In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: April 1, 2019

THERESA DEISHER, as Administrator of the Estate of H.S.,	*	PUBLISHED
Petitioner,	*	No. 17-294V
v.	*	Chief Special Master Nora Beth Dorsey
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Dismissal Decision; Measles, Mumps, Rubella ("MMR") Vaccine; Varicella Vaccine; Hepatitis A Vaccine; Burkitt Lymphoma; Insertional Mutagenesis.
Respondent.	*	

John F. McHugh, Law Office of John McHugh, New York, NY, for petitioner.
Heather L. Pearlman, U.S. Department of Justice, Washington, DC, for respondent.

DECISION DISMISSING CASE[1]

On March 2, 2017, Theresa Deisher ("petitioner") filed a petition pursuant to the National Vaccine Injury Compensation Program[2] on behalf of the estate of her deceased son, H.S. Petitioner alleges that "vaccinations this child received between 2002 and 2005 caused onset of lethal cancer." Petition at ¶ 2.

After carefully analyzing and weighing all of the evidence presented in this case in accordance with the applicable legal standards, the undersigned finds that petitioner has not met her legal burden. Petitioner has failed to demonstrate that any of the childhood vaccines

[1] Because this Decision contains a reasoned explanation for the action in this case, the undersigned is required to post it on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). **This means the Decision will be available to anyone with access to the Internet.** In accordance with Vaccine Rule 18(b), petitioner has 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, the undersigned agrees that the identified material fits within this definition, the undersigned will redact such material from public access.

[2] The Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-10 et seq. (hereinafter "Vaccine Act" or "the Act").

administered to H.S. caused his death from Burkitt lymphoma. Accordingly, petitioner is not entitled to compensation and her petition is dismissed.

I. BACKGROUND

A. Procedural History

Petitioner filed her claim on March 2, 2017, and she filed a number of medical records on March 7, 2017, and May 10, 2017. See Petitioner's Exhibits ("Pet. Exs.") 1-10. On July 10, 2017, respondent filed a Rule 4(c) Report, in which he recommended against compensation. Respondent's Report ("Resp. Rpt.") (ECF No. 14). Emphasizing that the Vaccine Act does not allow a special master to find entitlement based on petitioner's claims alone, respondent maintained that "H.S.'s medical records do not support a causal association between any of his vaccines and his condition." Id. at 7. He also noted a variety of medical records that had not been included in petitioner's filings. Id. at 2, 4.

Petitioner submitted additional medical records on August 19, 2017. Pet. Ex. 11. She subsequently filed an expert report from Dr. Judy Mikovits and Dr. Francis Ruscetti, as well as an expert report from Dr. Douglas Darnowski, on September 8, 2017. Pet. Ex. 12, 25. At respondent's request, the undersigned then ordered petitioner to file all medical literature referenced in the reports and to clarify certain assertions made by her experts. Order dated Mar. 12, 2018 (ECF No. 32). When petitioner failed to file all of the requested documentation by the deadline, the undersigned issued an order to show cause. Order to Show Cause dated May 21, 2018 (ECF No. 37).

On June 18, 2018, respondent filed an expert report from Dr. Lewis Chodosh. Resp. Ex. B. The same day, petitioner filed a response to the order to show cause, maintaining that she had now supplied all documentation requested by the Court. Pet. Response dated June 18, 2018 (ECF No. 45). Respondent filed his own response on June 20, 2018, asserting that petitioner's submission "reflect[ed] a misunderstanding" regarding the additional information necessary to move the case forward. Resp. Response dated June 20, 2018 (ECF No. 46). On June 21, 2018, the undersigned issued a second order to show cause, noting a number of deficiencies in petitioner's response. Second Order to Show Cause dated June 21, 2018 (ECF No. 47). Petitioner subsequently submitted several filings, each responsive to a different part of the second order to show cause, on June 27, 2018, July 11, 2018, and July 19, 2018. Status Rpt. dated June 27, 2018 (ECF No. 50); Status Rpt. dated July 11, 2018 (ECF No. 52); Notice of Compliance dated July 19, 2018 (ECF No. 53).

During a status conference on August 7, 2018, the undersigned provided the parties with her preliminary evaluation of petitioner's claim. Order dated Aug. 8, 2018 (ECF No. 59). After comparing the parties' expert reports, she concluded that petitioner had not offered a plausible mechanism that could satisfy any of the Althen prongs. Id. at 2. The undersigned thus ordered petitioner to file either a motion to dismiss or an expert report from a hematologist or oncologist. Id. Petitioner responded by filing a motion for a ruling on the record. Pet. Mot. for Ruling on the Record dated Oct. 4, 2018 (ECF No. 60). She made no substantive arguments in this motion,

stating only that "[p]ursuant to the Court's pending order, petitioner respectfully requests a decision on the record." Id. Respondent did not file a response.

This matter is now ripe for adjudication on petitioner's motion for a ruling on the record.

B. Summary of Relevant Facts

To reach this decision, the undersigned fully reviewed the entire record. This section is a summary of the facts deemed most relevant to the present determination.

H.S. was born on March 28, 2001. Pet. Ex. 1 at 26. His mother had a benign abdominal tumor removed at age 26, and his family history includes a maternal great uncle who died from Hodgkin's lymphoma and a paternal great uncle who has an optic tumor. Pet. Ex. 2 at 246. As a child, H.S. received the following vaccines on the following dates:

Diphtheria, Tetanus, acellular Pertussis ("DTaP")
- May 9, 2001
- July 26, 2001
- September 26, 2001
- September 20, 2002
- May 24, 2005

Haemophilus Influenzae Type B ("Hib")
- May 9, 2001
- July 26, 2001
- April 5, 2002

Inactivated Poliovirus ("IPV")
- May 9, 2001
- July 26, 2001
- September 20, 2002
- May 24, 2005

Hepatitis B
- May 9, 2001
- July 26, 2001
- January 7, 2002

Measles, Mumps, Rubella ("MMR")
- April 5, 2002
- May 24, 2005

Varicella
- April 5, 2002

Meningococcal
- October 31, 2002

Hepatitis A
- April 2, 2003
- May 19, 2004

Influenza
- October 17, 2003
- February 1, 2007
- October 25, 2007
- December 9, 2014

Pneumococcal Conjugate ("PCV")
- May 9, 2001
- July 26, 2001
- September 26, 2001
- September 20, 2002

Tetanus, Diphtheria, acellular Pertussis ("TDaP")
- October 31, 2012

Pet. Ex. 1 at 2.[3] Prior to 2014, H.S.'s medical history was remarkable only for a persistent cough in 2006; scoliosis concerns in 2008-2009; a right hydrocele in 2009; and a left thumb fracture in 2011. Id. at 12, 26-27; Pet. Ex. 2 at 55-56; Pet. Ex. 11 at 22-24. No other significant medical issues were revealed during his routine well-child examinations on September 1, 2009; August 27, 2010; September 5, 2011; and October 29, 2012. Pet. Ex. 1 at 18-28.

On July 28, 2014, H.S. presented to Dr. Michael S. Dudas, M.D., with a one-week history of fatigue, nausea, and bone pain.[4] Pet. Ex. 1 at 12. He also reported mild diarrhea and intermittent pain in a rib on his right side, and he was noted to be a "poor eater." Id. Although his abdominal x-ray was negative, a physical examination revealed non-tender fullness in the midline lower abdomen. Id. at 11, 13. H.S.'s labs showed an elevated white blood cell count, electrolyte abnormalities, elevated C-reactive protein, and elevated erythrocyte sedimentation rate. Id. at 13. A chemistry panel displayed low levels of albumin, sodium, and chloride. Id. at 9-10. An abdominal ultrasound conducted on July 30, 2014, further revealed a large right upper quadrant mass on the wall of the gallbladder, extensive peritoneal disease, and other

[3] Although H.S.'s medical records reflect a variety of vaccinations between 2001 and 2014, the petition only alleges injury from vaccines administered between 2002 and 2005. See Petition at 1. Additionally, the petition lists only MMR, Varicella, and Hepatitis A as "relevant vaccines." Id.

[4] Later, H.S. also reported the onset of a left testicular mass, beginning around April 2014. Pet. Ex. 2 at 245.

abnormalities in the pelvis. Id. at 13.

