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Association for Molecular Pathology

Letter Submitted to the Record for the

Senate Committee on the Judiciary, Subcommittee on Intellectual Property Hearing on:
"The Patent Eligibility Restoration Act – Restoring Clarity, Certainty, and Predictability to the U.S. Patent System"

January 23, 2024

Dear Chairman Coons, Ranking Member Tillis, and other members of the Subcommittee,

The Association for Molecular Pathology (AMP) is an international medical and professional association representing approximately 2,900 physicians, doctoral scientists, and medical technologists who perform or are involved with laboratory testing based on knowledge derived from molecular biology, genetics, and genomics. Membership includes professionals from the government, academic, private, and hospital-based clinical laboratories, as well as the in-vitro diagnostics industry. As professionals that populate most clinical molecular pathology laboratories in the United States, we hold various perspectives as licensees or users of patented technology and developers of innovative laboratory testing.

AMP was the named plaintiff in the *Association for Molecular Pathology v. Myriad Genetics Inc. (Myriad)* case heard by the Supreme Court in 2013 which led to a unanimous decision that human DNA, even when isolated from the body, is a product of nature and not patent eligible. AMP's longstanding position is that naturally occurring genetic sequences and other types of biomarkers, and their association with diseases and health conditions should not be patent eligible. Additionally, AMP also strongly supports the Supreme Court decisions in *Mayo Collaborative Services Inc. v. Prometheus Laboratories Inc. (Mayo) and Alice Corp. v. CLS Bank International (Alice).* Thus, we have significant concerns with S. 2140: the Patent Eligibility Restoration Act (PERA) which would reform Section 101 of the U.S. Patent Act by abrogating these important Supreme Court decisions. We are joined by nearly 200 other organizations that have previously sent a letter to you opposing similar reforms to Section 101 proposed in draft legislation distributed in 2019 that also would allow for patents of this kind.[1] While we disagree with the underlying premise of PERA that reforms to patent eligibility are needed, if the Subcommittee continues to believe that reforms to Section 101 of the U.S. Patent Act are warranted, we strongly request that modifications be made to this Act to protect the integrity of the Supreme

[1] https://www.amp.org/AMP/assets/2019-07-25%20Coalition%20Letter%20Opposing%20Draft%20Legislation%20of%20Section%20101%20of%20Patent%20Act.pdf

Court decisions in these three cases and continue to prohibit patents on abstract ideas, laws of nature, or natural phenomena.

Specific to the legislative text, AMP opposes the provisions that would effectively abrogate the *Mayo, Myriad, and Alice* Supreme Court decisions. Additionally, of significant concern is the language used in patent eligibility exclusion,

> "(D) An unmodified human gene, as that gene exists in the human body"

and the following condition,

> ''(2) CONDITIONS.—For the purposes of sub-paragraphs (D) and (E) of paragraph (1), a human gene or natural material shall not be considered to be unmodified if the gene or material, as applicable, is—
>
> ''(A) isolated, purified, enriched, or otherwise altered by human activity; or
>
> ''(B) otherwise employed in a useful invention or discovery.

The first step in any molecular diagnostic procedure is to isolate the biomarker of interest – which is often in the form of DNA or RNA – from the sample. Thus, by including the phrase "as that gene exists in the human body" and later by stating clearly that human activity to isolate a gene deems it to be modified and eligible to be patented, the legislation would directly overturn the *Myriad* decision. S.2140 would not only abrogate all existing case law on subject matter eligibility, but it actually doubles down on abrogating the *Myriad* decision to make it very clear that the intent of this legislation is to allow patents on products of nature, including human DNA.

We are aware of stakeholders pressing Congress to allow patents on natural phenomena and laws of nature to address false claims that the diagnostic industry in the United States is suffering. As professionals developing, validating, and performing laboratory tests, we see no evidence that these court decisions have had a "dramatic negative impact on investment, research, and innovation"[2] as it relates to molecular laboratory testing. Earlier this year on the 10th anniversary of the *Myriad* decision, Paul Diaz, the current CEO of Myriad Genetics Inc., stated, "The Supreme Court, I believe, ruled correctly that genes found in nature should not be patented."[3]

AMP members' efforts are central to the generation of novel, high quality, molecular pathology procedures that are applied daily in medical decision-making and informing patient care in various areas including molecular oncology, inherited diseases, infectious diseases, and histocompatibility testing. Prior to the *Mayo, Myriad, and Alice* decisions, patents on genetic sequences prevented the development and delivery of up-to-date and effective clinical genetic testing services. In 2001, a survey of 122 clinical laboratory professionals performing genetic testing demonstrated that most felt the patent environment was negatively impacting the cost, access,

