In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 18-1624V

Date: August 28, 2025

R.G.C *and* S.S.C., *as parents and legal representatives of their minor son, A.G.C.*,	*
Petitioners,	*
v.	*
SECRETARY OF HEALTH AND HUMAN SERVICES,	*
Respondent.	*

Ramon Rodriguez, Esq., Siri & Glimstad LLP, Richmond, VA, for petitioners.
Mary Holmes, Esq., U.S. Department of Justice, Washington, DC, for respondent.

RULING ON ENTITLEMENT[1]

Roth, Special Master:

On October 19, 2018, R.G.C and S.S.C.[2] ("petitioners") filed a petition on behalf of their son, A.G.C., under the National Vaccine Injury Compensation Program, 42 U.S.C. § 300aa-10 *et seq.*[3] ("Vaccine Act" or "the Program"). Petitioners alleged that the influenza ("flu") vaccine A.G.C. received on October 20, 2015 caused him to develop a seizure disorder, or in the alternative, significantly aggravated an underlying disorder resulting in his seizure disorder. *See* Petition ("Pet.") at 1-2, ECF No. 1.

[1] Because this Ruling contains a reasoned explanation for the action taken in this case, it must be made publicly accessible and will be posted on the United States Court of Federal Claims' website, and/or at https://www.govinfo.gov/app/collection/uscourts/national/cofc, in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). This means the Ruling will be available to anyone with access to the internet. In accordance with Vaccine Rule 18(b), the parties have 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. Any changes will appear in the document posted on the website.

[2] This Decision was originally filed on August 28, 2025. On September 9, 2025, petitioners filed a Motion to Redact. The Motion was granted on October 3, 2025. In this reissued version, petitioners' names were changed to reflect the redaction. The remainder of this Decision is unchanged.

[3] National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755. Hereinafter, for ease of citation, all "§" references to the Vaccine Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa (2018).

After carefully analyzing and weighing the evidence presented in accordance with the applicable legal standards, the undersigned finds that petitioners have provided preponderant evidence that the flu vaccine was a substantial factor in causing A.G.C.'s seizure disorder.

I. Procedural History

Petitioners filed their claim on October 19, 2018. The matter was assigned to me on that day. ECF Nos. 1, 4. Medical records were filed on November 12, 2018, and December 20, 2018 along with a Statement of Completion. Petitioners' Exhibits ("Pet. Ex.") 1-23, ECF Nos. 7-12.

Respondent filed his Rule 4(c) Report on April 2, 2019, advising against compensation. ECF No. 14. Additional medical records were filed on April 3, 2019. Pet. Ex. 24-25, ECF No. 15.

After several extensions, petitioners filed the expert report of Stephen Nelson, M.D. with corresponding medical literature on September 30, 2019. Pet. Ex. 29-38, ECF No. 28. Respondent filed a status report on December 30, 2019 claiming that the report was insufficient. He advised that he did not intend to file a responsive report unless petitioners filed a sufficient supplemental report. ECF No. 30.

After several more extensions, petitioners filed a supplemental report from Dr. Nelson along with a report from Lawrence Steinman, M.D. and additional medical literature, on July 13 and 17, 2020. Pet. Ex. 39-62, ECF Nos. 35, 37-38.

Respondent filed expert reports from Gregory Holmes, M.D. and Andrew MacGinnitie, M.D. with medical literature on December 2, 2020; January 19, 2021; and February 23, 2021. Respondent's Exhibits ("Resp. Ex.") A-F, ECF Nos. 43, 45-46.

The parties exchanged further expert reports on March 4, 2021; April 1, 2021; June 2, 2021; and July 26, 2021. Pet. Ex. 63-73, ECF Nos. 47, 50, 56; Resp. Ex. G, ECF No. 53. An entitlement hearing was scheduled for October 3-4, 2022. ECF Nos. 64, 67.

Additional medical records were filed on June 30, 2022 and July 19, 2022. Pet. Ex. 82-90, ECF Nos. 68, 70.

Pre-hearing submissions were filed, and a two-day entitlement hearing was held as scheduled on October 3 and 4, 2022. ECF Nos. 72, 75-83, 85-89.

Both parties presented new evidence just prior to and/or at the hearing. The experts were given the opportunity to review and respond to the new evidence following the hearing. ECF No. 90. Additional evidence and expert reports were filed. Resp. Ex. J-M, ECF Nos. 91, 95; Pet. Ex. 94, ECF No. 96.

A status conference was held on January 17, 2023, and the parties later agreed that post-hearing briefs were unnecessary. ECF Nos. 98-99.

This matter is now ripe for decision.

II. Background

A. Medical Terminology[4]

Encephalopathy is a clinical state of altered mental status, manifesting as confusion, disorientation, behavioral changes, or other cognitive impairments with or without inflammation of brain tissue. Encephalopathy without inflammation can be triggered by metabolic or toxic conditions and may be associated with specific infectious agents including influenza virus. Resp. Ex. A Tab 1 at 3.

Encephalitis is defined as brain inflammation. Resp. Ex. A Tab 1 at 3. The most common symptoms of encephalitis are fever, vomiting, headache, seizures, and focal deficits. Resp. Ex. A Tab 7 at 3; Resp. Ex. A Tab 2 at 1-2; Pet. Ex. 42 at 3.

Different types of encephalitis include infectious encephalitis, post-infectious, post-immunization encephalitis, or encephalomyelitis. Resp. Ex. A Tab 2 at 1. Autoimmune encephalitis is thought to be associated with antibodies against neuronal cell-surface or synaptic proteins. It resembles infectious encephalitis with neurological and psychiatric manifestations but without fever or CSF pleocytosis. Pet. Ex. 42 at 3. It was initially thought that autoantibodies targeted the voltage-gated potassium channels ("VGKC") itself. Pet. Ex. 50 at 1-2. Later research showed the target antigens of autoantibodies were actually the proteins leucine-rich glioma-inactivated 1 ("LGI1") and contactin-associated protein like-2 ("CASPR2"), which are complexed with the VGKC. Pet. Ex. 42 at 13.

Adenovirus is a common cause of childhood illnesses and often manifests as respiratory illness or gastroenteritis but may also have ocular, cutaneous, and urinary manifestations. Pet. Ex. 54 at 1; Resp. Ex. A Tab 9 at 1. Neurological manifestations like meningoencephalitis or acute necrotizing encephalopathy have also been observed, particularly in immunocompromised children. Resp. Ex. A Tab 5 at 1; Resp. Ex. A Tab 4 at 1.

B. Pre-Vaccination Medical History

A.G.C. was born full term without complications on January 7, 2010. He reached all developmental milestones in his first five years of life and received routine vaccinations including yearly flu vaccines without event. *See generally* Pet. Ex. 6.

A.G.C. has food allergies, asthma, eczema, and autoimmune alopecia with eosinophilia[5] since 2014. Pet. Ex. 6 at 40, 68; Pet. Ex. 8 at 1, 22; Pet. Ex. 77 at 64; Pet. Ex. 78 at 7; Pet. Ex. 89 at 10; *see generally* Pet. Ex. 5. He had frequent upper respiratory illnesses, with cough, wheezing, fever, and asthma exacerbation. *See generally* Pet. Ex. 6.

[4] The full citations to the medical literature are contained in an appendix.

[5] Eosinophilia is the formation and accumulation of an abnormally large number of eosinophils in the blood. Eosinophils are granular leukocytes with a nucleus that usually has two lobes connected by a slender thread of chromatin, and cytoplasm containing coarse, round granules that are uniform in size. Eosinophilia DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 622 (33rd ed. 2020) [hereinafter DORLAND'S]; Eosinophil, DORLAND'S 622.

He was noted to be a well child at his 4-year-old check up on May 9, 2014, meeting all milestones. Pet. Ex. 6 at 68. He received Hepatitis A and flu vaccines on October 3, 2014 without event. *Id*. at 93.

On September 28, 2015, A.G.C. was presented to the pediatrician with two days of fever and a cold for two weeks. He had a cough, low grade fever, and poor sleep. The assessment was sinusitis and exacerbation of his asthma. An antibiotic and prednisone were prescribed. Albuterol was ordered three times daily. Pet. Ex. 6 at 101.

C. Post-Vaccination Medical History

On October 20, 2015, A.G.C. was presented for his five-year-old well child checkup. Pet. Ex. 6 at 102. The subject flu vaccine was given on this date. *Id.*

A.G.C. was presented to the pediatrician two days later, on October 22, 2015, for strep exposure and a low-grade fever for two days. A flu shot two days prior was noted. He was positive for sore throat, congestion, nausea, rhinorrhea, abdominal pain, and headache for two days. A rapid strep test was negative. The assessment was pharyngitis. Tylenol was prescribed. Pet. Ex. 6 at 103.

On October 26, 2015, A.G.C. was presented to the University of Virginia emergency department by ambulance for a seizure. Pet. Ex. 9 at 171. His mother reported fever two days ago, three weeks of incontinence at night, including the night before, and one week of daytime urine leaking. There was no coordination change or headaches. Mom reported that he was hard to wake that morning and was very tired. While driving, she noticed he had a localized seizure with left-sided gaze then was completely unresponsive for about ten minutes. When EMS arrived, he was awake and alert but lethargic. Blood sugar was 107. He was incontinent during the seizure. Mom reported that he was active yesterday and played soccer. She denied recent trauma. He had no seizure history. *Id*. On examination he had no fever and appeared well nourished but was not speaking, was agitated, and was uncooperative. Examination was otherwise normal. *Id*. at 172. He had another seizure while in the ER that lasted 3-4 minutes with rightward eye deviation and lip smacking but no generalized movements. Ativan was successful. His head CT was normal. *Id.* at 173. Suspicion for meningitis was low because he was afebrile with no preceding "prodrome of not feeling well." Neurological consult recommended loading with Keppra. Blood work was unremarkable. *Id*.

A.G.C. was discharged on October 29, 2015 with a diagnosis which included: seizures of unknown etiology (viral vs. Anti-NMDA vs. onset of epilepsy). Pet. Ex. 9 at 181. The discharge summary included that his mom reported that the night before his presentation, he was not acting like himself, saying strange things, and not responding normally. He had a recent illness with fever two days ago with some URI symptoms. All siblings had the same. Rapid strep was negative. The day before the seizure he was playing soccer and was active. He had no tick bites, but multiple family members had tick exposure. The day of admission he awoke tired and fussy. Mom noted the first seizure while she was driving and that he was post-ictal when EMS arrived roadside. He was more awake upon arrival to the hospital but never fully returned to baseline. He had another seizure while in the ER that lasted about 5 minutes with eyes deviating to the right and lip and tongue smacking, which stopped with Ativan. He was loaded with Keppra after a neurological

consult. *Id.* During his hospitalization and following the Keppra load and Ativan, he had an unsteady gait, word finding difficulty, agitation, and some strange behaviors and speech. He had 4 more seizures not returning to baseline on the morning of October 28. Keppra was increased and Ativan was given during seizures. *Id*. An EEG was abnormal and showed slowing suggestive of an underlying moderate encephalopathy of nonspecific etiology but could have been due to sedatives. *Id*. at 181, 186, 213-14. MRI was normal. *Id.* at 186, 359-61. White blood count ("WBC") on cerebral spinal fluid ("CSF") was high at 13 but negative for HSV, enterovirus, antibodies for autoimmune encephalopathy, and NMDA-R. *Id*. at 182, 343-44, 346, 349. Lyme disease testing was negative. *Id*. at 345. He had no further seizures on increased Keppra with slightly improved gait. *Id*. at 181. He had occasional strange comments but improved greatly. The working diagnosis included epilepsy with uncommon presentation, viral encephalitis not from enterovirus, or anti-NMDA receptor encephalitis. *Id*. at 181-82. His blood work and urine were normal on discharge. *Id*. at 183-85.

The following day, A.G.C. was presented to Children's National Medical Center due to his parents' concern for focal seizures. Pet. Ex. 10 at 3. He had no fever, headache, vomiting, diarrhea, or stomach or muscle pain. *Id*. He was a 5-year-old boy with new focal seizures that started 4 days ago. *Id*. at 8. The UVA work up and hospitalization was noted. Mom reported 4 typical focal seizures today, with left eye gaze, lip smacking, and decreased responsiveness, lasting less than 3 minutes each. Diastat was not used. His last seizure was roughly 30 minutes prior to arrival. On arrival he was post-ictal, opening his eyes, following commands, but non-verbal. He returned to baseline while in the ER. *Id.* Neurological examination was normal. *Id.* at 9. The differential included new onset seizure, focal seizures, encephalitis/cerebritis with mild CSF pleocytosis.[6] He was afebrile, well appearing, and on a maximum dose of Keppra with continued concern for breakthrough seizures. He was admitted to Neurology for EEG, repeat MRI, and further monitoring. *Id.*

A.G.C. was discharged from Children's on November 13, 2015. Pet. Ex. 10 at 64. During his admission, he had multiple clinical and subclinical seizures. Keppra was discontinued, and Trileptal and fosphenytoin were started. EEG done on November 1, 2015 was diagnostic of epilepsy; seizure onset was bilateral, independent, arising out of the occipital and temporal regions, and associated with encephalopathy. *Id*. at 68. The results suggested multifocal onset of seizures, suggestive of channelopathy, meningoencephalitis, autoimmune etiology, or structural process. *Id*. Another EEG on November 7, 2015 was abnormal, indicative of mild to moderate encephalopathy but with no seizures observed. Pet. Ex. 6 at 206-07. He tested positive for adenovirus "per blood and csf", as well as on respiratory viral panel. He was also positive for arbovirus[7] in the serum. Pet. Ex. 10 at 65. The impression was encephalopathy due to viral encephalitis vs. post infectious/post vaccine encephalitis vs. mitochondrial disorder with new onset epilepsy. Pet. Ex. 6 at 232. He received a five-day course of methylprednisolone and two-day course of IVIG. Pet. Ex. 10 at 64. His alanine and lactate were elevated consistent with mitochondrial disorder. He was in the PICU for one day due to persistent seizures. His mental and other neurological findings had

[6] Pleocytosis is the presence of a greater than normal number of cells in the cerebrospinal fluid. Dorland's Online, *Pleocytosis*, https://www.dorlandsonline.com/dorland/definition?id=39556.

[7] Arbovirus refers to any member of an epidemiologic class of viruses that replicate in blood-feeding arthropods and are transmitted by bite to the host. Dorland's Online, *Arbovirus*, https://www.dorlandsonline.com/dorland/definition?id=3975&searchterm=arbovirus.

improved. He was seizure free for 48 hours prior to discharge. He was to follow up with neurology, infectious disease,[8] genetics, and physical therapy. Pet. Ex. 10 at 64; Pet. Ex. 6 at 215-16. The discharge diagnoses included dysautonomia, gait abnormality, CSF pleocytosis, altered mental status, balance problems, adenovirus infection, focal seizure, and nonconvulsive epilepsy; differential diagnoses of the neuroinflammatory condition included viral encephalitis vs. post infectious/post vaccine encephalitis vs. mitochondrial disorder with new onset epilepsy. Pet. Ex. 6 at 245; Pet. Ex. 10 at 69.