On July 30, 2014, H.S. was admitted to the Hematology-Oncology Clinic at Seattle Children's Hospital. Pet. Ex. 2 at 245-48. A CT scan that day found the following: a large right upper quadrant mass within the gallbladder fossa, compressing the inferior vena cava; extensive and diffuse peritoneal disease, involving the mesentery and omentum; moderate volume ascites; a 3mm non-obstructing renal calculus; an excrescence of the anterior right fourth rib,[5] with benign characteristics; mediastinal and pericardial lymphadenopathy; and moderate-sized bilateral pleural effusions. Id. at 247. Additional labs showed cell lysis, and an examination revealed several masses: a 5 x 5 cm hard mass in the right upper quadrant of the abdomen; a 10 x 10 cm hard mass in the median aspect of the lower abdomen; a 5 x 3 x 2 hard mass in the left testicle; and a 0.5 x 0.5 cm bony rib protuberance lateral of the left mamilla. Id. at 247.

The next day, July 31, 2014, H.S.'s testicular mass was biopsied. Pet. Ex. 2 at 234-35. The biopsy revealed no abnormal DNA content, but the scrotal fluid was positive for malignant cells, which stained positive for Ki-67 and CD20. Id. Furthermore, a clonal population of cells expressed CD45, CD19, and CD20, along with CD10, CD22, and HLA-DR. Id. Preliminary assessment of the scrotal fluid by fluorescence in situ hybridization also reflected rearrangement of the MYC oncogene.[6] Id. at 1421. Based on these results, H.S. was diagnosed with Burkitt lymphoma (mature B-cell non-Hodgkin lymphoma), Group B, and was later upgraded to Group C1. Id. at 234, 869. Doctors at Seattle Children's Hospital treated H.S.'s Burkitt lymphoma with several different regimens of chemotherapy. Pet. Ex. 2 at 184-242. An October 21, 2014 biopsy showed persistent disease, as did a second biopsy on December 12, 2014, although the tumor was noted to have shrunk. Id. at 869. A new chemotherapy regimen with rituximab, ifosfamide, carboplatin, and etoposide was administered, and plans were made for an autologous stem cell transplant. Id.

H.S.'s autologous stem cell transplant was conducted on March 21, 2015. Pet. Ex. 2 at 128. He experienced prolonged fevers during his recovery. Id. H.S. was discharged on April 8, 2015, but PET and CT scans conducted in May 2015 were "highly concerning for recurrent disease." Id. at 103, 1441-42, 1485-86. On May 14, 2015, H.S.'s treating physician informed his family that this recurrence signaled that the Burkitt lymphoma was "aggressive and likely incurable." Id. at 97. During the last few months of his life, H.S. underwent a wide variety of laboratory tests. Most significantly, a polymerase chain reaction ("PCR") test for Epstein-Barr Virus ("EBV")[7] conducted in March 2015 was negative, as was a June 2015 blood test for HIV.

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[5] According to the physical exam, this excrescence was found on the anterior left fourth rib, not the right. Id. at 247.

[6] An oncogene is "a gene capable under certain conditions of causing the initial and continuing conversion of normal cells into cancer cells." Dorland's Illustrated Medical Dictionary 1321 (32d ed. 2012).

[7] EBV is a virus that causes infectious mononucleosis and is also associated with Burkitt lymphoma and nasopharyngeal carcinoma. Dorland's at 2061. More than 90% of the healthy

Id. at 63, 1355.

On June 25, 2015, H.S. presented to Seattle Children's Hospital with complaints of "significant crampy abdominal pain and fullness in his upper abdomen," which had developed during his recent Make-A-Wish trip in Alaska. Pet. Ex. 2 at 468. He was admitted and administered palliative measures. Id. H.S. passed away on July 3, 2015, due to "progressive respiratory failure secondary to his underlying cancer." Id. at 468, 735.

C. Expert Reports

1. Petitioner's Experts

a. Judy Mikovits, Ph.D. and Francis Ruscetti, Ph.D.

i. Education and Background

Dr. Mikovits earned her B.A. in biology, with a specialization in biochemistry, from the University of Virginia. Pet. Ex. 12-a at 4. She earned her Ph.D. in biochemistry and molecular biology from George Washington University. Id. From 1992 to 1994, Dr. Mikovits was a post-doctoral fellow in molecular virology at the National Cancer Institute's ("NCI") Lab of Genomic Diversity, subsequently serving as a staff scientist at the NCI's Lab of Leukocyte Biology from 1994 to 1998. Id. at 3-4. From 1999 to 2001, she served as a Lab Director at the Laboratory of Antiviral Drug Mechanisms, a division of the NCI. Id. at 3. Dr. Mikovits worked in various capacities at several biotechnology start-up companies from 2002 to 2006, and she was the Research Director of the Whittemore Peterson Institute for Neuro-Immune Disease from 2006 to 2011. Id. at 2-3. From 2006 to 2012, she served as a scientist and consultant for a pharmaceutical company. Id. at 1-2. She is currently a consultant for MAR Consulting, a company she co-founded, and she also serves as an advisor for a private equity firm. Id. at 1. Her CV lists 51 publications that she has authored or co-authored. Id. at 5-9.

Dr. Ruscetti received his B.S. in biology from Boston University, and his Ph.D. in microbiology from the University of Pittsburgh. Pet. Ex. 12-b at 1. From 1972 to 1975, he was a Research Instructor at the University of Pittsburgh School of Medicine. Id. From 1975 to 1978, Dr. Ruscetti worked for a biotechnology company, and since 1978, he has held various senior positions at the NCI. Id. at 1-2. He currently serves as the Principal Investigator for the NCI's Leukocyte Biology Section and as an Adjunct Professor of biochemistry and molecular biology at George Washington University, a position he has held since 1988. Id. Dr. Ruscetti has authored or co-authored more than 300 scientific publications, has served on editorial boards of several scientific journals, and currently serves on the editorial board of Stem Cells. Id. at 2-32.

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population is infected with EBV as a "persistent, latent asymptomatic infection." Resp. Ex. B-37 at 2.

ii. Opinion

Dr. Mikovits and Dr. Ruscetti claim that "MMRII and Varivax are contaminated with trillions of base pairs of DNA from human cell lines . . . ." Pet. Ex. 12 at 6. These vaccines, along with the Hepatitis A vaccine, "may be contaminated with at least one animal retrovirus family, all of which have been associated with cancer." Id. at 7. For instance, Dr. Mikovits and Dr. Ruscetti posit that "[b]oth MMRII and Varivax have been documented to contain avian/chicken Retroviral DNA (from the chick embryo cell culture human endogenous and bovine leukemia virus DNA (from calf, guinea pig endogenous retroviral DNA, Human Endogenous retroviruses and murine leukemia virus DNA, which are CDC acknowledge excipient in the vaccine." Id. at 9. As a result, they assert, "HS was exposed to not only 100 billion retroviral DNA fragments but also EBV and SV40[8] cancer causing viruses . . . ." Id. at 6. Dr. Mikovits and Dr. Ruscetti claim that vaccines contaminated in this manner could have caused H.S.'s injury through the following mechanisms:

> 1) insertional mutagenesis 2) dysregulation of DNA methylation[9] machinery leading to aberrant expression of oncogenes, tumor suppressor genes and regulatory microRNA 3) altered immune cell function accelerate a stepwise selection of more malignant cells and the inability of the immune system to respond or repair the mutation and epi-mutations.

Id. at 11-12. The fact that H.S. was so young when first vaccinated, Dr. Mikovits and Dr. Ruscetti state, was his "primary risk factor" for the later development of Burkitt lymphoma. Id. at 4; see also id. at 6 (stating that because H.S. was "a child under three" at the time of the vaccination, he was "an immune incompetent individual"). Although they theorize that "one or two injections of an adventitious retrovirus likely does little damage to a healthy immune system," the fact that H.S. received multiple vaccinations at such a young age made him more susceptible to injury. Id. at 12. Dr. Mikovits and Dr. Ruscetti suggest that years after these vaccinations, onset of H.S.'s Burkitt lymphoma occurred "during puberty when the immune system [was] hyper-activated." Id.

