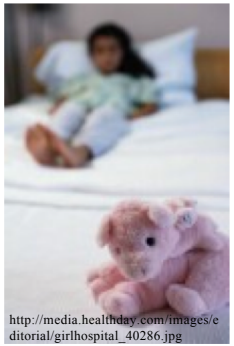
† The data shown from August 2015 to present are based on the AFM case definition adopted by the Council of State and Territorial Epidemiologists (CSTE): acute onset of focal limb weakness and an MRI showing spinal cord lesion largely restricted to gray matter and spanning one or more spinal segments, regardless of age.

Source - http://www.cdc.gov/acute-flaccid-myelitis/afm-surveillance.html

2014 Outbreak of Acute Flaccid Myelitis (AFM)

Mid-August 2014 – mid-January 2015:

- 120 cases of acute flaccid myelitis/paralysis (AFM) in the US with unknown etiology (Ayscue 2014, Messacar 2015, Van Haren 2015, Greninger 2015)
- 1,153 confirmed cases of EV-D68 infections, including 14 deaths in the US; likely many more cases of mild EV-D68 infections (CDC)
- EV-D68 etiology
  - 4/10 paralyzed children in CO were EV-D68 positive in respiratory samples
  - 2/23 AFM cases in CA (June 2012 – June 2014) were EV-D68 positive
  - EV-D68 positive AFM cases in Canada, France, Norway, and Australia (Skowronski 2015, Lang 2014, Bragstad 2015, Pfeiffer 2015, Levy 2015)



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Enterovirus clinical symptoms

Most infections are asymptomatic or mild respiratory symptoms

Genus: *Enterovirus*
Enterovirus A
Enterovirus B
Enterovirus C
Enterovirus D
Enterovirus E
Enterovirus F
Enterovirus G
Enterovirus H
Enterovirus J
Rhinovirus A
Rhinovirus B
Rhinovirus C
unclassified Enterovirus
unclassified Rhinovirus
uncultured enterovirus
unknown

Polioviruses, types 1-3

Paralysis (complete to slight muscle weakness)
Aseptic meningitis
Undifferentiated febrile illness, particularly during the summer

Coxsackieviruses, group A, types 1-24

Herpangina
Acute lymphatic or nodular pharyngitis
Aseptic meningitis
Paralysis
Exanthema
Hand-foot-and-mouth disease (A10, A16)
Pneumonitis of infants
"Common cold"
Hepatitis
Infantile diarrhea
Acute hemorrhagic conjunctivitis (type A24 variant)

Echoviruses, types 1-33

Aseptic meningitis
Paralysis
Encephalitis, ataxia, or Guillain-Barre syndrome
Exanthema
Respiratory disease
Others: Diarrhea
Pericarditis and myocarditis
Hepatic disturbance

Enterovirus, types 68-71

Pneumonia and bronchiolitis
Acute hemorrhagic conjunctivitis (type 70)
Paralysis (types 70, 71)
Meningoencephalitis (types 70, 71)
Hand-foot-and-mouth disease (type 71)