[2] https://www.tillis.senate.gov/services/files/04D9DCF2-B699-41AC-BE62-9DCA9460EDDA

[3] https://www.genomeweb.com/molecular-diagnostics/decade-after-scotus-gene-patents-ruling-precision-medicine-and-test

and development of genetic tests.[4] Ninety-one respondents said that their laboratories needed to obtain a license to use a patented method, device, or reagent. A quarter of the respondents had stopped performing a test altogether because of a patent or license. Moreover, fifty-three percent (53%) of respondents decided not to develop a new clinical genetic test because of a patent or license. In a thorough assessment by the U.S Department of Health and Human Services Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) in 2010, the Committee recognized the burden associated with negotiating numerous licenses and how the cost of these endeavors may render a clinically valuable test unworthy of financial investment.[5] As scientific understanding of genetics and genomics has increased over time, so has an appreciation of the polygenic (involving more than one gene) nature of disease. Today, the prospect of negotiating numerous licenses for multiple genes or genetic variants threatens standard medical practices that have evolved since *Mayo, Myriad, and Alice.*

Today, in a post-*Mayo, Myriad, and Alice* world, we are fortunate to have an environment where molecular professionals are not restricted by the existence of gene patents when developing and employing clinical laboratory tests in their practice. We implore you to consider these experiences and case studies exemplifying the importance of these Supreme Court decisions:

Hereditary Breast and Ovarian Cancer (HBOC) Syndrome

HBOC syndrome is an inherited disorder in which genetic alterations in various genes have resulted in a person having an elevated risk of developing breast cancer and ovarian cancer. People with HBOC syndrome may also have an increased risk of other types of cancer, including pancreatic cancer, prostate cancer, and melanoma. Over time, there has been increasing public awareness of the fact that alterations in genes known as *BRCA1* and *BRCA2* can dramatically contribute to a person's susceptibility to developing cancer and, prior to 2013, testing to glean information about a person's inherited risk for developing breast and ovarian cancer was largely focused on analyzing these two genes. Myriad Genetics, Inc., held patents on the *BRCA1* and *BRCA2* gene sequences and thus, was able to license the intellectual property (IP) for full DNA sequencing for the *BRCA* genes.[6] Myriad Genetics, Inc. unfortunately used the company's control over these patents to reduce competition for testing of the *BRCA* genes. In the study of laboratory professionals from 2001, there were nine reported instances of laboratories being contacted by Myriad Genetics, Inc., which led to those laboratories removing their tests from the market. However, upon the Supreme Court's decision in the 2013 *Myriad* case, five companies began offering testing for HBOC syndrome[7] immediately, with many more joining the market by 2014.[8] Today there are

[4] Cho MK, Illangasekare S, Weaver MA, Leonard DGB, Merz JF. Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services. J Mol Diagnostics. 2003;5(1):3-8. doi:10.1016/S1525-1578(10)60444-8

[5] Secretary's Advisory Committee on Genetics, Health, and Society, Department of Health and Human Services. Gene patents and licensing practices and their impact on patient access to genetic tests. https://osp.od.nih.gov/wp-content/uploads/2013/11/SACGHS_patents_report_2010.pdf. Published April 2010. Accessed August 17, 2021.

[6] University of Utah Research Foundation, et al. v. Ambry Genetics Corp. Case No. 2:13-cv-00640-RJS (D.Utah, filed July 9, 2013)

[7] https://www.nytimes.com/2013/06/14/business/after-dna-patent-ruling-availability-of-genetic-tests-could-broaden.html

[8] Cook-Deegan R, Niehaus A. After Myriad: Genetic Testing in the Wake of Recent Supreme Court Decisions about Gene Patents. Curr Genet Med Rep. 2014;2(4):223. doi:10.1007/S40142-014-0055-5

292 clinical tests involving the analysis of *BRCA1*, and 323 clinical tests involving the analysis of *BRCA2*, being performed in CLIA-certified laboratories in the United States according to the Genetic Test Registry.[9] This growth in *BRCA1* and *BRCA2* testing alone since the 2013 *Myriad* case decision is tremendous.