Dr. Mikovits and Dr. Ruscetti discuss at length "how DNA viruses like EBV and HIV cooperate to cause the initiation and progression of cancer." Pet. Ex. 12 at 3; see also id. at 4-6, 8-9. Although they acknowledge that H.S. tested negative for EBV, they hypothesize that he "could have still had EBV in his immune cells but the DNA would have been hypermethylated and silenced and thus be invisible to the immune system and show no evidence of infection." Id. at 3. In a later status report, petitioner clarified that Dr. Mikovits and Dr. Ruscetti "do not know

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[8] SV40 is "a species of the genus Polyomavirus that was isolated from Rhesus monkey kidney tissue and produces transformation in human and newborn hamster kidney cell cultures and has caused progressive multifocal leukoencephalopathy in humans." Dorland's at 2065.

[9] DNA methylation is "the postsynthetic addition of methyl groups to specific sites on DNA molecules. . . . Methylation is involved in gene expression, and plays a role in a variety of epigenetic mechanisms, including development, X chromosome inactivation, genomic imprinting, mutability of DNA, and uncontrolled cell growth in cancer." Dorland's at 1152.

nor does it change their opinion if HS's cancer was associated with [EBV]," asserting also that "if HS's cancer was associated with EBV, that EBV would have been from a contaminant of the vaccine." Status Rpt. dated July 11, 2018 (ECF No. 52).

b. Douglas Darnowski, Ph.D.

i. Education and Background

Dr. Darnowski earned a B.S. in biology from Yale University and a Ph.D. in plant biology from Cornell University. Pet. Ex. 25-a at 1-2. After completing his Ph.D., he served as a Postdoctoral Research Associate at the University of Illinois. Id. at 1. He has authored or co-authored 21 articles in journals such as Biotechniques, Plant Biology, and the Journal of the International Carnivorous Plant Society. Id. at 4-5. In addition to these peer-reviewed publications, Dr. Darnowski has engaged in a number of other scientific writing and research projects, focusing on subjects such as trigger plants and carnivorous plants in general. Id. at 6-11. He currently serves as an Associate Professor of biology at Indiana University Southeast, and he previously served as an Assistant Professor of biology at Washington College. Id. at 1.

ii. Opinion

Dr. Darnowski asserts that the MMR, Varicella, and Hepatitis A vaccinations that H.S. received between 2002 and 2005 "carr[ied] . . . human fetal DNA as a contaminant . . . ." Pet. Ex. 25 at 1. He alleges that the MMRII vaccine in particular "is contaminated with DNA from human fetal cells at about 2 µg per dose, far above the World Health Organization's recommended maximum of 10 ng/dose." Id. at 2 (internal citations omitted). These contaminants, Dr. Darnowski alleges, lead to "insertional mutations," a process by which an organism "absorbs DNA which it encounters in its environment and incorporates that DNA into its own genome due to the functioning of DNA repair mechanisms." Id. at 3. In turn, he states, these mutations "can include changes in the regulation of gene expression which can lead to cancer since upregulation of the expression of oncogenes leads to excessive cell division, cancer." Id. at 1. Similarly, he claims that some vaccines "are also contaminated with DNA of viruses which were used in vaccine production, a further cause of oncogenesis as seen in well-known clinical cases." Id. at 2 (internal citations omitted).

Relying on the mechanisms described above, Dr. Darnowski posits that "an immune system cell, such as a B cell which is the progenitor of cancers such as Burkitt lymphoma, can and will express DNA presented to them." Pet. Ex. 25 at 3. In the case of H.S. specifically, he maintains that the significant temporal gap between the administration of the vaccinations and the onset of cancer "can be explained by the dormancy of some immune system B cells which would have been subject to insertional mutation. When these B cells were later activated, they would then have caused Burkitt lymphoma in the patient." Id. at 2. Dr. Darnowski notes that B cells are activated "when the body is appropriately challenged," and that the activation is "likely to be random." Id. at 4.

In support of his theory of causation, Dr. Darnowski claims that "the introduction of MMRII and other similar fetal cell line-derived vaccines highly correlates with the rise of

various childhood disorders, including sporadic-type Burkitt Lymphoma . . . ." Pet. Ex. 25 at 2. He cites a graph which, he asserts, shows the "[c]hange in the incidence of Burkitt Lymphoma (sporadic type) with the introduction of MMRII."[10] Id. at 2-3.

2. Respondent's Expert – Lewis Chodosh, M.D., Ph.D.

a. Education and Background

Dr. Chodosh earned a B.S. from Yale University, an M.D. from Harvard Medical School, and a Ph.D. in biochemistry from the Massachusetts Institute of Technology. Resp. Ex. A at 1. His postgraduate training includes a medical residency at Massachusetts General Hospital and a postdoctoral research fellowship in the Department of Genetics at Harvard Medical School. Id. Over the course of his career, he has authored or co-authored over 100 peer-reviewed publications. Id. at 23-38. He has held multiple faculty appointments, and he currently serves as Chairman of the Department of Cancer Biology at the University of Pennsylvania School of Medicine. Id. at 2. Dr. Chodosh is licensed to practice medicine in Massachusetts and Pennsylvania. Id. at 3. He also serves as an editorial board member of the Journal of Mammary Gland Biology and Neoplasia, an associate editor of Cancer Biology and Treatment, and the editor-in-chief of Breast Cancer Research. Id. at 4.

b. Opinion

i. Theory of Causation

Dr. Chodosh begins by explaining that genetic mutations, such as those that cause cancer, generally "occur simply as a consequence of living." Resp. Ex. B at 7; see also Resp. Ex. B-16 at 17 ("[E]ndogenous biochemical processes usually make far greater contributions to genome mutation than do exogenous mutagens."). Discussing the normal damage and repair that human DNA endures on a daily basis, he observes that these "internal cellular processes" can cause mutations that "are almost certainly sufficient to cause human cancers . . . ." Resp. Ex. B at 7. Dr. Chodosh concludes that for H.S., "the presence of a characteristic MYC translocation in his cancer clearly indicates the presence of a well-known and powerful oncogene, and that oncogenic mutation almost certainly played a causal role in the development of his cancer." Id. at 8.

ii. Response to Dr. Darnowski

Dr. Chodosh responds to each of petitioner's expert reports individually. He first addresses Dr. Darnowski's assertion that "DNA which enters a cell can and often is inserted into that cell's genome." Resp. Ex. B at 11 (quoting Pet. Ex. 25 at 3). Dr. Chodosh calls this

[10] Petitioner later clarified that this graph had been constructed by Katy Doan, then a researcher at Sound Choice Pharmaceutical Institute. Status Rpt. dated June 27, 2018 (ECF No. 50) at 1. As respondent's expert noted, petitioner herself is the president of this Institute. Resp. Ex. B at 19. Petitioner stated that no effort had been made to publish the chart. Status Rpt. dated June 27, 2018, at 2.

statement "scientifically incorrect." Id. Mammalian cells, he explains, "do not typically take up exogenous DNA and incorporate it into their genome" because "there are numerous DNA sensing and genome protection mechanisms in the cell to prevent this." Id. Moreover, while Dr. Chodosh agrees that the MMR, Varicella, and Hepatitis A vaccines likely contain residual human DNA, he asserts that this DNA does not contain activated oncogenes or DNA from pathogenic exogenous viruses. Id. He later notes an additional safeguard: "[F]ragmentation of DNA would effectively destroy the transforming potential of any otherwise intact genes present in residual cell DNA." Id. at 12.

Next, Dr. Chodosh addresses Dr. Darnowski's claim that the digestion of the residual DNA in vaccines causes the uptake of DNA by B lymphocytes. Dr. Chodosh asserts that on the contrary, "B cells are highly resistant to taking up exogenous DNA fragments in culture, even when using methods designed to stimulate DNA uptake . . . ." Resp. Ex. B. at 12. Pointing to a study cited by Dr. Darnowski, Dr. Chodosh emphasizes that "because both the probability that DNA will integrate into the cellular genome and the probability that this exogenous DNA would disrupt a tumor-suppressor gene or activate a proto-oncogene have been considered to be extremely low . . . , any potential adverse consequences from integration have not been considered a significant risk." Id. at 14 (quoting Pet. Ex. 25-11 at 2); see also id. at 17-18 (further quantifying the extremely low risk of exogenous DNA being integrated into a cell's genome and causing a mutation). Moreover, even if this were a plausible mechanism, Dr. Chodosh disputes Dr. Darnowski's claim that the transformed lymphocytes would have remained dormant for 9-12 years, as would have been the case for H.S. Id. at 21.