A.G.C. was seen in the Neurology Clinic at Children's on November 16, 2015 for follow up. He required a rescue dose of Klonopin over the weekend. His behavior was still a little "off" with some trouble speaking. He had an occasional tic making a chirping noise not there prior to his illness. Mom learned over the weekend that her grandfather had a history of seizures between the ages of 8 and 10 and was taking Dilantin. She also had a first cousin who had two kids with neurologic problems including seizures. Pet. Ex. 15 at 1. CSF was consistent with possible viral encephalitis vs. post-infectious encephalitis. No virus was isolated in the CSF. *Id*. at 4. CSF continued to have pleocytosis with eosinophils present[9], even after IVIG and IV methylprednisolone, suggestive of a continued inflammatory process. Seizures were controlled by multiple medications, but he was not back to baseline and continued to have facial twitching at night. *Id*. The impression was encephalitis and focal seizures. *Id*. at 5.

At his pediatrician visit on November 17, 2015, his medications included Keppra and Trileptal twice daily, Dilantin and clonazepam if needed and rectal valium. He was taking a "mitochondrial cocktail" and lipoic acid. Pet. Ex. 6 at 254. He was scheduled for speech, physical, and occupational therapy appointments. Another EEG was scheduled in two weeks to try and wean Dilantin. The doctor wrote "? autoimmune vs viral- postinfectious enceph". He was to follow up with the specialists as planned. *Id.*

An occupational therapy ("OT") evaluation done on November 23, 2015 for lack of coordination determined that no formal OT was needed. Pet. Ex. 6 at 327, 330. Mom reported he was almost back to baseline. *Id.* at 330. Home programming recommendations were made. *Id*.

A.G.C. was examined at Johns Hopkins on December 1, 2015 for a second opinion. Mom provided the history of a well child until the end of October 2015 when A.G.C. had a viral febrile illness that "started 5 days prior and fever had resolved" before his first seizure on October 25. He also had a flu shot "6 days before". Pet. Ex. 23 at 7-8. In the 4 days prior to his first seizure, he showed some emotional lability and fatigue. On October 25, he had 4 episodes of bedwetting, appeared to be "out of it", and was saying "weird things." He was crying inconsolably and was taken to UVA. Head CT was normal, and EEG showed slowing. He had additional seizures that night with eye and head deviation to one side or the other, occasionally retained awareness, lasting 1-2 minutes sometimes with jerking. The head and eye deviation appeared more prominent on the left. He was prescribed Keppra and discharged. Lumbar puncture ("LP") showed mildly elevated WBC. MRI was normal. *Id*. After a cluster of seizures, A.G.C. seemed to have word finding issues and imbalance. Following discharged he was taken to Children's where repeat LP showed elevated WBC, lactate, and alanine, so he was started on a "mitochondrial cocktail". Seizures returned with

[8] No records from infectious disease were filed.
[9] It does not appear the neurologist knew A.G.C.'s history of eosinophilia prior to the flu vaccine.

face twitching and jerking of the arms, legs, and fingers; he also had auditory, visual, and olfactory hallucinations with odd vocalizations. *Id*. There was concern for autoimmune encephalitis. He was given a steroid load and started on IVIG. He had a questionable allergic reaction to Vimpat but it may have been from IV solumedrol. MRI was repeated and normal. He was switched to oral meds and discharged. Mom reported that an autoimmune encephalopathy panel and anti-NMDA testing was normal. *Id*. His lactate, pyruvate, and alanine were still elevated. *Id*. at 9. The only positive finding was adenovirus. *Id*. Prior to this, A.G.C. had met all milestones. He had appeared to lose some skills after the seizures, but they seemed to be returning and academically he seemed back to where he was. *Id*. There was a family history of seizures and neurological issues. *Id*. at 9-10. The assessment was a 5-year-old with focal seizures that were multifocal based on EEG. *Id*. at 10. He had a large cluster of seizures with encephalopathic presentation a few days after viral illness and flu shot. Mitochondrial screening suggested a possible disorder, so he was to follow up with genetics for mitochondrial DNA and epilepsy panel testing. *Id*. Differential included viral encephalitis, autoimmune encephalitis, underlying epilepsy worsened by illness, mitochondrial disorder worsened by illness/immunization. *Id*. at 11.

A.G.C. was admitted to Children's from December 3 to 4, 2015 for 23-hour EEG for "presumed viral vs. post-infectious encephalitis". Pet. Ex. 12 at 1104. The EEG was abnormal with "background slowing" sometimes more apparent on the left occipital and right posterior temporal regions. *Id*. at 1161. The results suggested non-specific diffuse cerebral dysfunction. "No epileptiform discharges were seen" and the clinical captures determined not to be due to seizure activity. *Id*. While at Children's, a VAERS report was submitted by Roberta DeBiasi which stated that A.G.C. developed seizure activity five days after a flu vaccine that "Resulted in Permanent Disability", "Required Hospitalization (10 days)", and "Required Emergency Room/Doctor Visit". Pet. Ex. 21 at 1-2.

A three-generation pedigree was obtained at a geneticist visit on December 15, 2015. Pet. Ex. 6 at 294-97; Pet. Ex. 15 at 45-49. The assessment was new onset non-motor seizures with unspecified convulsions accompanied by lactic acidosis. Levocarnitine was discontinued but the remainder of the mitochondrial cocktail continued. Additional testing was ordered. *Id*.

A.G.C. was presented to neurology that same day for follow up. The results of a December 3, 2015 EEG showed no epileptiform discharges but some multifocal areas of background slowing. Dilantin was decreased. His eosinophils were still high. An autoimmune panel came back negative. His seizures and mental status had improved with IVIG and IV methylprednisolone. There had been no further clear seizures, but mom reported intermittent, 1-second episodes of eye deviation and staring with a return to baseline right after. He had some disinhibited behaviors with outbursts and abnormal vocalizations mostly when tired. He had frequent myoclonic jerks during sleep that lasted for 30 minutes. He was seen by a neurologist at Johns Hopkins who agreed with the current plan. He was still taking a mitochondrial "cocktail" of vitamins and supplements. Mom felt he was returning to normal but is still not at baseline. Pet. Ex. 15 at 62.

A.G.C. was presented for physical therapy evaluation on December 17, 2015. Mom reported a history of virus-triggered encephalitis. Pet. Ex. 6 at 310. On evaluation, he was age-appropriate in gross motor skills and strength. He demonstrated mild endurance concerns secondary to hospitalization that were being addressed with soccer 2-4 times a week. Formal PT

was not recommended. *Id*. at 312.

A 23-hour EEG performed on January 19-20, 2016 was normal in awake and sleep state and showed no epileptiform abnormality. Pet. Ex. 6 at 336. A repeat EEG on March 28, 2016, showed slower frequency activity indicative of mild encephalopathy but no epileptiform discharges. There were no clinical or subclinical seizures. *Id*. at 397, 415-17.

Follow up with genetics on March 28, 2016 noted a 6-year-old with increasing frequency of myoclonic jerks at night, facial asymmetry, and seizure activity. He had elevated lactate, lactaturia, and hyperalaninemia. Additional testing for mitochondrial disorder was ordered. Pet. Ex. 6 at 400-01.

An MRI and MRA of the brain were performed on March 29, 2016. MRI showed no evidence of intracranial disease process and no abnormal contrast enhancement. There was decreased conspicuity of few small hyperintense bifrontal subcortical white matter lesions, likely sequela of old injury or infection. MRA was normal. Pet. Ex. 15 at 115.

A.G.C. returned to Hopkins on April 5, 2016 for neurology follow up. Pet. Ex. 6 at 419. It was noted that two weeks prior to that visit mom had emailed that A.G.C. was doing well until he was weaned from Keppra for an overnight EEG and suffered severe jerking that culminated in a seizure with drooling and facial asymmetry. *Id*. at 420. The finding on the overnight EEG did not correlate with mom's pushes. Keppra was reloaded and 3 days later he appeared to have improved, though mom reported personality changes with Keppra. *Id*. Mom also reported that one of her other sons used to have facial twitching or jerks when he was an infant which resolved on its own; another had some facial twitches and moderate jerks during sleep; another had some finger twitching and mild jerking during sleep. *Id*. at 421. A.G.C.'s recent recurrence seemed to be from weaning off Keppra. Previous EEGs suggested multifocality. *Id*. at 422.

A.G.C. followed up with neurology at Children's on April 12, 2016. His breakthrough seizures in the setting of weaning from Keppra were noted. His most recent CSF studies were reassuring with no CNS inflammatory process seen 5 months after the initial insult. His waxing and waning functional status was likely related to prolonged recovery from encephalitis. The impression was focal epilepsy and encephalitis and to "[c]onsider reporting as a vaccine related illness." Pet. Ex. 15 at 88-92.

At his neurological follow up at Children's on May 25, 2016, his history of encephalitis was noted to be of unknown etiology. A neuropsychology examination was performed due to difficulties with word retrieval. It was difficult to determine whether his behaviors and cognitive "clouding" were due to medication. The diagnosis remained encephalitis. Pet. Ex. 15 at 114-20.

At a July 18, 2016 neurology visit, the impression was encephalopathy and partial symptomatic epilepsy with complex partial seizures, not intractable, without status epilepticus. Pet. Ex. 6 at 436-40.

A.G.C. was presented to Hopkins for follow up on August 31, 2016 with continued concern for neurocognitive issues and lost skills. His speech was reportedly not clear or accurate, he was

sloppier when he ate, and he had become sensitive to sounds. He was hyper-emotional and seemed more off balance. His history included multifocal epilepsy beginning in the setting of an encephalopathy of unclear etiology, mild asthma, and alopecia areata. He was doing well on Keppra and Trileptal but continued to have some twitching and enuresis after physically stressful days. Genetics were investigating a possible metabolic etiology. Pet. Ex. 6 at 449-53.

On October 10, 2016, A.G.C. was presented to the neurogenetics clinic at Johns Hopkins. Mom reported a history of alopecia areata and eosinophilia. Genetic testing did not reveal any large deletions or known pathogenic variants in the mitochondrial genome. Various disorders were discussed but it was noted that "[t]he unusual feature here are the biochemical abnormalities, which were strongly suggestive of a mitochondrial etiology" and not other conditions discussed. His history of eosinophilia was to be monitored. There was also the concern for myoclonus. Additional blood work was recommended. Pet. Ex. 6 at 459-61.

An inpatient video EEG was performed at Hopkins from October 20, 2016 to October 25, 2016. A.G.C. "appear[ed] to have a complex partial seizure disorder associated with previous encephalitis or similar disorder." Pet. Ex. 6 at 477.

A.G.C. was examined at Kennedy Krieger Institute's Neuropsychology Department on December 15, 2016 for ongoing problems with attention and behavior. The evaluation was consistent with his history of encephalopathy and suggestive of a complex etiology for his symptoms. Pet. Ex. 6 at 482-92.

On January 23, 2017, Hopkins reported normal genetic testing. Mom reported new symptoms of executive dysfunction including attention deficit, disinhibition, dysarthria, and facial asymmetry when talking. The symptoms have worsened over the past two years. Pet. Ex. 23 at 507.

A speech therapy assessment on February 2, 2017 found no need for therapy. Pet. Ex. 6 at 503-07.

At his neurology follow on March 21, 2017, A.G.C. was noted to be a 7-year-old with focal seizures confirmed as multifocal by EEG. He was much improved on extended release Keppra. Pet. Ex. 6 at 509-12.

A.G.C. was noted to be doing better at his September 12, 2017 neurology follow up. Further genetic testing was encouraged with the possibility of coming off the mitochondrial cocktail following testing. Pet. Ex. 6 at 522. There had been no further concern for seizures. *Id*. at 524. The jerkiness overnight was less frequent. Enuresis has ended with stricter bedtimes. Balance and endurance had improved. He was doing third grade schoolwork but was age appropriate for second grade. Facial weakness episodes had stopped. Behavior was much improved. *Id.*

Additional genetic testing results at Hopkins on March 5, 2018 included "[k]nown mutations in *KCNA2* are associated with early infantile epileptic encephalopathy that often includes significant intellectual decline after onset of seizures, as well as poor or absent speech. Seizure types can include multifocal seizures, and early-onset ataxia and myoclonus are associated.

While it is possible that [A.G.C.] could be a very mild presentation of this condition with his mother not having any symptoms . . . as there are maternal family members with early-onset seizures, there is not enough information to confirm this at this point." Thus, genetic testing did not reveal and underlying genetic cause of A.G.C.'s symptoms. Pet. Ex. 23 at 594-95.

At the time of the hearing, A.G.C. had been evaluated for bouts of coughing consistent with paradoxical vocal cord movement, for which he saw a speech therapist. Pet. Ex. 84 at 22-25; Pet. Ex. 86 at 19. He was under the care of an allergist. His medications included albuterol, Flovent, Zaditor, Keppra, hydroxyzine, olopatadine, epinephrine, desloratadine, and levocetirizine. Pet. Ex. 75 at 29-32. He had alopecia, eczema, and eosinophilia but was not on immunotherapy. Pet. Ex. 83 at 1. He continued to follow up with neurology for focal seizures and epilepsy. He was taking extended release Keppra. Pet. Ex. 75 at 17-27; *see also* Pet. Ex. 84 at 55; Pet. Ex. 86.

D. Affidavits and Testimony of Petitioners

a. S.S.C. Affidavit

S.S.C. is A.G.C.'s mother and a board-certified pediatrician. Pet. Ex. 1. She described her son as a healthy baby and toddler who met all milestones. At age five, A.G.C. was an advanced soccer player, quick learner academically, and loved to play with his brothers. *Id*. at 1.

S.S.C. affirmed A.G.C.'s receipt of a flu vaccine at a routine pediatric visit on October 20, 2015 and his first seizure on October 26, 2015. Pet. Ex. 1 at 1-2. She affirmed driving with her five children on October 26, 2015 when she noticed that A.G.C. was not talking which was unusual. *Id*. at 2. She stopped to evaluate him. He was unresponsive but breathing, his body was stiff, neck turned to the right, staring to the right and drooling. He had lost bladder control. She called an ambulance that took him to UVA. When she arrived at UVA, A.G.C. was screaming and struggling against an IV placement, which triggered another partial seizure with neck and eyes deviating to the right and body stiffening. During his hospitalization, his seizures continued with blood draws or IVs, often requiring rescue medications and sedatives. *Id*. He also demonstrated severe and recurrent seizures that did not respond to medications. She grew concerned when she realized the doctors were having trouble finding a diagnosis and appropriate treatment. *Id*. at 3.

S.S.C. affirmed that following his discharge on October 29, 2015, A.G.C. continued to show abnormal neurological signs and recurrent seizures despite anti-seizure medication. He was acting strangely, did not interact normally with family, seemed confused, and his balance and coordination was off. She contacted a pediatric colleague, who suggested she immediately take A.G.C. to Children's Hospital D.C. for inpatient EEG monitoring. A.G.C. had stopped talking and only smiled when she hugged him. Pet. Ex. 1 at 3.

S.S.C affirmed that, while at Children's, testing confirmed that A.G.C. was continuously seizing and additional testing to determine a diagnosis was done. He was in the pediatric ICU for a time. Pet. Ex. 1 at 4.

According to S.S.C., A.G.C. did worse with high dose steroids which caused muscle weakness. He complained of an itchy throat after two infusions. There was no order for Benadryl

and his symptoms escalated with his screaming and clutching his throat. She became frantic and gave him Benadryl from her purse. He had another seizure. The same thing happened the next day. It was determined that he had an allergic reaction to the IV methylprednisolone. Pet. Ex. 1 at 4-5.

S.S.C. stated that whenever A.G.C. became emotional, he had seizures. He also seized upon falling asleep and upon waking. He was sent home after three weeks in the hospital, stabilized "precariously" and on four anti-seizure medications. Pet. Ex. 1 at 5.

He was hospitalized again for a seizure and further testing around Easter when his medications were weaned. Pet. Ex. 1 at 5-6.