Fields Virology, 2007

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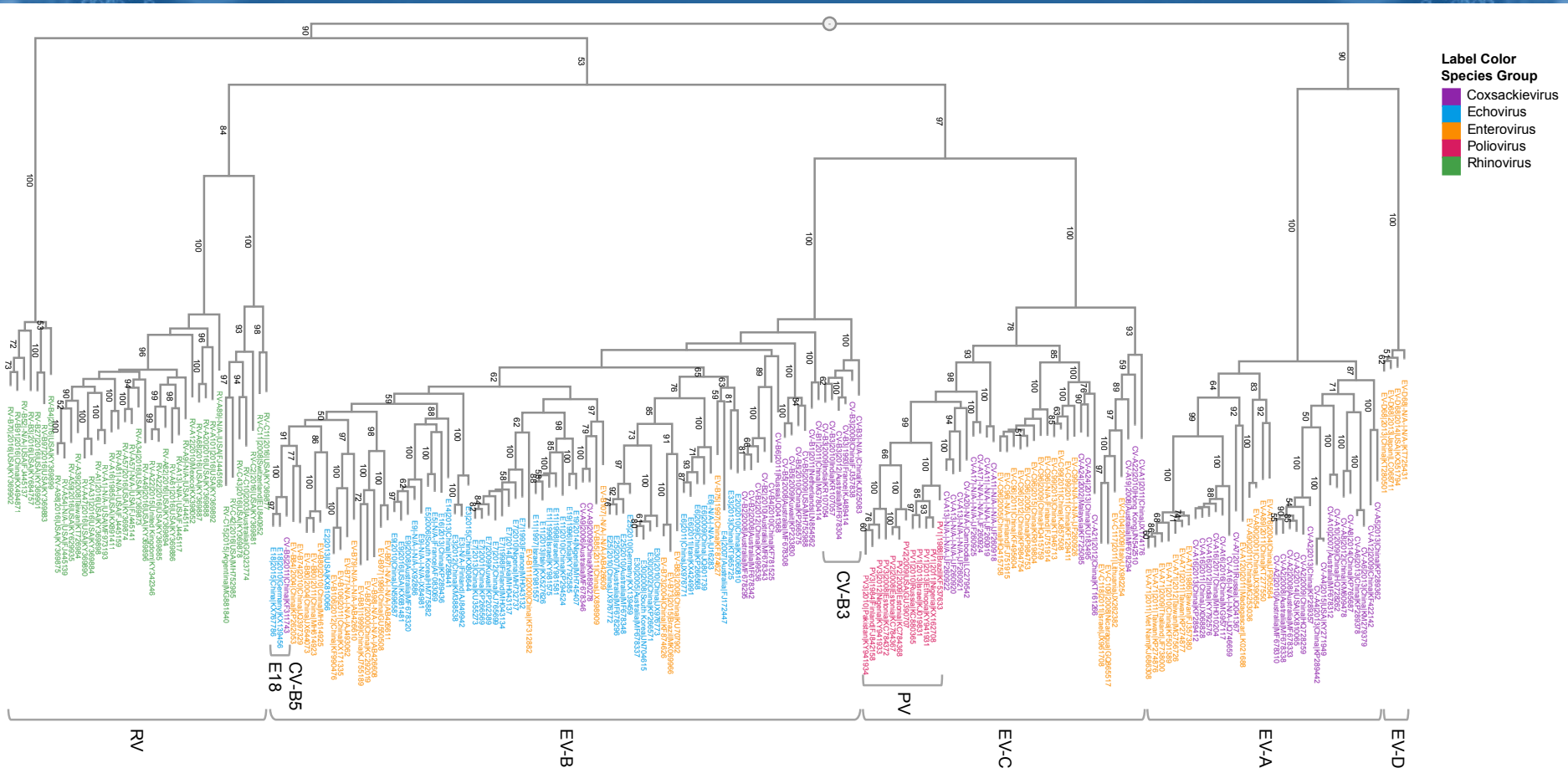
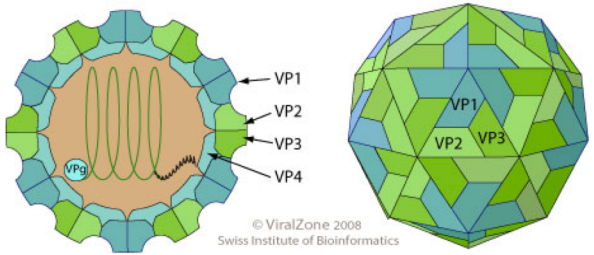
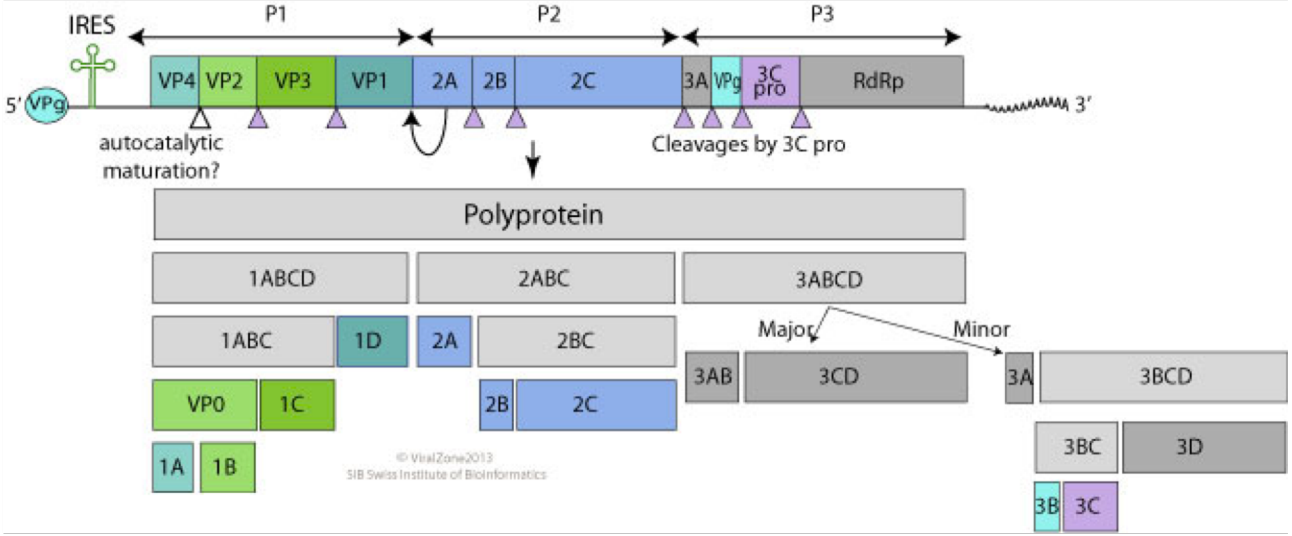
EV phylogenetic tree