Dr. Chodosh also questions the validity of Dr. Darnowski's "Burkitt Lymphoma Changepoint" graph. He emphasizes that surprisingly, Dr. Darnowski had not discussed the source of the graph's data or the methodology used to construct the graph. Resp. Ex. B at 19. Dr. Chodosh also observes that a wide variety of factors, other than childhood vaccinations, could have caused this alleged rise in the incidence of Burkitt lymphoma. Id. at 20. For instance, he notes, the hypothetical increase could have been prompted by changes in the demographic distribution of the U.S. population, or by changes in diagnostic practices. Id.

Dr. Chodosh disputes Dr. Darnowski's characterization of viral contamination in vaccines. Dr. Chodosh points out that the study discussed by Dr. Darnowski dealt only with the potential contamination of Rotarix, a vaccine not administered to H.S., and emphasized that the study "represents one of the very few examples in the modern history of vaccines in which an adventitious virus was identified as (potentially) being present." Resp. Ex. B at 21-22 (citing Pet. Ex. 25-7). Critically, he also notes that the virus found in Rotarix, porcine circovirus 1 ("PCV-1"), has "no known human health consequences." Id.

iii. Response to Dr. Mikovits and Dr. Ruscetti

Turning to the report of Dr. Mikovits and Dr. Ruscetti, Dr. Chodosh observes that "a substantial fraction of their report focuses on the biology of EBV and its potential role in cancer development." Resp. Ex. B at 24. He emphasizes that PCR testing like that conducted on H.S. "is extremely sensitive and specific for the presence of EBV DNA, particularly in the case of Burkitt lymphoma where sensitivity and specificity have been reported to approach 100%." Id.

at 24-25. Significantly, he notes that Dr. Mikovits and Dr. Ruscetti provided no citation for their claim that EBV DNA "is not detected by routine nucleic acid testing by [PCR]." Id. (quoting Pet. Ex. 12 at 3). Regardless of whether H.S. was EBV-positive, Dr. Chodosh further disagrees with Dr. Mikovits and Dr. Ruscetti's claim that sporadic Burkitt lymphoma is "clinically indistinguishable from EBV-associated [Burkitt lymphoma]." Id. (quoting Pet. Ex. 12 at 4). He notes several significant differences between the two varieties of lymphoma, such as "older age at presentation and abdominal (rather than facial) distribution of disease at presentation." Id.

Addressing the temporal relationship between H.S.'s vaccinations and the development of his cancer, Dr. Chodosh disputes Dr. Mikovits and Dr. Ruscetti's opinion that H.S.'s primary risk factor was "his young age at first exposure/infection." Resp. Ex. B at 26 (quoting Pet. Ex. 12 at 4). He emphasizes that if petitioner's experts were referring to the young age at which H.S. received his childhood vaccinations, "this would of course be true for nearly all vaccinated children in the U.S., and thus provides no insight as a 'risk factor' or a theory of causation." Id. at 26. Dr. Chodosh also disagrees that hyperactivation of H.S.'s immune system during puberty initiated the onset of his cancer, stating that Dr. Mikovits and Dr. Ruscetti provided no evidence to support this mechanism. Id. at 27. He concludes: "Suggesting that the rapid growth of his cancer was the result of immune system 'hyperactivation' is both counter-intuitive (the immune system fights cancer) and scientifically unfounded." Id.

Delving further into Dr. Mikovits and Dr. Ruscetti's proposed theory of causation, Dr. Chodosh disputes their claim that H.S.'s vaccinations had exposed him to "100 billion retroviral DNA fragments" and "EBV and SV40 cancer causing viruses." Resp. Ex. B at 28 (quoting Pet. Ex. 12 at 6). First, he notes that petitioner's experts provided no evidence that the vaccines at issue contained fragments of EBV or SV40 virus. Id. Similarly, he firmly rejects the claim of petitioner's experts that these vaccines "may be contaminated with at least one animal retroviral family." Id. (quoting Pet. Ex. 12 at 7). Second, Dr. Chodosh explains that any retroviral DNA fragments contained in vaccines would not be replication-competent,[11] and thus "cannot reasonably be equated with viral infection."[12] Id.

Dr. Chodosh contests Dr. Mikovits and Dr. Ruscetti's claim that vaccine contaminants could cause insertional mutagenesis. Not only did the experts fail to provide case reports or other evidence to support this claim, he observes, but "the theoretical risk of insertional mutations from DNA delivered by intramuscular injection has been estimated at $1.3x10^{-9}$, which is 1000-times lower than the spontaneous rate of gene-inactivating mutations." Resp. Ex. B at

[11] Replication-competent retroviruses replicate through the following process: "[G]enomic RNA serves as a template for DNA synthesis via reverse transcriptase; complementary DNA is synthesized from viral DNA and integrated into the host cell DNA, where is it used for transcription. Assembly occurs by budding through the plasma membrane." Dorland's at 1636. Replication-competent retroviruses are generally oncogenic. Id.

[12] Dr. Chodosh also questions the relevance of the FDA industry guidance that Dr. Mikovits and Dr. Ruscetti cited in support of this concept. Resp. Ex. B at 30 (citing Pet. Ex. 12-5). This FDA guidance, he notes, involved the production of concentrated retroviral stocks, not the incidental generation of retroviruses during vaccine production. Id.

30-31. He also cites several studies which, he asserts, failed to reveal evidence of insertional mutations in Burkitt lymphoma. Id. at 31. Dr. Chodosh similarly rejects Dr. Mikovits and Dr. Ruscetti's theory that vaccine contaminants could have caused dysregulation of DNA methylation machinery, emphasizing that no tests were conducted to evaluate H.S.'s DNA methylation specifically. Id. at 32.

Lastly, Dr. Chodosh addresses the theory that vaccine contaminants could alter immune cell function and hinder their ability to repair mutations. The inability of H.S.'s immune system to repair mutations, he states, is unremarkable "because it is true of all cancer patients, irrespective of their vaccination status." Resp. Ex. B. at 33. Dr. Chodosh also questions Dr. Mikovits and Dr. Ruscetti's claim that H.S.'s cancer could have developed "as a result of successive immunological challenges." Id. at 34 (quoting Pet. Ex. 12 at 5). On the contrary, Dr. Chodosh explains, mutations occur not as a result of immunological challenges, but rather "as a consequence of agents that damage DNA (i.e., mutagens), whether endogenous or exogenous." Id.

II. DISCUSSION

A. Standards for Adjudication

The Vaccine Act was established to compensate vaccine-related injuries and deaths. § 300aa-10(a). "Congress designed the Vaccine Program to supplement the state law civil tort system as a simple, fair and expeditious means for compensating vaccine-related injured persons. The Program was established to award 'vaccine-injured persons quickly, easily, and with certainty and generosity.'" Rooks v. Sec'y of Health & Human Servs., 35 Fed. Cl. 1, 7 (1996) (quoting H.R. Rep. No. 908 at 3, reprinted in 1986 U.S.C.C.A.N. at 6287, 6344).

Petitioner's burden of proof is by a preponderance of the evidence. § 300aa-13(a)(1). The preponderance standard requires a petitioner to demonstrate that it is more likely than not that the vaccine at issue caused the injury. Moberly v. Sec'y of Health & Human Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. Bunting v. Sec'y of Health & Human Servs., 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, petitioner must prove that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface v. Sec'y of Health & Human Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); see also Pafford v. Sec'y of Health & Human Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner who satisfies this burden 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." § 300aa-13(a)(1)(B).