According to S.S.C., about a year after being diagnosed with seizures and encephalopathy, A.G.C. was stable during the day but still had questionable seizures during sleep. He was on three anti-seizure medications, had confirmed neuropsychological memory loss, loss of balance, and issues focusing. School and soccer were both difficult. His behavior was "volatile and extremely aggressive". Pet. Ex. 1 at 6. They took him to a pediatric neurologist at Johns Hopkins Medical Center and had him evaluated at Kennedy Krieger for focusing difficulties and hyper behavior. His medications were adjusted, and he slowly improved. In October 2016, his medication was stopped while at Hopkins for continuous EEG monitoring, and he seized again. *Id.* at 6-7.

S.S.C. affirmed that A.G.C. is now stable and maintained on two anti-epileptic medications. He has improved academically and behaviorally but struggles with handwriting. He has returned to soccer, and sleeping is less of a concern. Bedwetting stopped and he has had no seizures since October of 2016. Pet. Ex. 1 at 7-8.

b. S.S.C. Testimony

At the time of the hearing, S.S.C testified to A.G.C.'s receipt of a flu vaccine on October 20, 2015 and first seizure on October 26, 2015. Tr. 36. Prior to that, he was a normal child, reaching all milestones, who was very active and loved to play soccer. Tr. 36. He had the occasional cough, cold or mild illnesses, some food and other allergies, mild asthma, and eczema. Tr. 37. She did have an Epipen and carried Benadryl. Tr. 37. A.G.C. and several of his brothers have alopecia. Tr. 37-38.

S.S.C testified that A.G.C. was up to date on all his vaccines on October 20, 2015 and received the flu vaccine which is recommended for children with asthma. Tr. 38. As of the date of hearing, he had received all required vaccination but no further flu vaccines. Tr. 39.

S.S.C recalled the events on October 26, 2015. They were headed to Charlottesville to visit family when she checked in her rearview mirror and saw that A.G.C. was unresponsive and stiff. Tr. 40-41. She pulled off the road to assess him and called 911. He had wet his pants. She handed him off to the ambulance, took the others to her in-laws then went to the ER at UVA. Tr. 41-42.

S.S.C stated that A.G.C. seemed fine that morning, was active and running around with the others. It was a routine morning of packing to go to grandma. He did not have a fever and ate breakfast. Tr. 42-43.

She had a vague memory that he might have had a mild illness before the first seizure and after the flu vaccine. Tr. 43-46. However, it was Octoberfest and they had gone to the mountains near Charlottesville with family and friends. A.G.C. was fine playing and running around with everyone. Tr. 44. When asked about a pediatric visit on October 22 for a URI, she stated that it "does not have a significant impact on [her] memory as any cause for concern." Tr. 46. She agreed that A.G.C. received the flu shot on a Tuesday, visited the pediatrician on Thursday and was diagnosed with pharyngitis, but the family left for Octoberfest and A.G.C. was fine, ran, and played. Tr. 47. She stated that he had no symptoms of illness "whatsoever" and it was a great weekend. Tr. 47-48. They then came home and were headed back up to Charlottesville on Monday when he had the seizure. Tr. 48. She stated that A.G.C. was fine Sunday night when they got home from Octoberfest, so it was surprising when he suddenly had the seizure on Monday. Tr. 77-78.

S.S.C was asked again about Monday morning, and she stated that maybe A.G.C. was tired and a little fussy, but all kids can be fussy. He was not sick enough to pause their plans due to concerns of a sick child. Tr. 48-49.

S.S.C stated that A.G.C.'s seizure was "out of the blue". When EMS arrived, she transferred his care to them and had to trust that they would make sure he was okay. He was stable, seemed to be coming out of it, and more to a normal conscious state. Tr. 49-50. When she got to the hospital, they were trying to put in an IV and he was screaming and crying. She believed the emotional trauma triggered another seizure. Tr. 50.

S.S.C described the stay at UVA as difficult. A.G.C. had repeated seizures particularly when they tried to put in new IVs. Tr. 50-51. She stated that in between episodes, A.G.C. was not sick just a little out of it. All testing was normal. Tr. 51. She recalled telling the doctor he seemed off balance, but the doctor said he was fine and discharged him. Tr. 51.

S.S.C stated that once home, A.G.C. was eating, drinking and playing but seemed off to her. He was on medications and at one point the side of his face "appeared paralyzed" and lasted for a couple of hours. She recalled telling her husband it was not normal and very strange. She thought he was having a stroke. She kept calling UVA with no response. She paged the doctor with no response. Tr. 52. She then called a pediatric friend, who told her to take A.G.C. to Children's in D.C. They took him on October 30, 2015. Tr. 53-54. At Children's, an EEG was performed and showed seizure activity. He was medicated by IV and his heartrate was going up and down. Tr. 53-55. In her mind, he was having refractory seizures because he was still seizing with all the medications. Tr. 55. He eventually stabilized enough for discharge. Since she and her husband are doctors, they felt it was safe to take him home. Tr. 56.

S.S.C stated that there were many differential diagnoses, with metabolic and infectious always at the top but A.G.C. did not have a fever. Tr. 57. They spoke to multiple specialists with no diagnosis confirmed. The obvious ones were excluded. They then discussed "with the specialist about whether or not this was a flu vaccine-triggered seizure and encephalopathy." Tr. 57. Mitochondrial disorder was considered but he did not improve with a mitochondrial cocktail and genetic testing later ruled out mitochondrial disorder. Tr. 57-58.

According to S.S.C, A.G.C. tested positive for adenovirus at Children's by nasal swab not CSF. He did not have any sickness symptoms, fever, or typical adenovirus meningoencephalitis. Tr. 58-59. In between seizures, he was eating drinking, being a kid, interacting. He had some confusion about different things but "it wasn't an ongoing impaired mental status." Tr. 59. He was on a regular hospital floor not ICU from a septic perspective; the only time he was in the ICU was for autonomic, heart rate instability from seizures. Tr. 59.

She and her husband discussed autoimmune etiologies with A.G.C.'s doctors, and he was given IVIg and high-dose IV steroids, but without improvement. Tr. 60. She described a severe anaphylactic response to the methylprednisolone with significant muscle weakness of the upper body. Tr. 60, 79-80. S.S.C stated that upon discharge there was no concrete diagnosis for A.G.C.'s fulminant seizures despite intensive therapies. That was when they discussed a flu vaccine related injury due to the timing being 6 days after the vaccination with Dr. Wells and his fellow, Dr. Julie. Tr. 61, 78-79, 83-85. After everything else was excluded, "we're looking at a flu vaccine-related seizure, meninges, encephalitis, encephalopathy." Tr. 62, 85. Autoimmune type epilepsy was "finally the diagnosis that we ended up arriving at after dealing with multiple other diagnoses first." Tr. 68. S.S.C explained that adenovirus was found only on nasal swab, not in the CSF and multiple specialists told them that A.G.C. did not have the "characteristics of an adenovirus encephalitis" which is pretty rare and it "was not contributing to any significant systemic illness". Tr. 71, 90-92. The positive adenovirus on the nasal swab was a "red herring". Tr. 90-92.

S.S.C claimed that after eliminating everything else and the conversation with the specialists shifted to flu vaccine as the cause, they asked that the doctors document that, and Dr. Julie said she did. Tr. 71-72, 85-86. Counsel interjected to provide citations in the medical record claiming that this was documented. Tr. 86-89; Pet. Ex. 10 at 69, 79; Pet. Ex. 6 at 436, 437. Upon review of the citations, I noted to counsel that the record repeatedly referred to various conditions in the differential with no conclusion ever reached. Tr. 88.

S.S.C stated that following his discharge from Children's, A.G.C. was on a lot of medications, and she watched him like a "hawk" for any signs of seizures. He had myoclonic jerks when he slept and behavior problems with the medications. Tr. 62-63. In October of 2016, they took him to an epilepsy specialist at Hopkins and they took him off the seizure medications for an EEG. He then had seizures and the medications were restarted. He was seizure free until January 2022 when they tried to wean him off medication but two days later, he had seizure on video EEG. Tr. 64-65.

S.S.C agreed that the medical records document that A.G.C. was positive for adenovirus and for arbovirus (from mosquito bites) and that they were treating him for post-infectious encephalitis. Tr. 72-73. She stated that A.G.C. had the flu vaccine 6 days before his first seizure, had a febrile illness five days before his first seizure but was fine and afebrile that weekend. She agreed the medical records stated otherwise. Tr. 73-74. She agreed that the medical records did not document vaccine related encephalitis. Tr. 73. However, she stated the medical record does not include the conversations they had with the doctors. Testing ruled out many questions that were raised, his seizures were refractory, his presentation did not fit any one thing. It was her understanding that adenovirus and any other infectious processes were ruled out as causes. Tr. 73-76.

When noted to S.S.C that the most recent medical records filed refer to a 12-year-old who began having focal seizures following a viral illness and flu shot, she stated that Dr. Kelly at Hopkins was not involved with A.G.C.'s care at the beginning, she got involved later and was not focused on the etiology but on the seizures and the medication. When they asked about the etiology of A.G.C.'s seizures, Dr. Kelly would not opine on that. Rather, she focused on managing his medications and controlling the seizures. Tr. 81-83.

S.S.C stated at the time of the hearing, A.G.C. was seizure free, in school in advanced classes with good grades, has friends, plays soccer, was thriving and was developmentally well at home and in school. Tr. 65. She has not given A.G.C. any further flu vaccinations. She believes that flu vaccine triggered the immune responses that resulted in A.G.C.'s seizure disorder. Tr. 68-69. No doctor suggested that A.G.C. not receive further flu vaccines; that was a decision made by her and her husband. Tr. 77.

c. R.G.C. Affidavit

R.G.C. is A.G.C.'s father and is board certified in internal medicine and nephrology. Pet. Ex. 2 at 1. He affirmed that A.G.C.'s first seizure was on October 26, 2015—roughly six days after receiving the flu vaccine. He briefly summarized A.G.C.'s condition and clinical course in the days and weeks following the vaccination. *Id.* at 1-2. He noted that A.G.C. suffered from breakthrough seizures or a side effect from a medication and required constant reevaluation. *Id*. at 2.

R.G.C. affirmed that A.G.C.'s personality and behavior changed "quite dramatically" after his first seizure. Pet. Ex. 2 at 2. "The most salient change was his emotional lability, manifested by frequent crying spells that seemed to come out of nowhere." *Id*. He described A.G.C.'s behavior post-vaccination and post-seizure as erratic, unpredictable, and combative. *Id.*

d. R.G.C. Testimony

R.G.C. described A.G.C. as a normal developing boy like the rest of his sons. He had some mild intermittent asthma and food allergies but no serious medical issues. Tr. 17. He had alopecia which did not alarm them because their oldest son has it too. Tr. 21.

He did not recall A.G.C. being sick before October 26, 2015 and stated they were all at Grave's Mountain Lodge with family and he was running around. Tr. 21-23; Pet. Ex. 6 at 101. He did not recall A.G.C. being sick after his flu vaccination. Tr. 29. He assumed that the October 20, 2015 visit was a well child visit. Tr. 23-24; Pet. Ex. 6 at 102.

He did not recall the morning of October 26, 2015. Tr. 24. He only recalled A.G.C. being in good health until he received the phone call from his wife stating that A.G.C. had a seizure while they were driving, and they were headed to UVA. Tr. 17, 29. That was his first seizure. Tr. 17.

R.G.C. went to UVA after work that night. Tr. 18. A.G.C. was placed on Keppra at UVA and sent home several days later. He recalled being concerned that they discharged A.G.C. too

soon. A.G.C. was not himself after discharge and the seizures continued. Tr. 18-19. His wife called a colleague, and they took A.G.C. to Children's where he had continuous EEG monitoring. Tr. 19.

According to R.G.C., at Children's, A.G.C. was put on several anti-seizure medications yet they still could not get control of the seizures. He was at Children's for roughly two weeks. Tr. 19-20. He was finally given IVIg and steroids, and "things seemed to calm down after that." Tr. 20. He recalled that the situation became very serious at one point, and he called a friend who is a priest for last rites. Tr. 20.

R.G.C. stated that after everything else was excluded as a cause for A.G.C.'s initial seizure, they had conversations with the specialists at Children's and concluded that there was no other good explanation other than the flu vaccine he received six days prior. Tr. 26. He recalled that at the end of his hospitalization at Children's there was a discussion about adenovirus, but he was not a sick appearing child, and it was not found in the CSF. Tr. 30-31. Viral encephalitis may have been in the differential, but he did not recall anyone saying that was the diagnosis. Tr. 31. He did not recall specific conversations with the doctors, only that there was a lot of confusion with no definitive conclusion as to etiology. He recalled speaking to Dr. Wells, who believed "the vaccine precipitated this or that hypothesis was . . . likely." Tr. 31-32. R.G.C. agreed that viral encephalitis was in the differential but "no one had any confidence as to what exactly had caused it." Tr. 32-33; Pet. Ex. 10 at 69. He did not recall any conversations with doctors other than with Dr. Wells. Tr. 33.

At the time of hearing, R.G.C. stated that A.G.C. was doing well academically, but they had some concerns with him physically. They are a big soccer family and all the boys play soccer. A.G.C. has dropped off a bit, but they are uncertain if it may be from the medication. Tr. 25. His last seizure was when they went to Hopkins to see if A.G.C. could be weaned off medication but after 3-4 days off medication, he had a seizure. The same thing happened the first time they took him to Hopkins and tried to wean his medication. Tr. 25.

R.G.C. believes A.G.C. has now "wrapped his head around" his seizure disorder. They are focal impaired awareness seizures, so he does not recall them, but he recalls being hooked up to electrodes in the hospital. R.G.C. believes A.G.C.'s alopecia bothers him more. He is generally very responsible in taking his medication. Tr. 26-27. They went to an air show recently, and A.G.C. mentioned wanting to possibly join the Air Force one day, so it is unlikely he has complete awareness of the long-term consequences of his seizure disorder. Tr. 27-28.

E. Expert Reports

1. Petitioners' Experts

a. Dr. Stephen L. Nelson

i. Qualifications

Dr. Nelson is a pediatric neurologist with a specialty in epilepsy. Pet. Ex. 30 at 1. He is board-certified in epilepsy, neurology with special qualification in child neurology, and general

pediatrics. *Id*. at 2. He obtained his PhD in biomedical sciences from University of California Riverside in 1996 and his MD from University of California San Diego in 2000. *Id*. at 3. He then completed residency at Wilford Hall Medical Center, then completed a child neurology fellowship at Stanford University School of Medicine. He is currently a practicing pediatric neurologist and is the Director of Pediatric Neurology and of Pediatric Neurodiagnostics at Tulane-Lakeside Hospital. *Id*. at 3-4.

ii. Opinion

Dr. Nelson provided a summary of A.G.C.'s medical history, noting him to be an overall healthy child until October 26, 2015 when he was presented to and admitted to UVA for seizures. He had received an influenza vaccine on October 20, 2015. Pet. Ex. 29 at 2; Tr. 115-16. He was then admitted to CHMC on October 30, 2015 for breakthrough seizures. An EEG was abnormal with focal and generalized and multifocal seizures requiring a variety of medications. CSF was negative for infection, but respiratory testing was positive for adenovirus. Pet. Ex. 29 at 2.