The existence of numerous clinical tests for a disease or condition is important for inter-laboratory comparisons, which helps to ensure that testing is high quality and allows patients to have confirmatory testing performed. For example, in 2006, a group of authors reported that approximately 12% of people with breast cancer who had severe family histories of cancer but tested negative for *BRCA1* and *BRCA2* alterations using Myriad's testing strategy at the time, were found by other testing methodologies to carry a large genomic deletion or duplication in one of these genes.[10] In other words, many patients who could have benefited from additional testing methods to detect these large rearrangements were being missed by the only clinical test that was available to them. That same year, Myriad Genetics, Inc., responded by offering testing for large rearrangements in *BRCA1* and *BRCA2*. It is speculated that this change was largely the result of considerable pressure from the scientific community consequent to the release of the critical study.

Our scientific understanding of HBOC syndrome has evolved and now molecular pathologists know that many more genes are involved in this disorder. For instance, the Current Procedural Terminology (CPT) code 81432 used for the billing of genomic sequence analysis panel (panel tests) for hereditary breast cancer-related disorders must include the sequencing of 14 genes including *ATM, BRCA1, BRCA2, BRIP1, CDH1, MLH1, MSH2, MSH6, NBN, PALB2, PTEN, RAD51C, STK11,* and *TP53*. A separate CPT code, 81433, is used for the payment of a duplication/deletion analysis panel that must include analyses for *BRCA1*, *BRCA2*, *MLH1*, *MSH2*, and *STK11.* In 2018[11], Concert Genetics reported that there were 374 panel tests that included *BRCA1* and *BRCA2* which compared to the 172 panel tests in 2016[12]. These highly complex tests greatly improve patient care by simultaneously evaluating multiple genes that can lead to similar disease presentations and Concert Genetics attributes the explosion of panel testing directly to the 2013 *Myriad* decision.[13] Panel tests are only possible because burdensome patents and/or licensing agreements do not interfere with the study of these genes, nor with the translation of scientific understanding into clinically actionable diagnostic tests. Furthermore, as the understanding of inherited genetic risk for cancer evolves, laboratories can readily update their testing to account for new scientific and medical information and deliver appropriate care to their patients.

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[9] Data accessed on January 18, 2024 from Genetic Testing Registry; https://www.ncbi.nlm.nih.gov/gtr/

[10] Walsh T, Casadei S, Hale Coats K, et al. Spectrum of mutations in BRCA1, BRCA2, CHEK2, and TP53 in families at high risk of breast cancer. JAMA. 2006;295(12):1379-1388. doi:10.1001/JAMA.295.12.1379

[11] Concert Genetics, "The Current Landscape of Genetic Testing: Market Growth, Reimbursement Trends, Challenges and Opportunities – 2018 Edition." 2018. http://www.concertgenetics.com/wp-content/uploads/2018/02/10_ConcertGenetics_CurrentLandscapeofGeneticTesting_2017Update.pdf Accessed August 31, 2021.

[12] Concert Genetics, "The Current Landscape of Genetic Testing – Market size, market growth and the practical challenges of the clinical workflow." 2016. http://concertgx.wpengine.com/wp-content/uploads/2017/02/ConcertGenetics_TheCurrentLandscapeOfGeneticTesting_March2016.pdf Accessed August 31, 2021.

[13] Concert Genetics, "The Current Landscape of Genetic Testing – Market size, market growth and the practical challenges of the clinical workflow." 2016. http://concertgx.wpengine.com/wp-content/uploads/2017/02/ConcertGenetics_TheCurrentLandscapeOfGeneticTesting_March2016.pdf Accessed August 31, 2021.

Canavan Disease

The National Institutes of Neurological Disorders and Stroke describes Canavan disease as a "gene-linked neurological disorder in which the brain degenerates into spongy tissue riddled with microscopic fluid-filled spaces."[14] This starts in infancy due to the lack of an essential enzyme resulting in the deterioration of white matter in the brain. Children with Canavan disease lack head control, have reduced visual responsiveness, and have abnormal muscle tone such as stiffness or floppiness.[15] Over time, children can also experience seizures, become paralyzed, developmentally delayed, blind, deaf, and have trouble swallowing. The prognosis for Canavan disease is poor with death usually occurring before the age of 10. This disease is caused when a child inherits two genetically altered copies of the *ASPA* gene.[16] Genetic testing is performed not only for diagnostic purposes, but the American College of Genetics and Genomics (ACMG) also recommends that all pregnant patients and those planning pregnancy should be offered carrier screening for over 100 inheritable autosomal recessive and X-linked conditions including Canavan disease.[17]