B. Legal Framework

To receive compensation through the Program, petitioner must prove either (1) that H.S. suffered a "Table Injury" – i.e., an injury listed on the Vaccine Injury Table – corresponding to a vaccine that he received, or (2) that H.S. suffered an injury that was actually caused by a vaccination. See §§ 300aa-13(a)(1)(A) and 11(c)(1); Capizzano v. Sec'y of Health & Human

Servs., 440 F.3d 1317, 1319-20 (Fed. Cir. 2006). Because petitioner does not allege that H.S. suffered a Table Injury, she must prove that a vaccine H.S. received caused his death. To do so, she must establish, by preponderant evidence: (1) a medical theory causally connecting the vaccine and H.S.'s injury ("Althen Prong One"); (2) a logical sequence of cause and effect showing that the vaccine was the reason for H.S.'s injury ("Althen Prong Two"); and (3) a showing of a proximate temporal relationship between the vaccine and H.S.'s injury ("Althen Prong Three"). § 300aa–13(a)(1); Althen v. Sec'y of Health & Human Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005).

The causation theory must relate to the injury alleged. Thus, petitioner must provide a reputable medical or scientific explanation that pertains specifically to this case, although the explanation need only be "legally probable, not medically or scientifically certain." Knudsen v. Sec'y of Health & Human Servs., 35 F.3d 543, 548-49 (Fed. Cir. 1994). Petitioner cannot establish entitlement to compensation based solely on her assertions. Rather, a vaccine claim must be supported either by medical records or by the opinion of a medical doctor. § 300aa-13(a)(1). In determining whether petitioner is entitled to compensation, the special master shall consider all material in the record, including "any . . . conclusion, [or] medical judgment . . . which is contained in the record regarding . . . causation." § 300aa-13(b)(1)(A). The undersigned must weigh the submitted evidence and the testimony of the parties' proffered experts and rule in petitioner's favor when the evidence weighs in her favor. See Moberly, 592 F.3d at 1325-26 ("Finders of fact are entitled – indeed, expected – to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence."); Althen, 418 F.3d at 1280 (noting that "close calls" are resolved in petitioner's favor").

C. Causation Analysis

1. Althen Prong One

Under Althen Prong One, petitioner must set forth a medical theory explaining how H.S.'s vaccines could have caused his Burkitt lymphoma, leading to his eventual death. Andreu v. Sec'y of Health & Human Servs., 569 F.3d 1367, 1375 (Fed. Cir. 2009); Pafford, 451 F.3d at 1355-56. Petitioner's theory of causation must be informed by a "sound and reliable medical or scientific explanation." Knudsen, 35 F.3d at 548; see also Veryzer v. Sec'y of Health & Human Servs., 98 Fed. Cl. 214, 223 (2011) (noting that special masters are bound by both § 300aa-13(b)(1) and Vaccine Rule 8(b)(1) to consider only evidence that is both "relevant" and "reliable"). If petitioner relies upon a medical opinion to support her theory, the basis for the opinion and the reliability of that basis must be considered in the determination of how much weight to afford the offered opinion. See Broekelschen v. Sec'y of Health & Human Servs., 618 F.3d 1339, 1347 (Fed. Cir. 2010) ("The special master's decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories."); Perreira v. Sec'y of Health & Human Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) ("An expert opinion is no better than the soundness of the reasons supporting it.") (citing Fehrs v. United States, 620 F.2d 255, 265 (Ct. Cl. 1980)).

Though petitioner's experts present slightly different medical theories, they all rely on

the claim that vaccines contain contaminants – either human or animal in origin – which cause mutations in the human genome, leading to cancer. Petitioner has failed, quite decisively, to establish that this is true. Throughout her expert reports, petitioner alternately claims that the vaccines at issue were contaminated with (1) residual human DNA, (2) retroviruses, (3) EBV, (4) SV40, or (5) animal retroviruses. Pet. Ex. 12 at 4, 6-7; Pet. Ex. 25 at 1. The undersigned will briefly address each alleged contaminant in turn.

Residual Human DNA

Although the vaccines at issue may contain residual human DNA, the undersigned is not persuaded that the human DNA in vaccines could cause Burkitt lymphoma, through insertional mutagenesis or any other mechanism.

"Insertional mutagenesis" is a "mutation caused by insertion of new genetic material into a normal gene." Farlex, Medical Dictionary for the Health Professions and Nursing (2012). In their advocacy for this mechanism, petitioner's experts critically underestimate the safety mechanisms that protect human cells and the genes within them. As Dr. Chodosh explained, "the stability of the genome is . . . heavily guarded to ensure that it remains largely invariant." Resp. Ex. B at 10; see generally Resp. Ex. B-16 (discussing the "maintenance of genomic integrity," including a variety of DNA repair mechanisms, as it relates to the development of cancer). "[T]he cell membrane at the perimeter of every mammalian cell presents a formidable barrier that prevents highly charged, often large, DNA molecules from entering the cell – so much so that great efforts must be made in the laboratory to disrupt the cell membrane in order to force some DNA into a cell." Resp. Ex. B at 11.

Thanks to these defense mechanisms, "[m]ammalian cells do not typically take up exogenous DNA and incorporate it into their genome." Resp. Ex. B at 11. On the contrary, studies of vaccines containing residual DNA "suggest that integration of exogenous DNA is an extremely low frequency event and thus the frequency of integration at a particular site [as would be required for cancer development] will be correspondingly lower." Resp. Ex. B-23 at 2 (internal citations omitted). These findings are unsurprising, given the various mechanisms that must cooperate for the DNA to achieve integration. In order to have any oncogenic effect, residual DNA must go through the following steps: "degradation by serum nucleases, adsorption to cells, uptake into cells, ligation to other DNA, mutation, expression of unintegrated DNA, integration, expression of integrated DNA, and activation of or inactivation of cellular genes." Resp. Ex. B-32 at 1. In other words, integration alone is not sufficient. The integrated DNA must activate an oncogene, or inactivate a tumor suppressor gene,[13] to initiate the development of cancer. Id.; see also Resp. Ex. B at 5 ("The process by which a normal cell is transformed into an initial cancer cell . . . is generally believed to require at least four to six different genetic mutations in critical genes, all of which must occur within the same cell."). Because successfully integrated DNA "is found at essentially random sites in the genome," rather than in critical genes, the risk of oncogenic mutations is "negligible." Resp. Ex. B-33 at 1-2.

[13] A tumor suppressor gene is "a gene whose function is to limit cell proliferation and loss of whose function leads to cell transformation and tumor growth." Dorland's at 769.

The undersigned is likewise unpersuaded by Dr. Darnowski's claim that B lymphocytes are "even more likely than other cells to take up DNA with which they are presented." See Pet. Ex. 25 at 3-4. Not only did Dr. Darnowski not provide citations to support this claim, but as Dr. Chodosh opined, "[I]t is widely known in the immunology community that B cells are highly resistant to taking up exogenous DNA fragments in culture, even when using methods designed to stimulate DNA uptake – methods that obviously would not be operative in the skin or muscle of vaccine recipients." Resp. Ex. B at 12. A study by Roberts, et al., for example, demonstrated that double-stranded DNA, measuring 44 base pairs ("bp") in length, was taken up poorly by B cells. Resp. Ex. B-22 at 1. Moreover, "B-cell DNA uptake was greatly reduced with increasing DNA length." Id. at 1. If B cells struggled to take up DNA at a length of 44 bp, it seems highly unlikely that it would take up the fragmented DNA contained in vaccines like MMR, which both Dr. Darnowski and Dr. Chodosh agree is significantly longer. See Pet. Ex. 25 at 2; Resp. Ex. B at 12.

The medical literature cited by petitioner's experts does little to bolster their argument; in some cases, the literature actively undermines it. For instance, Dr. Darnowski cites a study by Sheng, et al., in support of the proposition that residual DNA transmitted by injection can encourage the development of tumors. However, this study involved not simply residual DNA, but DNA containing a dominant activated oncogene.[14] Pet. Ex. 25-11 at 1-2. The researchers found that "plasmids expressing oncogenes could induce tumors in mice but only when [the T24 H-ras and c-myc oncogenes] were co-injected."[15] Id. at 2. Even then, the "efficiency of tumor induction was low." Id. The study concluded that "the risk of neoplastic transformation by cellular DNA that might be present in a biological product is low." Id. at 12. Elsewhere, Dr. Darnowski points to a study by Hacein-Bey-Abina, et al., as evidence of insertional mutagenesis leading to cancer. See Pet. Ex. 25 at 2. The study has nothing to do with vaccines. Instead, the study concerns patients with x-linked severe combined immunodeficiency disease ("SCID-X1") and the potentially oncogenic effects of a certain gene therapy.[16] Pet. Ex. 25-4; Pet. Ex. 25-3. This therapy, which intentionally alters genes, is not comparable to vaccination, which simply exposes cells to residual DNA. See Resp. Ex. B at 18; see also Resp. Ex. B-24 at 6 (noting that the dangers exhibited during SCID-X1 trials "are not to be regarded indicative for a similar risk potential being associated with the administration of plasmid DNA vaccines"). The undersigned is also puzzled by Dr. Darnowski's reliance on the TeGenero case study. See Pet. Ex. 25 at 3. In that instance, six volunteers were critically injured during a trial of a drug developed by a German immuno-therapeutics company. Pet. Ex. 25-15. Like much of petitioner's medical literature, this piece has no connection to vaccines.