Dr. Nelson opined that A.G.C. had an abrupt onset of intractable seizures and encephalopathy/encephalitis within days of his flu vaccine. He deferred to Dr. Steinman to explain the immunological process. Pet. Ex. 29 at 2-3; Pet. Ex. 39 at 1; Pet. Ex. 72 at 2; Tr. 126, 145. He submitted that the flu vaccine and flu infection have been associated with encephalopathy and encephalitis. Pet. Ex. 29 at 3. He testified at hearing that anything that causes brain dysfunction or brain injury may result in epilepsy because the body may continue to produce antibodies that could cause neuronal dysfunction, or prolonged seizures can cause injury to the brain resulting in epilepsy. Tr. 121-22. "Given that AC developed symptoms within days of the influenza vaccination, and no other etiology was found, the most likely cause for AC's abrupt symptom onset was the influenza vaccine that he received on 10/20/2015." Pet. Ex. 29 at 3.

He further submitted that A.G.C.'s clinical course, normal MRI, and abnormal EEG were "entirely consistent with autoimmune encephalitis". Tr. 116, 118-19, 141, 146. The imaging and CSF did not show evidence of viral encephalitis, nor was he very ill. Tr. 118, 146, 148-49. Typically, there are more abnormalities on lumbar puncture and on MRI in viral encephalitis, as well as evidence of elevated intracranial pressure. Tr. 129. In fact, the hallmark of viral encephalitis is elevated white blood cell count, but elevated WBC is seen in autoimmune encephalitis as well to a lesser degree. Tr. 130-32. A.G.C.'s WBC was only modestly elevated, suggesting he had autoimmune encephalitis. Tr. 132. He later agreed that lumbar puncture would not distinguish between autoimmune or post-infectious encephalitis; it would only differentiate active viral infection. Tr. 139-40. At hearing he stated that adenovirus was detected in the nasopharynx—not in the CSF or blood. Tr. 122. He concluded that the autoimmune encephalopathy was "either due to the vaccine or a vaccine in combination with the adenovirus." Tr. 119, 154-55.

Dr. Nelson agreed with Dr. Steinman and Dr. Holmes that the pre-existing adenovirus infection could have allowed multiple agents to pass through the blood brain barrier and enter the brain, including inflammatory cells activated in response to the flu vaccine. Pet. Ex. 72 at 1-2; Tr. 142-44. He agreed with respondent that "the vast majority of patients administered the influenza vaccine do not develop an autoimmune reaction," but argued "that does not prove that autoimmune

meningoencephalitis cannot occur in the right patient under the right set of conditions as in AC." Pet. Ex. 72 at 2; Tr. 134-35, 157, 332-37.

b. Dr. Lawrence Steinman

i. Qualifications

Dr. Steinman obtained his MD from Harvard University in 1973 and completed his residency in pediatrics and in pediatric and adult neurology at Stanford University in 1980. He is board-certified in neurology. Pet. Ex. 91 at 1-2. He has held various academic positions at Standford University and at the Weizmann Institute of Science and holds over forty patents related to immunotherapies. *Id*. at 2-3. He served on the advisory committee at the Institute of Medicine, Muscular Dystrophy Association, National Multiple Sclerosis Society, and more over the course of his career. *Id.* at 4.

ii. Opinion

Dr. Steinman summarized A.G.C.'s medical history and agreed the appropriate diagnosis was "viral encephalitis versus autoimmune encephalitis." Pet. Ex. 46 at 4. Testing ruled out genetic or metabolic causes of A.G.C.'s condition. He opined that A.G.C. had viral encephalitis from adenovirus, autoimmune encephalitis from the vaccine, or a combination of the two. *Id.*; Tr. 168-69.

Dr. Steinman provided that both the flu vaccine and adenovirus infection could trigger an immune response to contactin-associated protein like-2 ("CASPR2"), a protein associated with the ion channel known as the voltage-gated potassium channel ("VGKC") which is associated with epilepsy. Pet. Ex. 46 at 5, 8; Tr. 177. While he could not distinguish whether the adenovirus or the influenza vaccine was the trigger, the adenovirus infection and the influenza vaccine could have combined to create a "perfect storm". Pet. Ex. 46 at 8; Tr. 168-69. He added that the antigenic fragments of the vaccine might have breached the blood brain barrier that was "leaky" due to an adenoviral encephalitis. Pet. Ex. 63 at 3. Dr. Steinman offered three possible scenarios, the flu vaccine as the cause, the adenovirus as the cause, or the flu vaccine and the adenovirus combined as the cause. He concluded that two out the three involve flu vaccine making the flu vaccine more likely than not a substantial factor in contributing to A.G.C.'s seizure disorder. Pet. Ex. 46 at 1, 8; Pet. Ex. 73 at 1-2.

Dr. Steinman described adenovirus as a well-known tropism[10] that is highly cytotoxic, which explains its proclivity for triggering encephalitis. Pet. Ex. 63 at 3; Pet. Ex. 66. But CNS dysfunction following adenovirus is "rare" based on *Huang*, which observed encephalitis after adenovirus infection in only 3.3% of patients. This means that approximately 97% of people with adenovirus do not have CNS dysfunction or seizures. Further, it is unclear how soon or how often after adenoviral infection encephalitis might present. *Huang* observed a "minimal time of onset as 5 days". Pet. Ex. 63 at 3; Pet. Ex. 67; Pet. Ex. 73 at 2; Tr. 172. Dr. Steinman maintained that the

[10] Tropism refers to a reaction to a stimulus. Dorland's Online, *-tropism*, https://www.dorlandsonline.com/dorland/definition?id=51294&searchterm=-tropism.

flu vaccine, adenovirus infection, or the two combined caused A.G.C.'s seizure disorder. Pet. Ex. 73 at 1-2.

Dr. Steinman noted that the package insert for the 2015-2016 fluzone vaccine includes febrile convulsions and encephalomyelitis. Pet. Ex. 46 at 9; Pet. Ex. 51.

Dr. Steinman agreed that A.G.C. tested negative for antibodies to VGKC but noted that he was not tested for antibodies to CASPR2. He referenced *Michael* and *Kirschstein* to show that autoantibodies to CASPR2 are associated with some syndromes including limbic encephalitis and appear to be directly pathogenic. Pet. Ex. 46 at 5; Pet. Ex. 50; Pet. Ex. 52; Tr. 176-77, 192, 353-54. Further, VGKC antibodies that lack LGI1 or CASPR2 antibodies "are common in healthy controls and have no consistent associations with distinct syndromes." *Id*. Further, *Kirschstein* showed that antibodies to CASPR2 alter synaptic firing linked to epilepsy. Pet. Ex. 46 at 8; Pet. Ex. 52.

Dr. Steinman opined that molecular mimicry is the mechanism by which either the flu vaccine, adenovirus, or both triggered an immune response. Pet. Ex. 46 at 8; Tr. 169-70, 189-90. Relying on an article he authored, he described molecular mimicry as "an evolutionary adaptation whereby viruses and bacteria attempt to fool the body into granting them free access. Such mimicry works by showing the immune system stretches of amino acids that look like self." Pet. Ex. 56 at 4. He claimed that at least one molecule known to trigger seizures has a molecular mimic within both the 2015 influenza vaccine and adenovirus. However, adenoviruses are rarely associated with encephalitis and seizures. Pet. Ex. 46 at 8; Pet. Ex. 53; Pet. Ex. 54; Pet. Ex. 55; Tr. 169-70, 176.

Dr. Steinman explained that when vaccines are administered in the periphery, macrophages at the injection site ingest the flu vaccine components and present them to the immune system, beginning the immune response. Receptors in the T cells and B cells in the regional lymph nodes recognize the vaccine components and begin to expand. The B cells produce influenza-specific antibody response, while the T cells help the development of the antibody response and can mount a cytotoxic response to kill the influenza virus. Pet. Ex. 63 at 3. Alpha-4 integrin molecules located on T cells and B cells bind to VCAM-1 (vascular cellular adhesion molecule-1) on the surface of blood vessel endothelium, which is the initial entry to the brain, thus allowing the immune cells to cross the blood brain barrier. *Id.* at 4-5; Pet. Ex. 70. When the T cells and B cells target mimics present in the flu vaccine that are similar to antigens in the brain, like CASPR2, the T cells and B cells can trigger autoimmune epilepsy. Pet. Ex. 63 at 4; Tr. 179-80. Dr. Steinman agreed with Dr. MacGinnitie that little, if any, antigen from the vaccine would spread to the brain. However, the T cells and B cells reactive to influenza virus would be trafficked to and enter the brain with some of those T cells and B cells cross-reactive to antigens involved in autoimmune epilepsy. Pet. Ex. 63 at 6.

Dr. Steinman explained that molecular mimicry can induce autoimmunity even absent exact homology. Pet. Ex. 46 at 9; Pet. Ex. 56; Pet. Ex. 63 at 4; Tr. 177-78, 188, 197-98. He referenced *Gautam*[11] where he and his colleagues were able to trigger experimental

[11] Because the lead author in this study is the same as in two other studies filed, Exhibit 58 is referred to herein as *Gautam*; Exhibit 59 is referred to herein as *Gautam II*; and Exhibit 60 is referred to herein as *Gautam III*.

encephalomyelitis ("EAE") with only 5 of 12 amino acids identical—not even consecutive—between the virus and myelin basic protein. Pet. Ex. 46 at 9, 11; Pet. Ex. 58. In *Gautam II*, a six amino acid peptide with identity at 5 amino acids was sufficient to trigger neuroinflammation. Pet. Ex. 46 at 10; Pet. Ex. 59. In *Gautam III*, EAE was induced with 5 of 11 amino acids identical between the virus and MBP, only three of which were consecutive. Pet. Ex. 46 at 10; Pet. Ex. 60. He defended his reliance on the EAE models, explaining that EAE is a "classic model of neuroinflammation" and was not exclusively relevant to MS. Tr. 343-44. Dr. Steinman agreed that cross-reactive immune responses between viruses and hosts are somewhat common and that the cross-reaction must take place at a "disease related" epitope in order to cause autoimmune disease. Pet. Ex. 46 at 9; Pet. Ex. 57.

Dr. Steinman also agreed that a powerful adjuvant was used in the animal studies he relied on because the goal was not to inject hundreds/thousands of mice to see a rare condition, but to show that it is "uncontested that we could get paralysis not only with the native myelin peptide sequence, but with a peptide that matched this at 6 of 13 amino acids." Pet. Ex. 63 at 7; Tr. 188, 339-40, 345-46. Further, *Root-Bernstein* considered molecular similarities of at least 5 identical amino acids in 10 as significant. Pet. Ex. 63 at 7; Pet. Ex. 71.

Here, Dr. Steinman used BLAST searches for shared sequence homologies between CASPR2 and both the 2015-2016 influenza vaccine and adenovirus. Pet. Ex. 46 at 11; Tr. 177-78, 192. He then used a filtration system to eliminate sequence homologies that are below the threshold shown to induce neuroinflammation with clinical symptoms. Pet. Ex. 46 at 11-16. Finally, a third filter retains peptide sequences identified in the first two steps that have also been identified by other investigators using the Immune Epitope Database ("IEDB"). *Id.* at 16. This three step filtration process resulted in sequences shared between adenovirus and CASPR2 (RDSSSRVDNAP) and between influenza B and CASPR2 (ERNLIAQNAHAVERI). *Id.* at 16-17; Tr. 347-48.

Dr. Steinman argued that his BLAST searches and filtration system are the strongest scientific theory he could provide, short of doing actual experiments on A.G.C.'s blood samples at the onset of his seizures to prove with certainty that such a mimic was recognized by his immune system. Pet. Ex. 63 at 7; Tr. 180, 348-49. Further, molecular mimicry as a theory is shown by the IEDB, which indicates that humans mount an immune response to the component of the influenza virus that is shared with CASPR2 precursor found in humans. Pet. Ex. 63 at 8; Pet. Ex. 73 at 2-3.

In summary, Dr. Steinman argued that the flu vaccine, which is meant to mount an immune response, combined with the adenovirus that A.G.C. was fighting at the time he received the vaccine, and which is capable of breaching the BBB, allowed T cells and B cells to enter the brain. Pet. Ex. 63 at 6; Tr. 167. The T cells and B cells that recognize and target the flu vaccine antigens could also target molecular mimics found in the brain, such as CASPR2, thereby triggering encephalitis and seizures. Pet. Ex. 63 at 4-6; Tr. 189-90. He conceded his theory does not prove with certainty what triggered A.G.C.'s epilepsy without blood samples but shows how the seasonal flu vaccine could cause autoimmune epilepsy. Pet. Ex. 63 at 4; Tr. 180, 341-43, 348-49, 356.

As to prong two, Dr. Steinman submitted that A.G.C. had an upper respiratory infection a week prior to the October 20, 2015 influenza vaccination, which was likely the adenovirus he later

tested positive for. The admission notes from the pediatric neurologist at UVA documented that A.G.C. had a change in cognitive ability in the week leading up to his presentation for seizures. Pet. Ex. 46 at 17, citing Pet. Ex. 9 at 283, 287; Pet. Ex. 21 at 3, 6. Further, he argued that A.G.C. had a "noticeable" response to IVIG, which is typical of CASPR2-related seizure disorders. Tr. 355.

For prong three, Dr. Steinman used GBS and encephalomyelitis—both neuroinflammatory conditions—as a surrogate to show that a medically reasonable time for onset is a week following flu vaccine. Pet. Ex. 46 at 18; Pet. Ex. 61; Pet. Ex. 62; Tr. 185-87.

Dr. Steinman pointed out that Dr. Holmes agreed A.G.C. had meningoencephalitis but disagreed that the flu vaccine played any role. Dr. Steinman agreed while flu vaccine is generally very safe, that "does not mean that influenza vaccine is never involved in meningoencephalitis and seizures." Pet. Ex. 63 at 8; Tr. 353.

Dr. Steinman filed another report after the hearing discussing the new literature submitted by respondent. Pet. Ex. 94 at 1. He postured that when taken together, the new literature described patients with CASPR2 antibodies many with the features described in A.G.C.'s medical records and during hearing. *Id*. at 1-2; Resp. Ex. J; Resp. Ex. K; Resp. Ex. L; Resp. Ex. M.

Dr. Steinman also submitted two articles he co-authored after the hearing involving molecular mimicry and Epstein Barre Virus ("EBV") in multiple sclerosis ("MS"). Pet. Ex. 92; Pet. Ex. 93. He explained that the two articles demonstrate that 5 identical amino acids in a stretch of 12 consecutive amino acids, between a virus and a component of the nervous system, can trigger MS. Pet. Ex. 94 at 2-3. "The degree of homology that we were able to demonstrate directly in human specimens in the newly filed papers, adds weight to the importance of molecular mimics with a minimum of 5 identities out of 12." *Id*. at 3.

2. Respondent's Experts

a. Dr. Gregory L. Holmes

i. Qualifications

Dr. Holmes obtained his MD from the University of Virginia in 1974 then completed his residency in pediatrics at Yale University and pediatric neurology at the University of Virginia School of Medicine. Resp. Ex. H at 1. He is board-certified in pediatrics, neurology with special competence in child neurology, and clinical neurophysiology. *Id*. at 2. He has been on faculty in several positions at University of Connecticut Health Center, Medical College of Georgia, Harvard Medical School, Dartmouth Medical School, and Larner College of Medicine at University of Vermont. *Id*. at 2-3.

ii. Opinion

Dr. Holmes detailed A.G.C.'s medical history, summarizing that A.G.C. had no fever at the time he received the vaccine on October 20, 2015, developed a fever that evening, developed

pharyngitis on October 22, 2015, and developed focal seizures, altered awareness, and ataxia resulting in hospital admission on October 26, 2015. Once in the hospital he had an inflammatory CSF and an encephalopathic EEG. At a later hospital admission, he tested positive on PCR for adenovirus. Tr. 211-13. A.G.C. received aggressive treatment with IVIG, steroids, and a mitochondrial cocktail while in the hospital and showed some improvement. However, it is difficult to determine which of these treatment(s) caused his condition to improve. Tr. 223-24, 245. According to Dr. Holmes the adenovirus symptoms began the evening he received the vaccination when he developed a fever. Tr. 209, 234-35. He remains on antiepileptic drugs. Resp. Ex. A at 2-13.