In 1993, a patent application relating the sequence and genetic alterations associated with *ASPA* was filed by Dr. Reuben Matalon, and others, who at the time was affiliated with Miami Children's Hospital Research Institute, Inc.[18] A review by Colaianni et al. in 2010 described the actions of Miami Children's Hospital following the award of the a patent in 1997. The authors report that Miami Children's Hospital sent letters to laboratories and hospitals informing them that they would have to license access to the sequence or risk an infringement lawsuit. Findings from a survey conducted in 2001 confirm this report, indicating that at least four respondents stopped performing testing on *ASPA* as a result of receiving a patent enforcement letter.[19] Former AMP President, Dr. Debra Leonard, was the recipient of one letter which specified that Miami Children's Hospital would charge $12.50 per test in patent royalty fees and warned that volume limitations would likely be placed on her institution.[20] Unfortunately, Dr. Leonard was ultimately no longer able to perform testing for Canavan disease, in addition to other genetic diseases, because of patent enforcement actions taken by various entities.[21]

As reported by Colaianni et al. (2010), the Canavan disease community found this narrowing of access to affordable testing problematic and, in response, formed the Canavan Disease Screening Consortium to advocate for 1) removal of a testing volume cap, 2) reduction of royalty fees, 3) development of an educational program

[14] https://www.ninds.nih.gov/Disorders/All-Disorders/Canavan-Disease-Information-Page
[15] https://www.canavanfoundation.org/about_canavan_disease
[16] https://rarediseases.info.nih.gov/diseases/5984/canavan-disease
[17] Gregg AR, Aarabi M, Klugman S, et al. Screening for autosomal recessive and X-linked conditions during pregnancy and preconception: a practice resource of the American College of Medical Genetics and Genomics (ACMG). Genet Med 2021. 2021;10:1-14. doi:10.1038/s41436-021-01203-z
[18] Colaianni A, Chandrasekharan S, Cook-Deegan R. Impact of Gene Patents and Licensing Practices on Access to Genetic Testing and Carrier Screening for Tay-Sachs and Canavan Disease. Genet Med. 2010;12(4 Suppl):S5. doi:10.1097/GIM.0B013E3181D5A669
[19] Cho MK, Illangasekare S, Weaver MA, Leonard DGB, Merz JF. Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services. J Mol Diagnostics. 2003;5(1):3-8. doi:10.1016/S1525-1578(10)60444-8
[20] Terry M. Storming the Molecular Diagnostic IP Fortress. Biotechnol Healthc. 2006;3(1):49. /pmc/articles/PMC3571035/.
[21] Leonard D. Medical practice and gene patents: a personal perspective. Acad Med. 2002;77(12 Pt 2):1388-1391. doi:10.1097/00001888-200212001-00010

focused on carrier screening, and 4) dedicated funds to assist families unable to afford carrier testing. Miami Children's Hospital did not agree to the requests of the Consortium and, instead, pursued a plan to establish a single, large-volume licensee. The controversy culminated in a lawsuit being filed against Miami Children's Hospital which resulted in the United States District Court for the Southern District of Florida concluding that Miami Children's Hospital enriched itself at the expense of the patients and families who had donated tissue that aided in research for Canavan disease.[22]

Today, in the absence of gene patents, there are 108 tests that include the analysis for *ASPA* gene alterations being performed in 22 CLIA-certified laboratories in the United States.[23] It is also important to emphasize that testing for *ASPA* is often incorporated into panel testing that evaluates an array of many other genes. This serves two clinical purposes: 1) it offers patients a single, broad, symptom-based approach to diagnosing heritable conditions especially when it is not clear that a child has Canavan disease, and 2) it allows for affordable and efficient comprehensive carrier testing for many diseases and disorders to be performed so that patients can make informed reproductive decisions. If efforts to establish a single, large volume testing entity just for *ASPA* had been successful, the ability to provide optimal patient care would have been disrupted and fragmented across multiple laboratories. Notably, both the clinical and financial impact would have been disproportionate on those with an elevated risk of carrying an *ASPA* genetic alteration based on their ancestry. For this reason (among many others), ACMG now recommends that carrier screening be offered in an "ethnic and population neutral" approach to ensure those approaches comprehensively assess diverse populations and promote equity and inclusion.