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[14] Petitioner provides no evidence that any vaccine at issue here contains dominant activated oncogenes.

[15] Furthermore, as discussed by Dr. Chodosh, these mice developed sarcomas, not any kind of lymphoma or immune-cell tumor. Resp. Ex. B at 13.

[16] Gene therapy involves "the introduction of a biologically active gene into a cell to achieve a therapeutic benefit." Robert L. Nussbaum et al., Thompson & Thompson Genetics in Medicine 275 (8th ed. 2016).

The presence of residual human DNA in vaccines is not ominous, despite how it has been portrayed by petitioner. After all, residual human DNA is also routinely transmitted through blood transfusions, and "many decades of experience with millions of transfusion recipients [has] failed to reveal evidence of an increased risk of cancer."[17] Resp. Ex. B at 17; see also Resp. Ex. B-31 at 3 (acknowledging "the lack of evidence that the significant amounts of cellular DNA in blood for transfusion are associated with a risk of neoplastic or other disease"); J.M. v. Sec'y of Health & Human Servs., No. 02-10V, 2017 WL 7409771, at *42 (Fed. Cl. Spec. Mstr. Aug. 31, 2017) (noting that "DNA can also be introduced by blood transfusions . . . , which contain large amounts of cellular DNA," and explaining how this undermined the petitioners' theory of insertional mutagenesis). Petitioner has failed to establish that the introduction of residual human DNA through vaccination would be any more dangerous than its introduction through transfusion.

Dr. Mikovits and Dr. Ruscetti also assert that vaccine contaminants like human DNA could cause cancer through epigenetic mechanisms such as DNA methylation. This theory is also unworkable. First, epigenetic alterations are not necessarily pathogenic, and they can even be beneficial. See Resp. Ex. B at 31; Resp. Ex. B-44 (finding that "exercise induces genome-wide changes in DNA methylation in human adipose tissue"). Second, the medical records do not suggest that H.S.'s DNA methylation machinery had been altered, and even if it had, no evidence suggests that vaccine contaminants caused such an alteration. See Resp. Ex. B at 31. Third, much of Dr. Mikovits and Dr. Ruscetti's discussion of epigenetic mechanisms relies on the potential involvement of HIV or EBV. See Pet. Ex. 12 at 5-6. H.S. tested negative for both HIV and EBV.

Finally, the undersigned does not accept Dr. Mikovits and Dr. Ruscetti's claim that vaccine contaminants could cause "altered immune cell function [which] accelerate[s] a stepwise selection of more malignant cells and the inability of the immune system to respond or repair the mutation and epi-mutations." See Pet. Ex. 12 at 11-12. Petitioner's experts have cited no evidence to support this proposition. Additionally, the "inability of the immune system" to properly respond to mutations is true of all cancer patients, as Dr. Chodosh observed:

> [I]n every person in whom a cancer is clinically diagnosed, by definition the immune system has failed to adequately respond to the mutations that caused the cancer. That is, if a cancer came to clinical detection, that means that the immune system was not able to effectively combat it.

Resp. Ex. B at 33.

Retroviruses

Petitioner has not established that the vaccines at issue are contaminated with replication-competent retroviruses. Furthermore, petitioner's experts have failed to link hypothetical

[17] This is particularly significant because "[the] level of contaminating cellular DNA in biological products is five to six orders of magnitude lower than the amount of DNA in a unit of human blood for transfusion." Resp. Ex. B-31 at 3.

contamination by human endogenous retroviruses ("HERVs") to the development of Burkitt lymphoma. Retroviruses are a family of viruses whose genomes consist of single-stranded RNA. Dorland's at 1636. HERVs are "retroviruslike sequences found in the human genome, thought to constitute the remains of true retroviruses that were absorbed through evolution." Id. There is nothing unusual or sinister about these sequences: "Indeed, approximately 8% of human DNA is composed of sequences that are recognizably retroviral." Pet. Ex. 7 at 1. Because almost all HERVs are inactive due to various mutations, "no replication-competent endogenous HERVs have been identified in the human genome so far." Pet. Ex. 25-1 at 1. In other words, HERVs are "historical relics of viruses from eons in the past that are now incapable of acting as viruses." Resp. Ex. B at 28.

Petitioner expresses concern about one family of HERVs in particular.[18] HERV-K is "one possible exception" to the general rule that HERVs are inert. Pet. Ex. 30-11 at 2. Like all other HERVs, HERV-K is present in some vaccines. See Pet. Ex. 25-14 at 7. However, while "occasional reports link [the HERV-K family's] expression with human disease," their role in those diseases has not been established. See Pet. Ex. 7 at 1. It is unknown, for instance, whether these HERV-K elements are "the cause, rather than just markers," of these diseases. See Pet. Ex. 30-11 at 9; Pet. Ex. 12-8 at 30 ("[T]he mere presence of a virus in a tumor does not prove etiology."). Even if HERV-K were the cause of some diseases, petitioner has provided no evidence linking HERV-K to Burkitt lymphoma specifically.[19]

Ultimately, Dr. Mikovits and Dr. Ruscetti "conflate the biological properties of fragments of viral DNA with the properties of a functional, replication competent virus." Resp. Ex. B at 28. Neither of these alleged contaminants provides a plausible mechanism. For the same reasons discussed above, the undersigned is not persuaded that the fragmented viral DNA transmitted through HERVs could be introduced into the genome through insertional mutagenesis. Moreover, petitioner's lack of evidence for contamination by replication-competent retroviruses leaves the undersigned unable to accept this assertion.

In support of their claim that vaccines may contain replication-competent retroviruses, Dr. Mikovits and Dr. Ruscetti point to the xenotropic murine leukemia virus-related virus ("XMRV"), which they assert "most likely entered the human population via contaminated vaccines." See Pet. Ex. 12 at 2. This example fails for two reasons. First, Dr. Mikovits and Dr. Ruscetti provide no evidence that XMRV spread to humans through vaccines. Second, XMRV

[18] The undersigned notes that while the petition discusses HERV-K, petitioner's own experts do not mention it. For further discussion of the concerns raised by the petition, see Section II.D.3 of this Decision.

[19] Petitioner's HERV-K theory would face even more serious obstacles under Althen Prong Two. Even if petitioner had established a link between HERV-K and Burkitt lymphoma, petitioner has not demonstrated that members of the HERV-K family were present in H.S.'s genome. And even if members of the HERV-K family were present, petitioner has certainly not shown that the HERV-K was transmitted through vaccines, rather than occurring naturally in H.S.'s genome.

has not been shown to be pathogenic to humans. While early studies linked XMRV to prostate cancer and chronic fatigue syndrome, "[t]hese findings have been refuted by numerous independent laboratories, debunking any disease association with XMRV." Pet. Ex. 12-6 at 1; see also Resp. Ex. B-39 (finding no association between XMRV and prostate cancer); Resp. Ex. B-43 (retracting study that found association between XMRV and chronic fatigue syndrome).[20] Thus, "the production of such recombinant viruses is essentially a laboratory artifact with little, if any, relevance to the manufacture of vaccines." Resp. Ex. B at 29; see also Pet. Ex. 12-6 (noting that two endogenous murine leukemia virus proviruses "most likely recombined during xenograft passaging of a human prostate tumor in mice to generate [XMRV]").