In Dr. Holmes opinion, the most likely diagnosis was viral encephalitis due to adenovirus. A.G.C,'s new onset of focal seizures and mental status changes began several days after a clear viral illness supporting this diagnosis, along with CSF pleocytosis and encephalopathic EEG findings. Additionally, the infectious disease expert at Children's National Hospital noted that viral or post-viral encephalitis from adenovirus was the most likely diagnosis. Resp. Ex. A at 13, 17; Tr. 205.

Dr. Holmes defined encephalitis as an inflammation of the brain associated with neurologic dysfunction and characterized by altered mental status (decreased level of consciousness, lethargy, personality change, unusual behavior), seizures, and/or focal neurologic signs often accompanied by fever, headache, nausea, and vomiting. Resp. Ex. A at 13; Resp. Ex. A Tab 1. Post infectious encephalitis or acute disseminated encephalomyelitis is a monophasic illness thought to be autoimmune in response to a preceding antigenic challenge such as viral illness. Resp. Ex. A at 13; Resp. Ex. A Tab 2.

Dr. Holmes described the criteria for encephalitis or encephalopathy of presumed infection or autoimmune etiology. Resp. Ex. A at 14; Resp. Ex. A Tab 1. Neurologic dysfunction in the form of altered mental status lasting over 24 hours without alternative cause is present. Minor criteria (two for possible; 3 for probable) include fever within 72 hours, seizures, new focal neurological findings, CSF pleocytosis, neuroimaging with brain parenchymal changes, or encephalopathic EEG. For a definitive diagnosis, there must be pathologic confirmation on brain biopsy, evidence of infection with a microorganism associated with encephalitis, or laboratory evidence of an autoimmune condition associated with encephalitis. *Id*. He noted that the International Encephalitis Consortium does not distinguish between infectious and post-infectious processes. However, A.G.C. met the diagnostic criteria for encephalitis but whether the adenovirus resulted in direct brain invasion or caused a post-infectious encephalitis cannot be determined without brain biopsy. *Id*.

Dr. Holmes explained that adenovirus causes febrile illnesses in young children and is most often associated with upper respiratory syndromes like pharyngitis or coryza. Less often, it causes gastrointestinal, ophthalmologic, genitourinary, and neurologic diseases. Most are self-limiting and last 5-14 days but can be fatal in the immunocompromised and sometimes healthy children and adults. Resp. Ex. A at 14; Resp. Ex. A Tab 3; Tr. 213-14.

Dr. Holmes further explained that adenovirus can rarely cause CNS disease in immunocompetent children that ranges from mild aseptic meningitis and fully reversible

encephalopathy to severe, potentially fatal, acute necrotizing encephalopathy. Resp. Ex. A at 14; Tr. 217, 219, 236. Neurologic complications include febrile seizures, encephalitis, acute disseminated encephalomyelitis, and aseptic meningitis. In *Kumar*, an observational study of 73 patients with acute viral encephalitis, 11% were caused by adenovirus. Resp. Ex. A at 14; Resp. Ex. A Tab 7. Not all children with adenovirus encephalitis have virus detected in the cerebrospinal fluid, including A.G.C. Resp. Ex. A at 14. In *Schwartz*, a study of 48 immunocompetent children with adenovirus-associated brain disease, 85% had the virus detected in the respiratory or gastrointestinal tract but not in the cerebrospinal fluid. *Id*.; Resp. Ex. A Tab 6. In *Parisi*, another study of 24 children between the ages of 4-6 years with encephalitis, only 1 of 24 had a positive adenovirus PCR in the cerebrospinal fluid. Resp. Ex. A at 14; Resp. Ex. A Tab 12.

On the other hand, Dr. Holmes submitted that there is no association between influenza vaccination and encephalitis. Resp. Ex. A at 14, 16; Tr. 214, 219. If the two were linked, one would expect to see more cases of encephalitis because the flu vaccine is so common. Tr. 221-22. He referred to *Kawai*, which demonstrated no increased risk of encephalitis following 3.6 million first doses of inactivated flu vaccine and 250,000 first doses of live attenuated flu vaccine between 2012-2013. Resp. Ex. A at 14, 16; Resp. Ex. A Tab 15. *Baxter* demonstrated the same with the quadrivalent live attenuated influenza vaccine. Resp. Ex. A at 14-15; Resp. Ex. A Tab 16. The Canadian Immunization Monitoring Program Active showed 61 cases of encephalopathy/encephalitis reported between 1992 and 2012, none of which were causally associated with pertussis or influenza vaccine. Resp. Ex. A at 15; Resp. Ex. A Tab 17. Dr. Holmes added that A.G.C. did not have adverse events from six prior flu vaccines. Resp. Ex. A at 15.

Further, Dr. Holmes asserted that the evidence does not support that A.G.C. had anti-CASPR2 antibodies. He explained that children with anti-CASPR2 antibodies present clinically with insomnia, possibly encephalopathy, and dysautonomia, not epilepsy. He further explained that anti-CASPR2 antibodies are typically seen in elderly men. Tr. 225-27. However, he later agreed that A.G.C. was encephalopathic and had symptoms consistent with dysautonomia. Tr. 246-47.

In arguing that A.G.C.'s condition in the days leading up to his first seizure on October 26, 2015 were the result of adenovirus rather than flu vaccine, Dr. Holmes submitted that there is no evidence to support how molecular mimicry by a flu vaccine would result in upper respiratory symptoms. Resp. Ex. A at 15, 17; Tr. 235. However, he conceded that molecular mimicry is a well-accepted theory of autoimmunity. Tr. 244. Dr. Holmes took issue with Dr. Nelson's opinion that no other cause of A.G.C.'s encephalitis was found, stating evaluation showed that A.G.C. had adenovirus and it was A.G.C.'s adenovirus infection, which progressed to encephalitis as evidenced by inflammatory CSF and encephalopathic EEG. Resp. Ex. A at 15.

Dr. Holmes criticized Dr. Nelson's reliance on three abstracts, which generally do not provide enough information on methodology and data interpretation to evaluate a study's findings. Resp. Ex. A at 16. Nevertheless, Dr. Holmes addressed the abstracts noting that one discussed ADEM which A.G.C. did not have; one discussed an adult with encephalitis following flu vaccine but contained too few details to support causality; and the third lacked incidence figures to compare the rate of encephalitis in those who received a flu vaccine with those in an unvaccinated group during the same timeframe. *Id*.; Pet. Ex. 33; Pet. Ex. 35; Pet. Ex. 36. Dr. Holmes also took issue

with Dr. Nelson's reliance on *Segal and Shoenfeld*, noting that the article discussed the relationship between H1N1 vaccination, GBS and narcolepsy, neither of which A.G.C. had. Resp. Ex. A at 16; Resp. Ex. A Tab 25. Likewise, *Williams* deemed ADEM "possible" after H1N1 vaccine in 4 of 8 cases assessed. A.G.C. did not have ADEM. Resp. Ex. A at 16; Resp. Ex. A Tab 24.

Dr. Holmes instead offered *Machicado*, which showed a temporal relationship between ADEM and inactivated flu vaccine, but the authors cautioned that this alone was insufficient to show causation. Resp. Ex. A at 16; Resp. Ex. A Tab 22.

Dr. Holmes agreed that influenza infection may rarely cause CNS disease in immunocompetent children but "[f]ortunately, influena (sic) encephalitis is preventable with the influenza vaccine." Resp. Ex. A at 16; Resp. Ex. A Tab 6; Resp. Ex. A Tab 26; Resp. Ex. A Tab 27. He further stated that vaccines are recommended if a child presents with only a mild illness, but the decision is based on clinical judgment. Tr. 229-30. He agreed that if a child presented with a known adenovirus infection, he would hold off on vaccination because the child may have a reaction, and treaters would have no way to discern whether the reaction was due to the vaccine or to the infection. Tr. 229-33, 236-37, 248-49. Dr. Holmes conceded that he could not say whether receipt of the flu vaccination in this case may have "escalated things" but typically adenovirus infection clears within four days in an otherwise healthy child. Tr. 233.

Dr. Holmes agreed A.G.C.'s diagnosis was meningoencephalitis, which is inflammation of the membranes that surround the brain and spinal cord as well as of the brain itself. Resp. Ex. A at 17.

Dr. Holmes submitted that A.G.C. developed a fever the night of the flu vaccination then developed pharyngitis, congestion, nausea, rhinorrhea, and headache two days later—not the week before vaccination. He characterized A.G.C.'s symptoms of focal seizures, altered awareness, and ataxia as consistent with adenovirus infection. In Dr. Holmes's opinion "AC had a viral illness which resulted in entry of the virus into the brain, or the virus induced auto-immune response against the brain". He noted that Dr. Steinman agreed that adenovirus could induce an autoimmune response. Thus, in Dr. Holmes's opinion, there was no reason to implicate the flu vaccine. Resp. Ex. A at 17-18; Tr. 207-09, 211-14, 237-38.

Dr. Holmes then explained how adenovirus may enter the brain through disruption of the BBB and cause further damage to the BBB once inside the brain. In so doing, he submitted that at the time that A.G.C. received the flu vaccine, he already showed signs of adenovirus-induced encephalitis and "would have had impairment of the blood-brain barrier. This breach would have allowed entry of inflammatory cells, microorganisms, antigens and antibodies into the brain," but the small amount of antigen contained in the flu vaccine would be unlikely to result in "any meaningful brain concentration regardless of the integrity of the blood-brain barrier." Resp. Ex. E at 1-2. He agreed it was possible that antibodies against the flu vaccine could enter the brain through the disrupted BBB. But added that A.G.C.'s clinical course was consistent with a monophasic illness caused by the adenovirus infection and "highly improbable" that the flu vaccine caused a "second hit". *Id*.

Dr. Holmes commented that vaccine package inserts contain reports from the public and are not a reliable tool to establish causation. Resp. Ex. A at 18; Tr. 219, 240-42.

Dr. Holmes concluded that A.G.C. had adenovirus infection that resulted in encephalitis. There is no plausible link between the influenza vaccine on October 20, 2015 and A.G.C.'s neurological injury. Resp. Ex. A at 18; Resp. Ex. E at 2; Tr. 220-21.

b. Dr. Andrew MacGinnitie

i. Qualifications

Dr. MacGinnitie obtained his PhD in pathology in 1996 and his MD in 1998 from University of Chicago Pritzker School of Medicine. He completed his residency in pediatrics in 2001 and was then a fellow in allergy/immunology at Children's Hospital Boston and a clinical fellow in pediatrics at Harvard Medical School until 2004. Resp. Ex. I at 1. As of his most recent CV filed, he was on faculty in pediatrics at Harvard Medical School and was an attending physician in pediatrics and allergy/immunology at Children's Hospital Boston. *Id.* at 1-2.

ii. Opinion

Dr. MacGinnitie opined that the flu vaccination played no role in A.G.C.'s development of epilepsy. Tr. 258. He provided a detailed summary of A.G.C.'s medical history but his focus was on petitioner's theory that there was molecular mimicry between the components of the flu vaccine and human proteins that led or contributed to A.G.C.'s new onset seizures and encephalopathy/encephalitis. *See generally* Resp. Ex. C.

Dr. MacGinnitie proposed several weaknesses in petitioner's causation theory including a lack of significant homology between the components of the flu vaccine and human proteins, a lack of evidence to show the presence of antibodies, failure to respond to immune modulating therapies, and his testing positive for adenovirus or other infection in the month prior to his seizures being a more plausible trigger of his seizures. Resp. Ex. C at 5. Dr. MacGinnitie added that epidemiology clearly shows that epilepsy, seizures, and encephalitis are not increased after flu vaccine. *Id.*; Tr. 262-63, 302-04.

More specifically, in response to Dr. Steinman's theory of causation, Dr. MacGinnitie argued that homology between influenza B nucleoprotein ("NP")[12] and CASPR2 is not significant. The studies Dr. Steinman relied on to support his theory are 20 years old, used a mouse model for multiple sclerosis to cause EAE, and used powerful adjuvants not suitable for humans. Resp. Ex. C at 5-6; Pet. Ex. 58; Pet. Ex. 59; Pet. Ex. 60; Resp. Ex. C Tab 1; Resp. Ex. G at 2; Tr. 265-68, 307, 310. In these studies, pertussis toxin was simultaneously injected, which is thought to damage the BBB and allow access to pathogenic cells and antibodies into the CNS. Resp. Ex. C at 6; Resp. Ex. C Tab 3. Mouse models are "poorly representative of human disease", and the subject flu vaccine had no adjuvant. Resp. Ex. C at 6; Resp. Ex. C Tab 4; Resp. Ex. C Tab 5; Tr. 267, 270.

[12] Nucleoprotein is a substance composed of a simple basic protein, usually a histone or protamine, combined with a nucleic acid. Dorland's Online, *Nucleoprotein*, https://www.dorlandsonline.com/dorland/definition?id=34464&searchterm=nucleoprotein.

Dr. MacGinnitie added that the BLAST algorithm used by Dr. Steinman includes a statistical measure called the Expect Value, which evaluates how probable or improbable a particular match is by chance. Dr. Steinman's reported values of 1.2, 2.9, and 3.8 indicate that the degree of homology is expected by chance. Notably, he demonstrated that homology with adenovirus had an Expect Value of 0.44, which was better than those with CASPR2 but still not notably significant. Resp. Ex. C at 6; Resp. Ex. C Tab 6; Resp. Ex. G at 2; Tr. 272-75. Dr. Steinman then used the IEDB and identified the sequence (ERNLIAQNAHAVERI); however, the sequence he identified is from the NP component of influenza B and shows that the sequence is highly homologous to NP from other influenza B viruses, which is "hardly surprising and is in no way informative about possible molecular mimicry in this case." Resp. Ex. C at 6-7.

Dr. MacGinnitie referenced more recent studies showing that there are significant overlaps between viral and bacterial DNA with that in humans. *Kanduc* illustrated that each viral genome studied had multiple instances of 5, 6, and even 7 amino acids peptides identical to human peptides. He proposed that "[i]f molecular mimicry was truly a trigger of autoimmune disease, such illnesses should 'theoretically approach a 100% real incidence' which is obviously not observed." Resp. Ex. C at 7; Resp. Ex. C Tab 7; Tr. 276-79; *see also* Resp. Ex. C Tab 8. Thus, limited sequence homology is not significant. Resp. Ex. C at 7.

Dr. MacGinnitie agreed that sequence homology is necessary, but alone is not sufficient to induce autoimmunity. Tr. 264-67, 275, 280. He added that The Institute of Medicine ("IOM") also noted that sequence homology does not equate to human disease. Resp. Ex. C at 7; Resp. Ex. C Tab 9. In Dr. MacGinnitie's opinion, Dr. Steinman did not identify significant homology between the influenza vaccine and CASPR2; homology alone is not enough to trigger autoimmunity. Resp. Ex. C at 7. He then questioned the adequacy of molecular mimicry as a theory of autoimmunity, referencing *Root-Bernstein* and noted that "[i]f [molecular mimicry] is sufficient to induce autoimmune disease, then one would expect much higher rates of disease than are observed. . . Another problem is that according to many investigators, very little evidence exists for MM playing a role in human diseases." Resp. Ex. G at 2; Pet. Ex. 71; Tr. 281-83. Dr. MacGinnitie added that, "all current animal models based on [molecular mimicry] require adjuvants, in addition to the molecular mimic, to induce a hyperinflammatory response", which suggests that mimicry alone is insufficient to induce autoimmunity. Resp. Ex. G at 2.