The current environment for the development of comprehensive carrier screening is robust. In 2016, 20 laboratories offered comprehensive carrier testing.[24] Additionally, several market analyses indicated that North America was the highest-revenue-generating carrier screening market from 2014-2019 and will continue to dominate the market into the future.[25,26,27] One report emphasized that a number of partnerships have been formed to improve testing solutions and advance technology. If naturally occurring genetic sequences and their association to diseases and health conditions remained patent eligible, the rapid expansion of the carrier screening market would have not occurred, and patients would have faced restrictions in access to testing as evidenced in the case of patients with Canavan disease.

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[22] Fla SD, editor. Greenberg v. Miami Children's Hospital Research Institute, Inc. 264 F. Supp. 2d 1064 (S. D. Fla. 2003). https://pubmed.ncbi.nlm.nih.gov/15776537/

[23] Data accessed on January 18, 2024 from Genetic Testing Registry; https://www.ncbi.nlm.nih.gov/gtr/

[24] Concert Genetics, "The Current Landscape of Genetic Testing – Market size, market growth and the practical challenges of the clinical workflow." 2016. http://concertgx.wpengine.com/wp-content/uploads/2017/02/ConcertGenetics_TheCurrentLandscapeOfGeneticTesting_March2016.pdf Accessed August 31, 2021.

[25] https://www.researchandmarkets.com/reports/5128884/carrier-screening-market-research-report-by Accessed August 18, 2021.

[26] https://www.psmarketresearch.com/market-analysis/carrier-screening-market Accessed August 18, 2021.

[27] https://www.marketwatch.com/press-release/carrier-screening-market-key-companies-business-opportunities-competitive-landscape-and-industry-analysis-research-report-by-2027-2021-08-11?siteid=bigcharts&dist=bigcharts&tesla=y Accessed August 18, 2021.

Comprehensive Genomic Profiling in Cancer/Whole Genome or Exome Sequence for Pediatric Conditions

Technological advancements in genetic sequencing that allowed for the development of a comprehensive genomic profile of a person's cancer have dramatically improved patient care. Comprehensive Genomic Profiling (CGP) refers to the use of sequencing technology by molecular professionals to simultaneously detect multiple classes of genomic alterations, which include DNA base substitutions, insertions and deletions, copy number alterations, and rearrangements or fusions, across hundreds of genes with a single test on a patient's tumor sample. Not only can CGP detect actionable mutations in any one of hundreds of genes, but it can also provide information about microsatellite instability, tumor mutational burden, homologous recombination repair deficiency, and other genomic signatures, which are properties of the cancer genome as a whole and are not specific to any one gene. This approach allows clinicians to match patients with advanced cancer to targeted therapies already in clinical use and investigational therapies being evaluated in clinical trials.

Increasingly, CGP has been adopted as a required tool for efficient and effective assessment in advanced cancer care. Moreover, as genomic diagnostic criteria and the number of targeted therapies associated with genomic targets increases over time, CGP will only become more essential. In oncology, the percentage of clinical trials incorporating biomarkers rose from 18 percent in 2000 to 61 percent in 2019.[28] This important work has led to the availability of 286 targeted therapies for patients in 2020, a greater than 350% increase from the 81 therapies available in 2012. Taken together, this indicates that more comprehensive approaches to cancer testing will be a focus for molecular professionals well into the future. Allowing patenting of biological phenomena associated with disease is likely to limit advances in application of diagnostic criteria and slow uptake of emerging therapies and biomarkers in the oncology setting.

Similarly, using whole exome and genome sequencing (WES/WGS), which evaluates all known genes or the full human genome, is an important option for identifying genetic causes of disease, including pediatric genetic testing for rare diseases. These testing approaches may be appropriate when 1) the gene or genes involved in a disease are not obvious or known in a patient who is undergoing a diagnostic odyssey, 2) the patient has complex clinical presentations or multiple diagnoses, 3) the patient has a disorder that can be associated with a large number of different genes, and/or 4) the patient is in need of immediate critical care.