EBV

H.S. tested negative for EBV, and petitioner has not convinced the undersigned that these test results are unreliable. Dr. Mikovits and Dr. Ruscetti claim that despite the negative test, H.S. "could have still had EBV in his immune cells but the DNA would have been hypermethylated and silenced and thus be invisible to the immune system and show no evidence of infection." Pet. Ex. 12 at 3. They later elaborated that while H.S. "did not encounter the [EBV] wild virus as that would have been detected in the clinical blood test that was administered [during his March 2015 hospital admission]," such a test would not have detected EBV transmitted through vaccination. Status Rpt. dated July 11, 2018 (ECF No. 52). However, Dr. Mikovits and Dr. Ruscetti offer no support for their claim that PCR testing would have failed to detect EBV, no matter what the transmission route. As Dr. Chodosh opined, PCR testing is "one of the most sensitive techniques in molecular biology," and is "extremely sensitive and specific for the presence of EBV DNA . . . ." Resp. Ex. B at 24-25; see also Resp. Ex. B-37 at 1 (finding that when used to detect EBV, PCR assays showed a sensitivity rate of 96% and a specificity rate of 100%). Thus, the undersigned finds no reason to doubt the accuracy of H.S.'s negative test results.

SV40

Petitioner offers no citations to support the claim that the vaccines at issue contain SV40. While one of petitioner's studies notes that "many individuals who received poliovirus vaccine in the 1950s were likely exposed to SV40," it also explains that once the contamination was discovered, SV40-free formulations of the vaccine were quickly manufactured. Pet. Ex. 25-7 at 7-8.

Animal Retroviruses

Petitioner presents evidence that some vaccines may contain viral fragments derived from animal cell lines, but no evidence that these contaminants are dangerous to humans.

[20] Dr. Mikovits and Dr. Ruscetti are two of the authors of the retracted study, published in Science in 2009, linking XMRV and chronic fatigue syndrome. Resp. Ex. B-42. Science retracted the study because (1) other laboratories were unable to replicate the results, (2) some of the experiments documented by the study showed poor quality control, and (3) the authors had omitted probative information from one of the figures in the study. Resp. Ex. B-43 at 1.

Although Dr. Darnowski cites a study that reported the detection of PCV-1 in Rotarix, H.S. did not receive that vaccine. See Resp. Ex. B at 21-22. The same study further noted that PCV-1 "seem[s] to be ubiquitous in pork products and thus the risk . . . to humans is believed to be negligible." Pet. Ex. 25-7 at 8 (internal citation omitted); see also Resp. Ex. B-34 (demonstrating that the PCV-1 detected in Rotarix is not infectious). Another study cited by Dr. Darnowski reported that viruses such as avian leukosis virus and endogenous avian virus have been reported in live-attenuated viral vaccines, but the study observed that these viruses are "noninfectious to humans." Pet. Ex. 25-14 at 9. The authors concluded: "Given that live-attenuated viral vaccines are safe, effective, and relatively inexpensive, their use against human and animal pathogens should be encouraged." Id. at 10.

In short, petitioner's experts have piled speculation atop speculation in an effort to connect H.S.'s childhood vaccinations to his Burkitt lymphoma. Speculation as to possible causes, however, is not sufficient to support a finding that a vaccine caused an injury. See Cedillo v. Sec'y of Health & Human Servs., 617 F.3d 1328, 1348 (Fed. Cir. 2010) (noting that physician speculated that fever experienced after vaccination might have caused neurological abnormalities and determining that this was not a conclusion that the vaccine caused petitioner's alleged injury). Thus, for the reasons discussed above, the undersigned concludes that none of petitioner's medical theories satisfy Althen Prong One.

2. Althen Prong Two

Althen Prong Two requires petitioner to prove, by preponderant evidence, a "logical sequence of cause and effect showing that the vaccination was the reason for the injury." Capizzano, 440 F.3d at 1324 (quoting Althen, 418 F.3d at 1278). "[P]etitioner must show that the vaccine was the 'but for' cause of the harm . . . or in other words, that the vaccine was the 'reason for the injury.'" Pafford, 451 F.3d at 1356 (citation omitted).

Petitioner has failed to connect H.S.'s vaccinations to his illness through a logical sequence of cause and effect. While petitioner's experts suggest risk factors that could have made H.S. particularly susceptible to injury, none of the suggested risk factors apply uniquely to H.S. If, as Dr. Mikovits and Dr. Ruscetti claim, H.S.'s "primary risk factor for disease development was his young age at first exposure/infection," the same risk would apply to any individual who had ever received childhood vaccinations. See Resp. Ex. B at 26. Likewise, if the onset of H.S.'s cancer was triggered by puberty, as Dr. Mikovits and Dr. Ruscetti suggest, or by some unspecified "immune challenge," as Dr. Darnowski asserts, all vaccine recipients would be at equal risk. Thus, petitioner's experts leave the undersigned no way to differentiate between H.S.'s illness, allegedly caused by vaccines, and other cases of Burkitt lymphoma, demonstrably caused by naturally occurring mutations. The undersigned concludes, as did Dr. Chodosh, that "the more straightforward explanation of the cause of this extremely rare event (developing Burkitt lymphoma) is that it was unrelated to the extremely common event (vaccination)." See Resp. Ex. B at 25.

H.S. fits the profile a typical patient with sporadic Burkitt lymphoma. He first presented with abdominal Burkitt lymphoma at 13 years of age. See Resp. Ex. B-1 at 2 (noting that abdominal presentation is more common in older children, between 10-14 years old). He was a

male. See id. (study results suggesting that males make up a larger portion of Burkitt lymphoma patients that females); Pet. Ex. B-2 at 2 (noting a male-to-female ratio or 2 or 3:1 in sporadic Burkitt lymphoma cases). His cancer grew quickly and aggressively. See Resp. Ex. B at 27 ("Unfortunately, the aggressive clinical course of H.S.'s Burkitt lymphoma is typical for this disease, which represents one of the fastest growing human cancers."). And most critically, he carried the MYC mutation that appears so crucial to the development of this cancer. See Resp. Ex. B-4 at 3 (describing the MYC translocation as the "defining feature" of Burkitt lymphoma). Petitioner has given the undersigned no reason to believe that anything other than usual oncogenesis caused H.S.'s death.

3. Althen Prong Three

Under Althen Prong Three, petitioner must provide "preponderant proof that the onset of symptoms occurred within a timeframe for which, given the 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). Because petitioner has failed to articulate a plausible theory of causation, she necessarily has also failed to demonstrate that the onset of H.S.'s cancer occurred within a medically acceptable timeframe. See Langland v. Sec'y of Health & Human Servs., 109 Fed. Cl. 421, 443 (2013) (describing Althen Prong One as a prerequisite to Althen Prong Three). However, some specific flaws in the proposed timeline are worth noting.

H.S.'s first symptoms of Burkitt lymphoma arose in 2014, over a decade after he first received MMR, Varicella, and Hepatitis A vaccinations. Petitioner's experts each offer slightly different explanations for this prolonged latency period. Dr. Mikovits and Dr. Ruscetti assert, without citation, that Burkitt lymphoma may remain latent until its rapid development "during puberty when the immune system is hyper-activated." Pet. Ex. 12 at 12. Dr. Darnowski states, also without citation, that insertionally-mutated B cells "go dormant until activated when the body is appropriately challenged." Pet. Ex. 25 at 4. Neither of these explanations is sufficient. Dr. Mikovits and Dr. Ruscetti provide no citation or other foundational evidence for the alleged role of puberty in the onset of H.S.'s cancer. Considering that Burkitt lymphoma often afflicts children long before puberty begins,[21] the relationship between puberty and onset seems quite attenuated. Dr. Darnowski's theory is similarly unworkable. If, as he claims, mutated cells "can lie dormant in the body for long periods of time," and "[t]he activation of these cells is likely to be at random," any vaccinee who develops Burkitt lymphoma at any point later in life could blame the vaccine. See Pet. Ex. 25 at 4. The undersigned is not willing to accept such an indefinite timeframe.