Dr. MacGinnitie pointed out that A.G.C. tested negative for VGKC antibodies making it unlikely that he had CASPR2 antibodies. The article Dr. Steinman relied upon showed that the vast majority of patients (85%) with CASPR2 antibodies also had positive anti-VGKC testing. He agreed that A.G.C.'s negative VGKC test did not rule out the presence of CASPR2 antibodies but argued that the negative testing for anti-VGKC suggested that he was also likely negative for CASPR2. Resp. Ex. C at 8; Pet. Ex. 21; Pet. Ex. 50; Tr. 286, 288, 316-17, 326, 328-29.

Dr. MacGinnitie described the blood brain barrier as "formidable", explaining that it protects the central nervous system from infectious, toxic, and autoimmune attacks. *Getts* detailed the practically impermeable physical wall between the circulatory system and the CNS. Resp. Ex. C at 8; Resp. Ex. C Tab 10. Dr. MacGinnitie postured that any plausible theory of how vaccination could trigger seizures would have to account for a breach of the blood brain barrier and Dr.

Steinman did not. He relied on mouse models that require an injection of pertussis toxin to open up the BBB. Resp. Ex. C at 8. In contrast, data from mice studies on adenovirus show the virus can directly damage the BBB, suggesting some strains of adenovirus have a special ability to cause CNS infection and damage. Resp. Ex. F at 2; Tr. 258-59.

According to Dr. MacGinnitie, the incubation period for adenovirus is 2 days to 2 weeks and A.G.C. manifested symptoms of adenovirus the day of his vaccination, therefore, his adenovirus exposure preceded the vaccination. Resp. Ex. F at 3; Tr. 259-61; Pet. Ex. 6 at 103. Dr. MacGinnitie was then asked if A.G.C. already had adenovirus when he received the flu vaccine, could the virus have caused BBB breakdown that would have allowed flu vaccine antigens to enter the brain. He responded that the inactivated flu vaccine antigen administered intramuscularly is not thought to be systematically available or capable of replicating due to its formulation, therefore little if any antigen is available to circulate to the brain and cause encephalopathy or seizures. Resp. Ex. F at 1-3. However, he conceded he "cannot exclude the possibility that compromise of the BBB by adenovirus could have allowed antibodies against influenza vaccine components to reach the brain" and agreed that Dr. Steinman "spelled out a process that could happen," but he thought it was unlikely. *Id*. at 3; Tr. 290, 317-18, 324.

Finally, Dr. MacGinnitie noted that studies show that anti-CASPR2 mediated neurological disorders generally have "dramatic" improvement with immunotherapies but A.G.C. did not have a notable response to high-dose corticosteroids or IVIG and required care in the pediatric ICU after completing such therapies. Resp. Ex. C at 8; Pet. Ex. 50; Tr. 259, 287-90, 318; Pet. Ex. 10 at 94.

Dr. MacGinnitie maintained that the adenovirus infection is known to trigger meningoencephalitis and seizures, so it was unnecessary to implicate the vaccine as a cause other than for purposes of the Program. Resp. Ex. G at 1, 4; Tr. 293. Further, epidemiological studies show no relationship between influenza vaccine and encephalopathy, seizures, or epilepsy. Resp. Ex. C at 9; Resp. Ex. G at 1. *Ghaderi* showed no increased risk of encephalitis in any timeframe after vaccination. Resp. Ex. C at 9-10; Pet. Ex. 32. *Haberg* found no increased risk of new onset epilepsy after influenza vaccine. Resp. Ex. C at 10; Resp. Ex. C Tab 15.

Dr. MacGinnitie criticized the literature Dr. Nelson relied on noting that case reports and abstracts provide only temporal associations, not causality. Resp. Ex. C at 8-9; Pet. Ex. 33; Pet. Ex. 34; Pet. Ex. 35. VAERS reports are unreliable in showing an increase of the rate of illness following a vaccination. Other literature did not address seizures or encephalopathy, and one study he filed, *Williams*, concluded it was difficult to assess causality in vaccine triggered injuries. Resp. Ex. C at 9; Pet. Ex. 36; Pet. Ex. 37; Pet. Ex. 38; Pet. Ex. 39. Finally, the vaccine package insert contains reports during the post-approval use of the vaccine and specifically notes that it is not possible to establish a causal relationship. Resp. Ex. C at 10; Pet. Ex. 51.

In summarizing, Dr. MacGinnitie noted that A.G.C. and other family members were sick the week prior to A.G.C.'s vaccination. A.G.C. was sick enough to require a visit to the pediatrician. An NP swab was positive for adenovirus. Adenovirus is associated with neurological complications. *Huang* and *Schwartz* both support neurological complications including seizures and encephalopathy associated with adenovirus. Resp. Ex. C at 10; Resp. Ex. C Tab 16; Resp. Ex. C Tab 17. *Huang* reported CNS dysfunction in 3.3% of pediatric patients with adenovirus

infection, the majority of which had seizures. Resp. Ex. G at 1; Tr. 259; Resp. Ex. C Tab 16. Unfortunately, A.G.C. falls into that category of children who develop CNS symptoms after adenovirus. Resp. Ex. G at 1-2. He probably would not vaccinate a child with known adenovirus because it is his understanding that vaccinations are not given to sick children because their body will not mount a sufficient immune response if they are simultaneously fighting off an infection. Tr. 295-97, 320-22, 326-28.

Dr. MacGinnitie concluded that the homology between the influenza vaccine and CASPR2 is not significant, sequence homology itself does not demonstrate molecular mimicry as a trigger for autoimmunity, and there was no evidence of anti-CASPR2 antibodies in A.G.C.'s case, nor did he respond to immunomodulatory therapy. Epidemiology shows no increased risk of encephalopathy or seizures after flu vaccine. Therefore, A.G.C.'s encephalopathy and seizures were unrelated to his vaccination. Resp. Ex. C at 10-11; Resp. Ex. G at 2; Tr. 290-91.

In his report filed following the hearing, Dr. MacGinnitie discussed the papers that Dr. Steinman submitted after the hearing and agreed there is strong support for EBV infection leading to MS, with several theories as to how this occurs. Resp. Ex. M at 3. He noted that the "ability of infected B cells to move into and take up residence in the CNS [is] thought to be key." *Id*. However, unlike EBV infection which is life-long, vaccination is a self-limited process, and vaccines cannot replicate once injected. *Id*. at 5. Dr. MacGinnitie was unaware of any evidence that showed that a small amount of protein contained in the inactivated flu vaccine is distributed throughout the body or transported into the CNS. *Id*. Timing of onset also weakens Dr. Steinman's analogy; MS following acute EBV infection generally takes years, while A.G.C.'s seizures began only six days after vaccination. *Id*. at 5-6. He argued that the example of EBV infection leading to MS "demonstrates just how extreme conditions must be for molecular mimicry to cause autoimmune disease." *Id*. at. 7.

III. Legal Standard

Petitioners are required to establish their case by a preponderance of the evidence. 42 U.S.C. § 300aa-13(1)(a). The preponderance of the evidence standard requires a "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [they] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010) (citations omitted). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Human Servs.,* 931 F.2d 867, 873 (Fed. Cir. 1991).

Distinguishing between "preponderant evidence" and "medical certainty" is important because a special master should not impose an evidentiary burden that is too high. *Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1379-80 (Fed. Cir. 2009) (reversing a special master's decision that petitioners were not entitled to compensation); *see also Lampe v. Sec'y of Health & Human Servs.*, 219 F.3d 1357 (Fed. Cir. 2000); *Hodges v. Sec'y of Health & Human Servs.*, 9 F.3d 958, 961 (Fed. Cir. 1993) (disagreeing with the dissenting judge's contention that the special master confused preponderance of the evidence with medical certainty). At the same time, mere conjecture or speculation is insufficient under a preponderance of evidence standard. *Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984).

The Vaccine Act provides two avenues for petitioners to receive compensation. First, a petitioner may demonstrate a "Table" injury—i.e., an injury listed on the Vaccine Injury Table that occurred within the provided time period. 42 U.S.C. § 300aa-11(c)(1)(C)(i). "In such a case, causation is presumed." *Capizzano v. Sec'y of Health & Human Servs*., 440 F.3d 1317, 1320 (Fed. Cir. 2006); *see* § 13(a)(1)(B). Second, where the alleged injury is not listed on the Vaccine Injury Table, a petitioner may demonstrate an "off-Table" injury, which requires that the petitioner "prove by a preponderance of the evidence that the vaccine at issue caused the injury." *Capizzano*, 440 F.3d at 1320; *see* § 11(c)(1)(C)(ii). A petitioner need not show that the vaccination was the sole cause, or even the predominant cause, of the alleged injury; showing that the vaccination was a "substantial factor" and a "but for" cause of the injury is sufficient for recovery. *Pafford v. Sec'y of Health & Human Servs*., 451 F.3d 1352, 1355 (Fed. Cir. 2006); *Shyface v. Sec'y of Health & Human Servs*., 165 F.3d 1344, 1352 (Fed. Cir. 1999). Petitioners are not required "to eliminate alternative causes as part of establishing [their] prima facie case." *Doe v. Sec'y of Health & Human Servs*., 601 F.3d 1349, 1357-58 (Fed. Cir. 2010); *see Walther v. Sec'y of Health & Human Servs*., 485 F.3d 1146, 1152 (Fed. Cir. 2007) (holding that a "petitioner does not bear the burden of eliminating alternative independent potential causes"). Once a petitioner has proven causation by preponderant evidence, "the burden then shifts to the respondent to show by a preponderance of the evidence that the injury is due to factors unrelated to the administration of the vaccine." *Deribeaux ex rel. Deribeaux v. Sec'y of Health & Human Servs*., 717 F.3d 1363, 1367 (Fed. Cir. 2013) (citing 42 U.S.C. § 300aa-13(a)(1)(B)).

To prove causation, a petitioner must satisfy the three-pronged test established in *Althen v. Sec'y of Health & Human Servs*., 418 F.3d 1274 (Fed. Cir. 2005). *Althen* requires that a petitioner show by preponderant evidence that a vaccination they received caused their injury "by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." *Id*. at 1278. Together, these prongs must show "that the vaccine was 'not only a but-for cause of the injury but also a substantial factor in bringing about the injury.'" *Stone v. Sec'y of Health & Human Servs*., 676 F.3d 1373, 1379 (Fed. Cir. 2012) (quoting *Shyface*, 165 F.3d at 1352-53). The received vaccine, however, need not be the predominant cause of the injury. *Shyface*, 165 F.3d at 1351. Causation is determined on a case-by-case basis, with "no hard and fast per se scientific or medical rules." *Knudsen v. Sec'y of Health & Human Servs*., 35 F.3d 543, 548 (Fed. Cir. 1994). Petitioners are not required to identify "specific biological mechanisms" to establish causation, nor are they required to present "epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities." *Capizzano*, 440 F.3d at 1325 (quoting *Althen*, 418 F.3d at 1280). "[C]lose calls regarding causation are resolved in favor of injured claimants." *Althen*, 418 F.3d at 1280.

Each *Althen* prong requires a different showing. Under the first prong, a petitioner must provide a "reputable medical theory" demonstrating that the vaccine received can cause the type of injury alleged. *Pafford*, 451 F.3d at 1355-56 (citation omitted). To satisfy this prong, a petitioner's "theory of causation must be supported by a 'reputable medical or scientific explanation.'" *Andreu*, 569 F.3d at 1379 (quoting *Althen*, 418 F.3d at 1278). This theory need only be "legally probable, not medically or scientifically certain." *Id*. at 1380 (emphasis omitted)

(quoting *Knudsen*, 35 F.3d at 548). Nevertheless, "petitioners [must] proffer trustworthy testimony from experts who can find support for their theories in medical literature." *LaLonde v. Sec'y of Health & Human Servs*., 746 F.3d 1334, 1341 (Fed. Cir. 2014).

The second *Althen* prong requires proof of a "logical sequence of cause and effect." *Capizzano*, 440 F.3d at 1326 (quoting *Althen*, 418 F.3d at 1278). Even if the vaccination can cause the injury, a petitioner must show "that it did so in [this] particular case." *Hodges v. Sec'y of Health & Human Servs*., 9 F.3d 958, 962 n.4 (Fed. Cir. 1993) (citation omitted). "A reputable medical or scientific explanation must support this logical sequence of cause and effect," *Id*. at 961 (citation omitted), and "treating physicians are likely to be in the best position to determine whether a logical sequence of cause and effect show[s] that the vaccination was the reason for the injury," *Paluck v. Sec'y of Health & Human Servs*., 786 F.3d 1373, 1385 (Fed. Cir. 2015) (quoting *Andreu*, 569 F.3d at 1375).

The third *Althen* prong requires that a petitioner establish a "proximate temporal relationship" between the vaccination and the alleged injury. *Althen*, 418 F.3d at 1281. This "requires preponderant proof that the onset of symptoms occurred within a timeframe for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." *De Bazan v. Sec'y of Health & Human Servs*., 539 F.3d 1347, 1352 (Fed. Cir. 2008). Typically, "a petitioner's failure to satisfy the proximate temporal relationship prong is due to the fact that onset was too late after the administration of a vaccine for the vaccine to be the cause." *Id*. However, "cases in which onset is too soon" also fail this prong; "in either case, the temporal relationship is not such that it is medically acceptable to conclude that the vaccination and the injury are causally linked." *Id*.; *see also Locane v. Sec'y of Health & Human Servs*., 685 F.3d 1375, 1381 (Fed. Cir. 2012) ("[If] the illness was present before the vaccine was administered, logically, the vaccine could not have caused the illness.").

A petitioner who satisfies their burden in proving causation is entitled to compensation unless respondent can prove, by a preponderance of the evidence, that the vaccinee's injury is "due to factors unrelated to the administration of the vaccine." § 13(a)(1)(B); *Whitecotton v. Sec'y of Health & Human Servs.,* 17 F.3d 374, 376 (Fed. Cir. 1994), *rev'd on other grounds sub nom., Shalala v. Whitecotton*, 514 U.S. 268 (1995); *see also Walther*, 485 F.3d at 1151. To prove an alternative cause unrelated to the vaccine, respondent must demonstrate that the proposed alternative cause was the "sole substantial factor" that caused petitioner's injury. *de Bazan*, 539 F.3d at 1354 (holding that Respondent's burden is to "identify[] a particular [unrelated] factor (or factors) and present[] sufficient evidence to establish that it was the sole substantial factor in bringing about the injury," thus "excluding the vaccine as a substantial factor"); *Deribeaux ex rel. Deribeaux v. Sec'y of Health & Human Servs.,* 105 Fed. Cl. 583, 595 (2012), *aff'd,* 717 F.3d 1363 (Fed. Cir. 2013); *Stone v. Sec'y of Health & Human Servs.,* 95 Fed. Cl. 233, 237 (2010); § 13(a)(1)(B).