WES/WGS allows molecular professionals to explore whether the underlying reasons for a patient's symptoms can be attributed to any known pathogenic or likely pathogenic DNA sequence alterations, and can also identify new gene associations and genetic alterations that have not been previously associated with a disease.[29] Using this information, molecular professionals work to improve testing – when evaluating the number of new genetic tests in 2017, one report found that the number of pediatric and rare disease tests grew faster than any other

[28] Personalized Medicine Coalition, "The Personalized Medicine Report: 2020, Opportunity, Challenges, and the Future." 2020. http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PM_at_FDA_The_Scope_and_Significance_of_Progress_in_2019.pdf Accessed August 19, 2021.
[29] As one example, see https://www.wired.com/story/one-scientists-quest-to-bring-dna-sequencing-to-every-sick-kid/

domain.[30] Moreover, they reported that between January 2016 and March 2018, the number of exome sequencing tests in the market grew from 72 to 125 (a 74 percent increase).

Recognizing the clinical utility of WES/WGS testing the in pediatric population, Congressmen Swalwell (D-CA), Peters (D-CA), and Emmer (R-MN) introduced the H.R. 5989, the "Precision Medicine Access for Kids Today Act," which would establish a demonstration program for up to 15 state Medicaid programs to financially assist with covering genetic and genomic testing for certain individuals under the age of 21 and would direct the Centers for Medicare and Medicaid Services to issue guidance to Medicaid programs clarifying coverage for these innovative tests. Allowing patents on any of the >20,000 human genes analyzed in these tests would significantly threaten patient access to this testing.

CGP, WES, and WGS are made possible because information about thousands of genes and the role of various segments of genetic sequences in human health and disease can be incorporated into a single test. Prior to *Mayo, Myriad, and Alice*, this was not possible as it would have required a laboratory to obtain a license for every gene patent that existed or to exclude potentially clinically relevant genes from the analysis. Instead of promoting an environment for growth and innovation, patents on genetic information would have siloed testing and inhibited patient access to more comprehensive testing options. In fact, since these court decisions, there has been increasing support by researchers and genetic testing laboratories to share and provide open access to information on genetic variants.

In 2017, the ACMG published a statement on data sharing, noting that "information that underpins health-care service delivery should be treated neither as intellectual property nor as a trade secret when other patients may benefit from the knowledge being widely available."[31] Additionally, AMP has recently released its own position statement on data sharing outlining numerous recommendations for hospitals, academic medical centers, commercial diagnostic laboratories, patient organizations, policymakers, and others, to support and facilitate the sharing of molecular genetic variant data.[32] As relayed in the statement, data sharing is "essential both for understanding the contribution of genetic and genomic variation to disease and conditions, and for translating that information through the development, validation, and interpretation of clinical testing… Submissions of de-identified data to [curated databases] accelerates the process for re-assignment of variants of unknown significance (VUS) to clinically actionable categories (e.g., benign or pathogenic), which [the National Institutes of Health] considers a critical aspect of the quality assurance process for accurate genetic and genomic testing."

[30] Concert Genetics, "The Current Landscape of Genetic Testing: Market Growth, Reimbursement Trends, Challenges and Opportunities – 2018 Edition." 2018. http://www.concertgenetics.com/wp-content/uploads/2018/04/12_ConcertGenetics_CurrentLandscapeOfGeneticTesting2018.pdf Accessed August 19, 2021.
[31] American College of Medical Genetics and Genomics Board of Directors, "Laboratory and clinical genomic data sharing is crucial to improving genetic health care: a position statement of the American College of Medical Genetics and Genomics." Genetics in Medicine January 5, 2017. https://www.nature.com/articles/gim2016196
[32] Association for Molecular Pathology, "Association for Molecular Pathology Position Statement: Variant Data Sharing." July 29, 2021 https://www.amp.org/AMP/assets/File/advocacy/AMP_Position_Variant_Data_Sharing_7_29_2021.pdf

Should associations between observed variants and health conditions once again become patent eligible, this type of data sharing would come to a standstill, dramatically slowing the pace of precision medicine research, harming quality genetic variant interpretation, and restricting the ability of molecular professionals to keep their tests current. Ultimately, these effects would render CGP, WES, and WGS unusable, to the detriment of patient care.