Enterovirus D68

Picornaviridae family of non-enveloped +ssRNA





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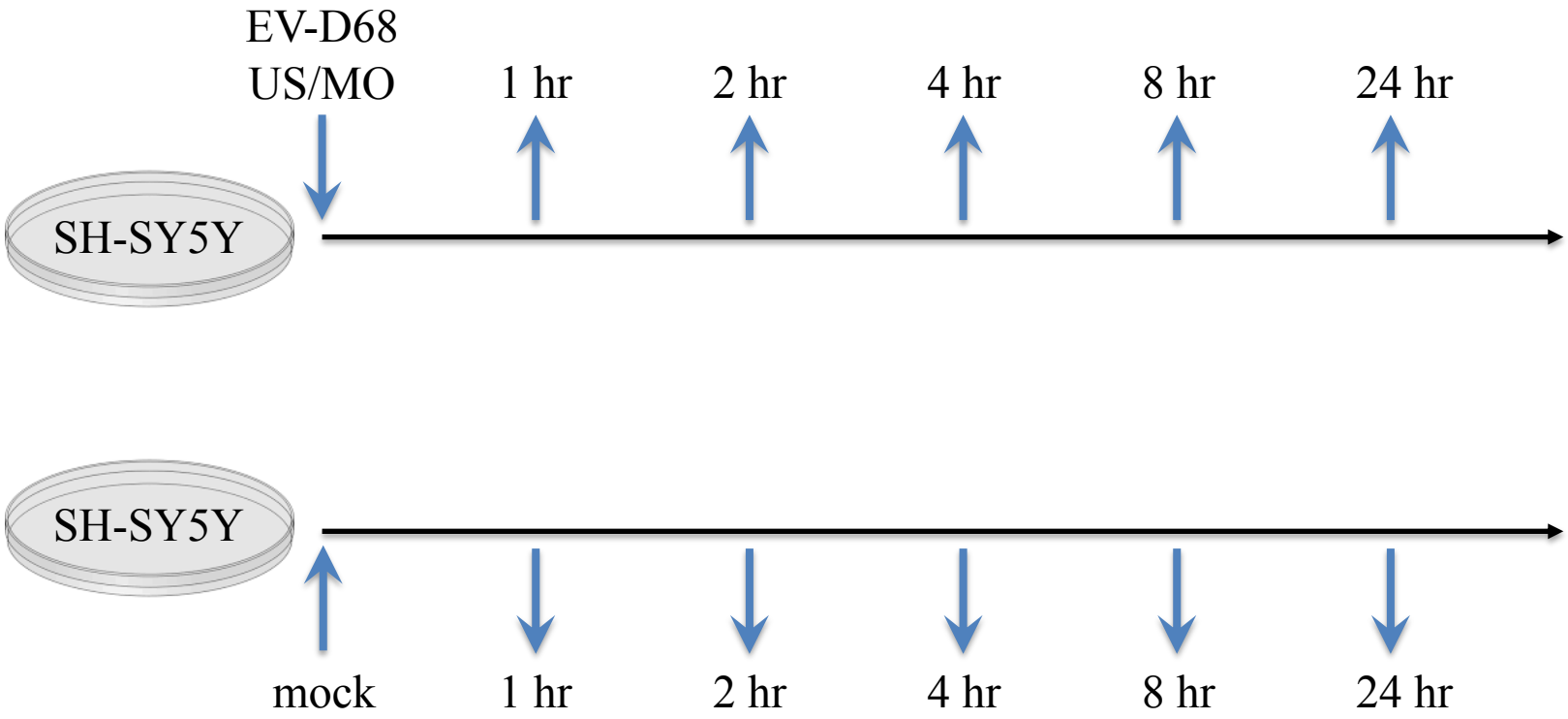
Contemporary Circulating Enterovirus D68 Strains Have Acquired the Capacity for Viral Entry and Replication in Human Neuronal Cells

David M. Brown,[a] Alison M. Hixon,[b] Lauren M. Oldfield,[a] Yun Zhang,[c] Mark Novotny,[c] Wei Wang,[a*] Suman R. Das,[a*] Reed S. Shabman,[a*] Kenneth L. Tyler,[d,e,f,g] Richard H. Scheuermann[c,h]

Transcriptional response to D68 infection



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