Finally, although this decision discusses some but not all the literature in detail, I have reviewed and considered all of the medical records and literature submitted in this matter. *See Moriarty ex rel. Moriarty v. Sec'y of Health & Human Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("We generally presume that a special master considered the relevant record evidence even though [s]he does not explicitly reference such evidence in h[er] decision."); *Simanski v. Sec'y of*

Health & Human Servs., 115 Fed. Cl. 407, 436 (2014) ("[A] Special Master is 'not required to discuss every piece of evidence or testimony in her decision.'" (citation omitted)), *aff'd*, 601 F. App'x 982 (Fed. Cir. 2015).

IV. Discussion

There is no dispute that A.G.C. has a seizure disorder and that his first observed seizure occurred on October 26, 2015, six days after his receipt of the flu vaccine. The experts agreed that A.G.C. had adenovirus at the time he received the subject flu vaccination. They agreed he developed a fever the night of the flu vaccination with symptoms of adenovirus two days later for which he was taken to the pediatrician. The experts agreed that adenovirus has the propensity to breach the blood brain barrier on rare occasion and cause CNS dysfunction. They disagreed that the flu vaccine played any role in A.G.C.'s onset of seizures.

At hearing, petitioners testified that they were on a family trip on October 24 and 25, 2015, and A.G.C. was fine with no illness and no fever. They denied that he had adenovirus or that it was a contributing factor to the onset of his seizures. They believed that the flu vaccine he received on October 20, 2015 caused his seizures. However, petitioners' testimony was contrary to the medical records and to the opinions of their own experts, which was discussed at length with counsel.

With all due respect to the petitioners, their testimony was inconsistent with what S.S.C reported to the medical providers at the time of the events and to a great extent with her own affidavit filed closer in time to the events. I therefore afforded greater weight to the contemporaneous medical records.

A. Petitioners Have Provided a Sound and Reliable Theory.

Under the first prong of *Althen*, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received can cause the type of injury alleged. *Pafford*, 451 F.3d at 1355-56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen*, 35 F.3d at 548.

I find that petitioners have proven by preponderant evidence that the flu vaccination in combination with the adenovirus infection can cause encephalitis and epilepsy through the immune-mediated process described by Dr. Steinman.

Dr. Nelson submitted that anything that causes brain dysfunction or brain injury may result in epilepsy; prolonged seizures can cause injury to the brain resulting in epilepsy. Tr. 121-22. He opined that both flu vaccine and flu infection have been associated with encephalopathy and encephalitis but deferred to Dr. Steinman to elaborate on the immunological process. Pet. Ex. 29 at 2-3; Pet. Ex. 39 at 1; Pet. Ex. 72 at 2; Tr. 126, 145. He agreed that a pre-existing adenovirus infection could have allowed inflammatory cells activated in response to the flu vaccine to pass through the blood brain barrier and enter the brain. Pet. Ex. 72 at 1-2; Tr. 142-44. While he agreed with respondent that the flu vaccine is largely safe, that does not prove that autoimmune meningoencephalitis cannot occur. Pet. Ex. 72 at 2; Tr. 134-35, 157, 332-37.

Dr. Steinman opined that both the flu vaccine and adenovirus infection could trigger an immune response to CASPR2, a protein associated with an ion channel known as VGKC and associated with epilepsy. Pet. Ex. 46 at 5, 8; Tr. 177. *Michael* and *Kirschstein* showed that autoantibodies to CASPR2 are associated with encephalitis and epilepsy and appear to be directly pathogenic. Pet. Ex. 46 at 5, 8; Pet. Ex. 50; Pet. Ex. 52; Tr. 176-77, 192, 353-54. Dr. Steinman proposed molecular mimicry as the mechanism by which both the flu vaccine and adenovirus together triggered an immune response. Pet. Ex. 46 at 5, 8; Pet. Ex. 73 at 1-2; Tr. 168-70, 189-90. He described molecular mimicry as "an evolutionary adaptation whereby viruses and bacteria attempt to fool the body into granting them free access. Such mimicry works by showing the immune system stretches of amino acids that look like self." Pet. Ex. 56 at 4. Using a three-step filtration process, he identified at least one molecule known to trigger seizures (CASPR2) that has a molecular mimic in both the subject influenza vaccine and adenovirus. Pet. Ex. 46 at 8, 11-17; Pet. Ex. 53; Pet. Ex. 54; Pet. Ex. 55; Pet. Ex. 73 at 2-3; Tr. 169-70, 176-78, 192, 347-48.

He acknowledged that adenovirus is a tropism shown to rarely cause encephalitis and seizures, which is why he believed the flu vaccine played a role here. Pet. Ex. 63 at 3; Pet. Ex. 66; Pet. Ex. 67; Pet. Ex. 73 at 1-2; Tr. 172. He opined that the flu vaccine, an adenovirus infection, or a combination of the two could trigger molecular mimicry involving CASPR2, ultimately resulting in encephalitis and epilepsy. Pet. Ex. 46 at 5, 8; Pet. Ex. 73 at 1-2; Tr. 168-70, 177, 189-90.

Dr. Steinman explained the immune process following a flu vaccination that would allow antigenic immune T cells and B cells to cross the BBB and enter the brain. *See* Pet. Ex. 63 at 3-5; Pet. Ex. 70. He added that it was also possible that adenovirus caused encephalitis, causing permeability of the BBB and allowing immune cells activated by the vaccine to pass into the brain. Pet. Ex. 63 at 3. Once in the brain, these immune cells designed to target flu antigens may instead target the mimics found in the brain, triggering epilepsy. Pet. Ex. 63 at 4; Tr. 179-80. Dr. Steinman agreed with Dr. MacGinnitie that little, if any, antigen from a flu vaccine would spread to the brain; rather, his argument was that the T and B cells reactive to influenza vaccine would be trafficked to the brain and could cross the BBB via the mechanisms he described. Pet. Ex. 63 at 6.

Dr. Steinman opined that molecular mimicry can induce autoimmunity absent exact homology, with only 5 of 12 amino acids identical. Pet. Ex. 46 at 9-11; Pet. Ex. 56; Pet. Ex. 58; Pet. Ex. 59; Pet. Ex. 60; Pet. Ex. 63 at 4, 7; Pet. Ex. 71; Pet. Ex. 94 at 2-3; Tr. 177-78, 188, 197-98. He defended his use of the EAE models to support molecular mimicry, explaining that EAE is a "classic model of neuroinflammation" and the results could be extrapolated to conditions beyond just MS. Pet. Ex. 63 at 7; Tr. 188, 339-40, 343-46.

He agreed with respondent's experts that sequence homology is not uncommon but argued that sequence homology at a "disease related" epitope may cause autoimmune disease such as epilepsy. Pet. Ex. 46 at 9; Pet. Ex. 57. He agreed that the flu vaccine is generally very safe, but that "does not mean that influenza vaccine is never involved in meningoencephalitis and seizures." Pet. Ex. 63 at 8; Tr. 353.

Dr. Steinman concluded that the flu vaccine, which is meant to mount an immune response, combined with the adenovirus A.G.C. was already fighting, allowed the T cells and B cells reactive to influenza vaccine virus to enter the brain, and created the "perfect storm." Pet. Ex. 46 at 8; Pet.

Ex. 63 at 6; Tr. 167-69. The antigenic fragments of the vaccine could have breached the BBB that was "leaky" from adenovirus, targeted molecular mimics found in the brain, such as CASPR2, and triggered encephalitis and seizures. Pet. Ex. 63 at 3-6; Tr. 189-90. He conceded his theory does not prove with certainty what triggered A.G.C.'s epilepsy but shows how the seasonal flu vaccine could combine with an already present adenovirus and cause autoimmune epilepsy. Pet. Ex. 63 at 4; Tr. 180, 341-43, 348-49, 356. Therefore, the flu vaccine was more likely than not a substantial factor in contributing to A.G.C.'s seizure disorder. Pet. Ex. 46 at 1, 8; Pet. Ex. 73 at 1-2.

Dr. Holmes argued that there is no association between influenza vaccination and encephalitis. Resp. Ex. A at 14-16; Resp. Ex. A Tab 15; Resp. Ex. A Tab 16; Resp. Ex. A Tab 17; Tr. 214, 219-22. He agreed, however, that influenza infection may cause CNS disease in rare cases but stated that "[f]ortunately, influena (sic) encephalitis is preventable with the influenza vaccine." Resp. Ex. A at 16; Resp. Ex. A Tab 6; Resp. Ex. A Tab 26; Resp. Ex. A Tab 27. He asserted that adenovirus, on the other hand, has been demonstrated to cause CNS disease, including encephalitis in rare cases. Resp. Ex. A at 14; Resp. Ex. A Tab 6; Resp. Ex. A Tab 7; Tr. 213-14, 217, 219, 236. In *Kumar*, a study of 73 patients with acute viral encephalitis, 11% were caused by adenovirus. Resp. Ex. A at 14; Resp. Ex. A Tab 7. Dr. Holmes disagreed that CASPR2 antibodies were associated with epilepsy but rather manifested in children as weakness, sleep dysregulation, dysautonomia, autonomic dysfunction, and encephalopathy. Tr. 225-27; Resp. Ex. J; Resp. Ex. K; Resp. Ex. L.

Dr. Holmes explained that adenovirus may enter the brain through disruption of the BBB and cause further damage to the BBB once inside the brain. An individual with adenovirus infection "would have had impairment of the blood-brain barrier. This breach would have allowed entry of inflammatory cells, microorganisms, antigens and antibodies into the brain." Resp. Ex. E at 1. However, he argued that the small amount of antigen contained in the flu vaccine would be unlikely to result in "any meaningful brain concentration regardless of the integrity of the blood-brain barrier." *Id.* at 2. Nevertheless, Dr. Holmes agreed that it was possible that antibodies from the flu vaccine could enter the brain through an already disrupted BBB. *Id*.

Dr. Holmes argued that since Dr. Steinman conceded that adenovirus could induce an autoimmune response, there was no reason to implicate the flu vaccine. Resp. Ex. A at 17-18; Tr. 207-09, 211-14, 237-38.

Dr. MacGinnitie argued that epidemiology clearly established no relationship between influenza vaccine and epilepsy, seizures, or encephalitis. Resp. Ex. C at 5, 9-10; Resp. Ex. C Tab 15; Pet. Ex. 32; Resp. Ex. G at 1; Tr. 262-63, 302-04.

Dr. MacGinnitie further argued that homology alone is insufficient to trigger autoimmunity. Additionally, the homology between flu vaccine and CASPR2 in the brain is not significant. The homology between adenovirus and CASPR2 is even closer, yet still insufficient to trigger autoimmunity. Resp. Ex. C at 6-7; Resp. Ex. C Tab 6; Resp. Ex. C Tab 7; Resp. Ex. C Tab 9; Resp. Ex. G at 2; Tr. 264-67, 272-80; *see also* Resp. Ex. C Tab 8. Dr. MacGinnitie questioned molecular mimicry in general as a theory of autoimmunity, citing *Root-Bernstein* to show that "[i]f [molecular mimicry] is sufficient to induce autoimmune disease, then one would expect much higher rates of disease than are observed. . . Another problem is that according to

many investigators, very little evidence exists for MM playing a role in human diseases." Resp. Ex. G at 2; Pet. Ex. 71; Tr. 281-83.

Dr. MacGinnitie criticized Dr. Steinman's reliance on the mouse models of EAE, which required the use of a powerful adjuvant not present in any vaccines. Resp. Ex. C at 5-6; Pet. Ex. 58; Pet. Ex. 59; Pet. Ex. 60; Resp. Ex. C Tab 1; Resp. Ex. C Tab 4; Resp. Ex. C Tab 5; Resp. Ex. G at 2; Tr. 265-70, 307, 310. Further, those studies also used pertussis toxin to damage the BBB and allow access to pathogenic cells and antibodies to the CNS. Resp. Ex. C at 6; Resp. Ex. C Tab 3.

Dr. MacGinnitie argued that petitioners failed to show how any antigen from a vaccination could cross the BBB, which is practically impermeable, while the literature shows that adenovirus can directly damage the BBB and cause CNS infection or damage. Resp. Ex. C at 8; Resp. Ex. C Tab 10; Resp. Ex. F at 2; Tr. 258-59. Specifically, *Huang* and *Schwartz* show that seizures and encephalopathy are associated with adenoviral infection. Resp. Ex. C at 10; Resp. Ex. C Tab 16; Resp. Ex. C Tab 17. Dr. MacGinnitie argued that since adenovirus is a known trigger of meningoencephalitis and seizures, there was no reason to implicate the vaccine as a cause other than for purposes of the Program. Resp. Ex. G at 1, 4; Tr. 293.

When asked whether adenovirus could have caused a breakdown of the BBB that then allowed circulating vaccine antigens into the brain, Dr. MacGinnitie responded that there is little, if any, antigen from the flu vaccine available to circulate to the brain to cause encephalopathy or seizures. Resp. Ex. F at 1-3. Nevertheless, he could not "exclude the possibility that compromise of the BBB by adenovirus could have allowed antibodies against influenza vaccine components to reach the brain". *Id*. at 3. He agreed Dr. Steinman "spelled out a process that could happen" but believed it to be unlikely. Tr. 290, 317-18, 324.

It is undisputed that adenovirus is associated with upper respiratory syndromes and can rarely cause encephalopathy and neurological manifestations like encephalitis. However, Dr. Holmes stated and the literature he cited included that neurologic dysfunction from adenovirus more often occurs in immunocompromised children. Resp. Ex. A at 14; Resp. Ex. A Tab 5 at 1; Resp. Ex. A Tab 4 at 1; Tr. 217, 219, 236. The issue herein then is whether a flu vaccination—on its own or in combination with an adenovirus infection—could cause the same. I find petitioners' theory that the combination of adenovirus infection and flu vaccine[13] could trigger epilepsy to be scientifically sound and reliable.

Dr. Steinman explained how immunogenic T and B cells produced in response to a flu vaccine could cross the blood brain barrier in an individual already incubating an adenovirus infection. Both Dr. Holmes and Dr. MacGinnitie agreed that A.G.C. already had adenovirus when he received the flu vaccine and that adenovirus can damage the BBB. Neither effectively rebutted petitioner's argument that antibodies to the flu vaccine could cross an already-damaged BBB. In fact, they both agreed that this was possible. Resp. Ex. E at 1-2; Resp. Ex. F at 3. Dr. MacGinnitie

[13] Given the facts of this case wherein both parties agreed A.G.C. had an infection and a flu vaccination, my findings relate only to petitioners' combination theory. To be clear, I make no findings as to whether a flu vaccination on its own can cause encephalopathy or epilepsy.

conceded that Dr. Steinman's theory "spelled out a process that could happen". Tr. 290, 317-18, 324.

Medical certainty is not required for a petitioner to prevail on prong one, but this "does not absolve [a petitioner] from [their] burden to present a 'persuasive' theory supported by 'reputable' scientific or medical evidence." *Trollinger v. Sec'y of Health & Human Servs.*, 167 Fed. Cl. 127, 138 (2023). I find petitioners' combination theory persuasive. Dr. Steinman, who is one of the foremost experts on molecular mimicry, supported this theory with medical literature that discussed the association between CASPR2 antibodies and epilepsy. He identified a molecular mimic between CASPR2 and both the subject flu vaccination and adenovirus. He also provided animal studies on EAE to demonstrate how molecular mimicry may induce neuroinflammation.