The undersigned also finds Dr. Darnowski's analysis of the "Burkitt Lymphoma Changepoint" graph unpersuasive as an explanation for the delayed onset of H.S.'s illness. First, this graph was created by petitioner's own organization and was not subject to a peer-review publication process, presenting a potential conflict of interest. See Pet. Ex. 25 at 3; Resp. Ex. B

[21] A study of Burkitt lymphoma cases reported to the NCI's Surveillance, Epidemiology, and End Results program demonstrated that the "[a]ge-specific incidence rate for [Burkitt lymphoma] peaked by age 3-5 years." Resp. Ex. B-1 at 1.

at 19; Pet. Status Rpt. dated June 27, 2018, at 2 (stating that no effort had been made to publish the graph). Second, petitioner provided no information regarding the methodology used to create this graph. Third, Dr. Darnowski's interpretation of the graph seems to contradict his own theory of causation. He asserts that the graph "shows a change point about 10 years after the introduction of MMRII, i.e. establishing a time from exposure to clinical symptoms consistent with this child's case." Pet. Ex. 25 at 3. However, as pointed out by Dr. Chodosh, this statement would seem to contradict his earlier claim that the activation of mutated cells "is likely be to random." See id. at 4; Resp. Ex. B at 21.

D. Persuasiveness of the Parties' Experts

The undersigned rejected petitioner's theories of causation only after careful consideration of her expert reports, medical literature, and the other expert materials filed in this case. However, the undersigned has additional concerns about the quality of petitioner's experts that are worth addressing separately from the causation analysis above.

1. Dr. Mikovits and Dr. Ruscetti

The undersigned found the report of Dr. Mikovits and Dr. Ruscetti unhelpful for a number of reasons. First, the report devoted an inordinate amount of space to discussing EBV and HIV, two conditions for which H.S. tested negative. Although the experts acknowledged that H.S. had tested negative for EBV, it was often difficult to ascertain how their theory of causation applied to an EBV-negative, HIV-negative patient like H.S. Second, the report is generally speculative, difficult to follow, and outside the experts' area of expertise.[22] The undersigned is especially concerned by the experts' lack of citation to appropriate medical literature, or misuse of the medical literature they do cite. For instance, the experts display a table in their report entitled "Relations between coinfecting viruses and HIV-1," which they describe as follows: "The table below shows co-expression of retroviruses and herpes viruses including EBV critical pathways necessary to stop the progression of the cancer. Immune deficiency and HIV infection are risk factors for the development of aggressive Burkitt's lymphoma and support our plausible theory of causation." Pet. Ex. 12 at 10 (internal citation omitted). This table does not mention cancer. Furthermore, the undersigned struggles to comprehend how a table documenting "coinfecting viruses and HIV-1" is applicable to an HIV-

[22] Other special masters have shared these concerns. See Rogero v. Sec'y of Health & Human Servs., No. 11-770V, 2017 U.S. Claims LEXIS 1200, at *58, 129-30, 138-39 (Fed. Cl. Spec. Mstr. Sept. 1, 2017) (discussing Dr. Mikovits' dubious use of medical literature and observing that her testimony "often veer[ed] into opinions concerning medical disciplines in which she was wholly unqualified"); McCabe v. Sec'y of Health & Human Servs., No. 13-570V, 2018 U.S. Claims LEXIS 726, at *40-51, 60-63, 97-100 (Fed. Cl. Spec. Mstr. May 17, 2018) (chronicling a series of problems with Dr. Mikovits and Dr. Ruscetti's expert reports, including their failure to cite support for many of their assertions); Dominguez v. Sec'y of Health & Human Servs., No. 12-378V, 2018 U.S. Claims LEXIS 724, at *11-14 (Fed. Cl. Spec. Mstr. May 25, 2018) (discussing Dr. Mikovits' questionable scientific credentials and lack of recent research experience). The undersigned shared these examples with the parties during a status conference. See Order dated Aug. 8, 2018 (ECF No. 59).

negative patient like H.S. These issues critically undermine the persuasiveness of Dr. Mikovits and Dr. Ruscetti's report.

2. Dr. Darnowski

Additionally, the undersigned questions whether Dr. Darnowski is qualified to opine on these matters at all. Dr. Darnowski received his Ph.D. in the field of plant biology, and his work has focused on topics such as profilin distribution in tomatoes; transgenic soybean seeds; aquatic bladderworts; triggerplants; carnivorous seaweeds; and carnivorous plants in general. See generally Pet. Ex. 25-a. His 16-page CV contains no references to cancer, vaccinations, or any other medical issues applicable to humans. Id. Although Dr. Darnowski appears quite accomplished in his field, the opinion he has offered in this case is far outside his area of expertise. See Piscopo v. Sec'y of Health & Human Servs., 66 Fed. Cl. 49, 54-55 (2005) (finding that the special master did not abuse his discretion when he determined that Dr. Mark Geier, who had been trained in genetics, obstetrics, and gynecology, could not reliably testify on immunology).

3. A Note Regarding Petitioner, Theresa Deisher

Lastly, the undersigned has concerns about the role played in this litigation by petitioner, Theresa Deisher. Dr. Deisher, who holds a Ph.D. in molecular and cellular physiology, testified as an expert witness in J.M. v. Sec'y of Health & Human Servs., the autism proceeding adjudicated by the undersigned. See J.M., 2017 WL 7409771, at *11-12. There, in her attempt to establish a link between autism and the MMR, Varicella, and Hepatitis A vaccines, Dr. Deisher proposed some of the same mechanisms that she now offers in this case: primarily, insertional mutagenesis and retroviral contamination.[23] See id. at *32-35. Her testimony was met with considerable skepticism. First, the undersigned rejected Dr. Deisher's theories of causation, for many of the same reasons discussed above. See id. at *40-47. Second, the undersigned observed that Dr. Deisher's testimony was tarnished by her "conceptual bias against the use of human fetal cells for vaccines."[24] Id. at *62.

Dr. Deisher was not proffered as an expert in this case. Indeed, the undersigned specifically informed the parties that she would not allow Dr. Deisher to serve as an expert for

[23] In fact, some of the medical literature filed in this case still bear their original J.M. Bates stamps. See, e.g., Pet. Exs. 4, 10.

[24] The undersigned is not alone in her concerns regarding Dr. Deisher's potential bias. As the undersigned discussed in J.M., Dr. Deisher once applied for a National Institute of Health grant for a "Safety Study of Human Fetal DNA and HERVK Contaminants in Childhood Vaccines." J.M., 2017 WL 7409771, at *62. One member of the Scientific Review Group that evaluated her proposal "acknowledged the importance of ongoing safety evaluations for vaccines, but expressed concern that Dr. Deisher's approach was 'heavily biased, including an assessment of the current literature that fails to adequately consider the recent data that has rebuked the association between vaccination and autism.'" Id. The other two written critiques issued by the Scientific Review Group contained similarly negative commentary. Id.

her own claim. Order dated Apr. 12, 2017 (ECF No. 8) ("Petitioner agreed that Dr. Deisher will not be an expert in this case."). Nevertheless, the undersigned notes that the petition in this matter essentially constitutes an expert report from Dr. Deisher, equipped with its own mechanism of causation and medical literature. See Petition at 2-14; Pet. Exs. 5-10. Given Dr. Deisher's ideological and financial stake in this litigation, the undersigned gives very little weight to the opinions expressed in the petition, particularly where they differ from the opinions of petitioner's proffered experts.

III. CONCLUSION

"In a very real sense this lawsuit is an understandable search for reasons." Canterbury v. Spence, 464 F.2d 772, 776 (D.C. Cir. 1972). Petitioner has suffered an immense loss, and the undersigned empathizes with her desire to find a clear cause for her son's illness. However, the outcome of this case is dictated not by empathy, but by the evidentiary and causation requirements of the Vaccine Program. Thus, for all of the reasons discussed above, the undersigned must find that H.S.'s vaccinations did not cause him to develop Burkitt lymphoma, and that petitioner is therefore not entitled to compensation in the Vaccine Program. Accordingly, the petition is **DISMISSED**.

In the absence of a motion for review filed pursuant to RCFC Appendix B, the Clerk of the Court shall enter judgment in accordance herewith.[25]

IT IS SO ORDERED.

s/Nora Beth Dorsey
Nora Beth Dorsey
Chief Special Master

[25] Pursuant to Vaccine Rule 11(a), entry of judgment can be expedited by each party, either separately or jointly, filing a notice renouncing the right to seek review.