I recognize respondent's argument that epidemiology has not shown a link between the flu vaccine and seizures, encephalitis, or encephalopathy. However, epidemiology is not designed to identify rare events such as vaccine injuries. For that reason, epidemiological evidence is not necessary for a petitioner to sustain their burden in proving prong one. I also understand Dr. MacGinnitie's issue with using mouse models to study human disease. Nevertheless, the medical literature provided in Program proceedings must be viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Andreu*, 569 F.3d at 1380. Experts who testify in this Program often must extrapolate a study's findings then apply that to the case before them. Although doing so does not prove that the subject vaccine can cause the alleged injury to the degree of scientific certainty, it may provide circumstantial evidence that advances a sound and reliable theory. *Doles v. Sec'y of Health & Human Servs*., 2023-2404, 2025 WL 1177875, at *5-9 (Fed. Cir. 2025) (The Federal Circuit "has expressly disavowed the requirement that petitioners under the Vaccine Act proffer a theory . . . that is grounded in medical certainty and backed by medically certain (statistically significant) evidence.") (internal citations omitted).

For the reasons set forth above, I find that petitioners have provided preponderant evidence of a sound and reliable theory to show that the combination of the flu vaccine with an active adenovirus infection can cause encephalitis and epilepsy. Petitioners have satisfied prong one.

B. Petitioners Have Provided a Logical Sequence of Cause and Effect.

To satisfy the second prong of *Althen*, a petitioner must establish a "logical sequence of cause and effect showing that the vaccination was the reason for the injury." *Althen*, 418 F.3d at 1278. The sequence of cause and effect need only be "logical and legally probable, not medically or scientifically certain." *Knudsen*, 35 F.3d at 548-49; *accord Capizzano*, 440 F.3d at 1326.

Where there are two potential causes for an illness/injury, a petitioner is not required to eliminate the other potential cause in order to be entitled to compensation. *Walther*, 485 F.3d at 1149-52. Moreover, case law instructs that where two causes combine to cause a vaccine-related illness, and it is not possible to determine which of the causes was most responsible, it is appropriate to find in favor of compensation. *See, e.g., Althen*, 418 F.3d at 1280 (noting that "close calls" are resolved in petitioners' favor).

The experts agreed that A.G.C. was exposed to adenovirus prior to the receipt of the subject flu vaccination and that A.G.C. manifested symptoms of adenovirus beginning the evening of his flu vaccination when he developed a fever followed two days later by symptoms of adenovirus including pharyngitis. Dr. Holmes explained that adenovirus incubates for 2 days to 2 weeks before symptoms begin. Resp. Ex. F at 3; Tr. 209, 211-13, 234-35, 259-61; Pet. Ex. 6 at 103. The experts also agreed that a pre-existing adenovirus infection could have damaged A.G.C.'s BBB and allowed agents, such as inflammatory cells activated in response to the flu vaccine, to enter the brain. Pet. Ex. 46 at 17; Pet. Ex. 63 at 6; Pet. Ex. 72 at 1-2; Resp. Ex. E at 1-2; Resp. Ex. F at 1-3.

The literature shows that adenovirus is rarely associated with encephalitis and seizures. Pet. Ex. 46 at 8; Pet. Ex. 53; Pet. Ex. 54; Pet. Ex. 55; Pet. Ex. 63 at 3; Pet. Ex. 66; Tr. 169-70. Dr. Steinman cited *Huang* which observed encephalitis after adenovirus infection in only 3.3% of patients, meaning that approximately 97% of people with adenovirus do not have encephalitis, which is why Dr. Steinman believed the flu vaccination played a causative role in A.G.C.'s encephalitis and development of epilepsy. Pet. Ex. 63 at 3; Pet. Ex. 67. Additionally, the records show that A.G.C.'s siblings had similar URI symptoms at the time, yet he was the only child who went on to develop encephalitis and seizures and the only one who received a flu vaccination at the time. Pet. Ex. 9 at 181.

Dr. Holmes explained that adenovirus typically clears within four days. Tr. 233. This would mean that, in a healthy child like A.G.C., the adenovirus infection should have resolved by or around October 24. Clearly, that did not occur in this case. A.G.C. had received the flu vaccination on October 20, became encephalopathic then developed seizures on October 26 and was ultimately diagnosed with epilepsy. At hearing, Dr. Holmes conceded that he could not say whether the flu vaccination here may have "escalated things". Tr. 233. Dr. Holmes also stated that he would not vaccinate a child with known adenovirus, because if they had a reaction, treaters would have no way to discern whether the reaction was due to the vaccine or to the infection. Tr. 229-33, 236-37, 248-49.

Dr. Holmes initially argued that the small amount of antigen contained in the flu vaccine would not likely result in "any meaningful brain concentration regardless of the integrity of the blood-brain barrier". Resp. Ex. E at 2. Interestingly, he also opined that A.G.C. showed signs of adenovirus-induced encephalitis when he received the flu vaccine and "would have had impairment of the blood-brain barrier", thereby allowing inflammatory cells, microorganisms, antigens, and antibodies to enter the brain. *Id.* at 1. Dr. MacGinnitie conceded that he "cannot exclude the possibility that compromise of the BBB by adenovirus could have allowed antibodies against influenza vaccine components to reach the brain". Resp. Ex. F at 3.

As detailed in prong one, Dr. Steinman showed that there are shared homologies between CASPR2 and components of the subject flu vaccine and adenovirus. Pet. Ex. 46 at 11; Tr. 177-78, 192. The literature filed also supports that CASPR2 antibodies are associated with some syndromes including encephalitis. Pet. Ex. 46 at 5; Pet. Ex. 50; pet. Ex. 52; Tr. 176-77, 192, 353-54. *Kirschstein* showed that antibodies to CASPR2 alter synaptic firing linked to epilepsy. Pet. Ex. 46 at 8; Pet. Ex. 52.

Dr. Steinman opined that the flu vaccine activated T and B immune cells that crossed the adenovirus-damaged BBB, allowing T cells and B cells to enter the brain. Those T and B cells then recognized and targeted molecular mimics found in the brain, such as CASPR2, triggering encephalitis and seizures. Pet. Ex. 46 at 17; Pet. Ex. 63 at 4-6; Tr. 167, 189-90.

Petitioners provided medical literature to support the assertion that A.G.C. may have had CASPR2 antibodies. While he tested negative for VGKC antibodies, he was not tested for CASPR2 antibodies. The literature shows that CASPR2 antibodies may be present in a patient where VGKC antibodies are negative. Pet. Ex. 50. Additionally, in arguing that A.G.C. likely did not have CASPR2 antibodies, Dr. Holmes submitted that anti-CASPR2 antibodies typically present clinically as encephalopathy and dysautonomia (among other symptoms), both of which he agreed were consistent with A.G.C.'s clinical presentation. Tr. 225-27, 246-47; Resp. Ex. J; Resp. Ex. L. To invoke the age-old adage, absence of evidence is not evidence of absence; I cannot conclude that A.G.C. did not have CASPR2 antibodies when petitioners demonstrated that VGKC testing is not dispositive on this issue, when Dr. Holmes agreed that A.G.C. presented clinically with symptoms associated with anti-CASPR2 antibodies, and when caselaw instructs that the benefit be afforded to petitioners. *See Althen*, 418 F.3d at 1280.

Further, the evidence shows that A.G.C.'s condition did improve with immunotherapy. Both Dr. Steinman and Dr. MacGinnitie argued CASPR2-related neurological disorders show dramatic improvement with immunotherapy. Tr. 355; Pet. Ex. 50 at 3; Pet. Ex. 94 at 1-2; Resp. Ex. C at 8. Dr. MacGinnitie disagreed that A.G.C. improved with the immunotherapies he received; however, Dr. Holmes and Dr. Steinman submitted that A.G.C. responded to immunotherapy. Resp. Ex. C at 8; Tr. 223-24, 245, 259, 287-90, 318; Pet. Ex. 10 at 94; *see also* Tr. 20. The discharge record from November 13, 2015 noted that A.G.C.'s "[e]ncephalopathy improved with seizure control on 3 [anti-epileptic drugs], s/p 5 days of [IV methylprednisolone] and 2 g/kg of IVIG." Pet. Ex. 10 at 69, 94. Similarly, the visit notes from a neurology follow up on December 15, 2015 noted that A.G.C. had improvement in seizures and in mental status following immunotherapy while admitted at Children's. Pet. Ex. 15 at 62. Thus, the contemporaneous records support Dr. Holmes' and Dr. Steinman's opinions that A.G.C. improved with immunotherapy, thereby supporting Dr. Steinman's assertion that A.G.C.'s disorder was CASPR2-related.

Respondent argued that adenovirus is a known cause of encephalitis and thus, there is no reason to implicate the flu vaccine as a cause here. Resp. Ex. A at 17-18; Resp. Ex. G at 1, 4. However, "[t]he bare statistical fact that there are more reported cases of viral encephalopathies than there are reported cases of [vaccine-caused] encephalopathies is not evidence that in a particular case an encephalopathy following a [] vaccination was in fact caused by a viral infection present in the child and not caused by the [subject] vaccine. *Knudsen,* 35 F.3d at 550.

Most importantly, all four experts agreed that a pre-existing adenovirus infection could have damaged the BBB and allowed agents, such as inflammatory cells activated in response to the flu vaccine, to enter A.G.C.'s brain. Pet. Ex. 46 at 17; Pet. Ex. 63 at 6; Pet. Ex. 72 at 1-2; Resp. Ex. E at 1-2; Resp. Ex. F at 1-3.

The caselaw is clear that a petitioner may sustain their burden by demonstrating that the vaccination was a "substantial factor" and a "but for" cause of the injury, even if the vaccination is not the sole cause. *Pafford*, 451 F.3d at 1355; *Shyface*, 165 F.3d at 1352.

The Federal Circuit in *Shyface* held that a petitioner need not prove the vaccination was the predominant factor in bringing about the injury, just that it was a substantial factor. In *Shyface*, the child received a DPT vaccine while incubating an E. coli infection. Because it was not possible to determine whether the vaccine or the infection was the predominant factor, the Federal Circuit found that both were substantial factors in bringing about the child's death. *Shyface*, 165 F.3d at 1352-53.

Special masters have since found that where there is a concurrent infection with vaccination, both are substantial factors in bringing about the injury alleged. *Herkert v. Sec'y of Health & Human Servs.*, No. 97-518V, 2000 WL 141263, at *1 (Fed. Cl. Spec. Mstr. Jan. 19, 2000) (finding petitioner proved the DTaP vaccine and cytomegalovirus infection were both substantial factors in causing his son's transverse myelitis); *Nash v. Sec'y of Health & Human Servs*., No. 00-149V, 2002 WL 1906501, at *1 (Fed. Cl. Spec. Mstr. June 27, 2002) (finding both meningitis infection and DPT vaccination were substantial factors in causing the child's condition). Likewise, where there are concurrent factors of infection and vaccination, I have found that both are substantial factors in the resulting injuries or death. *See Lehrman v. Sec'y of Health & Human Servs*., No. 13–901, 2018 WL 1788477, at *1 (Fed. Cl. Spec. Mstr. Mar. 19, 2018); *Matten v. Sec'y of Health & Human Servs*., No. 12-155V, 2021 WL 5768148, at *1 (Fed. Cl. Spec. Mstr. Nov. 2, 2021).

With a concurrent adenoviral infection and flu vaccination, I find both were substantial factors in causing A.G.C.'s encephalitis and epilepsy. Accordingly, I find that petitioners have provided preponderant evidence to satisfy prong two.

C. Petitioners Have Provided a Medically Acceptable Timeframe.

The third *Althen* prong requires a petitioner to establish the "timeframe for which it is medically acceptable to infer causation" and that the onset of the disease occurred in this period. *Shapiro v. Sec'y of Health & Human Servs.,* 101 Fed. Cl. 532, 542-43 (2011), *recons. denied after remand on other grounds*, 105 Fed. Cl. 353 (2012), *aff'd without op.,* 503 F. App'x 952 (Fed. Cir. 2013). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury utilized to satisfy the first prong. *Shapiro*, 101 Fed. Cl. at 542 (internal citations omitted).

Prong three is largely uncontested. Dr. Steinman relied on *Schonberger* and used GBS as a surrogate to show the onset of neuroinflammation within one week of flu vaccination. Pet. Ex. 46 at 18; Pet. Ex. 61. He also submitted *Bennetto & Scolding*, which observed the onset of encephalomyelitis between 1-14 days after vaccination. Pet. Ex. 46 at 18; Pet. Ex. 62. Additionally, in *Huang*, the authors observed a "minimal time of onset [of encephalitis] as 5 days" of adenoviral infection. Pet. Ex. 63 at 3; Pet. Ex. 67. Here, the onset of A.G.C.'s adenovirus was the day of vaccination. His clinical presentation six days later on October 26, 2015 is consistent with the

proposed timeframes of both adenovirus-caused and vaccination-caused encephalitis. Neither Dr. Holmes nor Dr. MacGinnitie provided any disagreement with the onset.

Therefore, petitioners have provided preponderant evidence to satisfy prong three.

D. Respondent Has Failed to Prove an Alternative Cause.

Because petitioners have established a prima facie case of causation under *Althen*, they are entitled to compensation unless respondent can show by a preponderance of the evidence that A.G.C.'s injury was in fact caused by a factor unrelated to the vaccine. *Deribeaux*, 717 F.3d at 1367; *see* § 13(a)(1)(B). To meet this standard, respondent must "present sufficient evidence to prove that the alternative factor was the *sole* substantial factor in bringing about the injury." *Deribeaux*, 717 F.3d at 1367 (emphasis added).

The experts agreed that A.G.C. had an antecedent or concurrent infection at the time A.G.C. received the flu vaccination and prior to the onset of seizures, encephalitis, and epilepsy. As detailed above, I have found that where infection and vaccination collide, both are substantial factors in bringing about the injury alleged. Thus, respondent cannot sustain his burden in proving that adenovirus was the *sole* substantial factor in causing A.G.C.'s injury.

V. Conclusion

For the reasons discussed above, I find that petitioners have established by preponderant evidence that A.G.C.'s flu vaccination was a substantial contributing factor to his condition. Therefore, petitioners are entitled to compensation. A separate damages order will issue.

IT IS SO ORDERED.

s/ Mindy Michaels Roth
Mindy Michaels Roth
Special Master

Appendix: Medical Literature

Exhibit	Citation
Pet. Ex. 32	Sara Ghaderi et al., *Encephalitis after influenza and vaccination: a nationwide population-based registry study from Norway*, 46 INT'L J. EPIDEMIOLOGY 1618 (2017).
Pet. Ex. 33	Nazish Ilyas, MD et al., *"Possessed" or flu shot encephalitis? A rare complication of the influenza vaccine*, Hospital Medicine (2018).
Pet. Ex. 34 Resp. Ex. A Tab 22	Jorge D. Machicado et al., *Acute Disseminated Encephalomyelitis following Seasonal Influenza Vaccination in an Elderly Patient*, 20 CLINICAL & VACCINE IMMUNOLOGY 1485 (2013).
Pet. Ex. 35	Priya Narwal et al., *Recurrent Encephalitis after Seasonal Influenza Vaccine (P5.100)*, 84 NEUROLOGY 14 Supplement (2015).
Pet. Ex. 36	Zaid Al Qudah et al., *Encephalitis after Vaccination in United States. A Report from the CDC/FDA Vaccine Adverse Event Reporting System [1990–2010] (P03.151)*, 78 NEUROLOGY 1 Supplement (2012).
Pet. Ex. 37 Resp. Ex. A Tab 25	Yahel Segal & Yehuda Shoenfeld, *Vaccine-induced autoimmunity: the role of molecular mimicry and immune crossreaction*, 15 CELLULAR & MOLECULAR IMMUNOLOGY 586 (2018).
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