COVID-19

Lastly, we call attention to the COVID-19 pandemic and the response effort which largely relied upon highly effective and broadly accessible testing for SARS-CoV-2. AMP shares the concerns expressed by others that, if allowed, patents on the SARS-CoV-2 genetic sequence would have greatly hampered the United States' response efforts.[33] In addition, AMP joined thirty-seven other organizations in calling President Biden's attention to how the COVID-19 pandemic compared to the 2003 outbreak of severe acute respiratory syndrome (SARS).[34] As described in our letter, during the 2003 outbreak, biotechnology and pharmaceutical companies raced to patent everything from the genetic sequences within the virus' genome to the virus itself.[35] In competition with these companies was the Centers for Disease Control and Prevention (CDC), which sought to defensively patent the virus and its entire genetic content "to make sure access to the virus remains available to anyone" as stated by then CDC Director Julie Gerberding.[36]

The necessity for molecular professionals to operate, innovate, and develop testing for patients in an environment free of considerations related to the patent-status of SARS-CoV2 and COVID-19 are crystalized when considering the necessity of frequent shifts in testing strategy due to external challenges experienced repeatedly since February 2020. AMP members were on the frontlines of responding to the COVID-19 pandemic by developing and providing molecular-based diagnostics for patients across the United States. We surveyed our membership multiple times over the course of 2020 and collected over 250 responses from molecular laboratory professionals to understand their successes and hurdles when developing and providing the crucial and timely diagnostic services that patients needed during the COVID-19 pandemic.[37] In August and April of 2020, respondents reported that supply chain interruptions were having a significant impact on their work. To overcome testing supply shortages and maintain their testing capacity, molecular professionals deployed multiple testing methodologies, i.e. they built redundancy in test protocols within their laboratories. Our findings indicated that testing diversity played an important role in the public health emergency to meet the clinical need. If laboratories and manufacturers had been required to navigate multiple patent and licensing

[33] As an example: Park, S. "The Dangers of Expanding What Can Be Patented In the Age of COVID-19." October 30, 2020. https://www.aclu.org/news/privacy-technology/the-dangers-of-expanding-what-can-be-patented-in-the-age-of-covid-19/ Accessed August 19, 2021.

[34] https://www.amp.org/AMP/assets/File/advocacy/Coalition%20Letter%20to%20Biden%20Administration%20on%20Patent-Eligibility_6_8_2021.pdf

[35] https://apnews.com/article/145b4e8d156cddc93e996ae52dc24ec0

[36] https://www.wsj.com/articles/SB105226807345954200

[37] https://www.amp.org/advocacy/sars-cov-2-survey/

arrangements related to SARS-CoV-2 genetic sequence with each assay adjustment or introduction, the observed testing response would not have been possible.

SARS-CoV-2 is made up of ribonucleic acid (RNA, a similar material to DNA) that contains all the genes the virus needs to function within a human cell and, on January 10 of 2021, scientists in China made the full sequence of the virus' genome available to the public. Fortunately, genetic sequences and their association to health conditions are not patentable in the United States, which allowed for multiple molecular tests for SARS-CoV-2 to be developed and performed in CLIA high complexity certified laboratories across the United States.[38] Current patent eligibility jurisprudence has allowed molecular professionals to be adaptable, to rapidly detect different emerging strains, and to ensure that testing in a geographic area is sensitive and specific for that particular population. Flexible regulatory policy during the public health emergency and the lack of patents on the virus' RNA sequence were crucial to our members ability to meet the testing needs of this nation.

Taking a broader view than specific case studies and the experiences of molecular professionals, AMP believes it is critical to also take into consideration how genetic testing and the field of molecular pathology have grown over time since the *AMP v Myriad* Supreme Court decision. We know from public reports from Concert Genetics that in 2022, there were over 175,000 genetic tests in the US market[39] -- an over 180 percent increase compared to the number of genetic tests in 2016.[40] It has been estimated that 14 genetics tests are entering the market *every day*.[41] As articulated previously, we also know that genetic tests are becoming more complex. For instance, during the 12 months ending March 1, 2018, a net total of 801 new genetic testing panels entered the market.[42] This growth is also having a tremendous positive impact on the economy. According to a 2019 report issued by the American Society of Human Genetics (ASHG), human genetics and genomics contributed $265 billion to the US economy in that year alone, and for every federal dollar invested in human genetics and genomics research in 2019, it yielded a $4.75 return.[43]

AMP believes it is also critically important to consider how this rich environment impacts molecular professionals. The ASHG report on the economy found that the US human genetics and genomics research and industrial domain employs nearly 166,000 workers which includes researchers, medical geneticists, and genetic

[38] https://chs.asu.edu/diagnostics-commons/testing-commons
[39] Concert Genetics, "Genetic Test Price Transparency Report." 2023. http://www.concertgenetics.com/wp-content/uploads/2023/11/Concert-Genetics-2023-Genetic-Test-Price-Transparency-Report-07Nov2023.pdf Accessed January 18, 2024.
[40] Concert Genetics, "The Current Landscape of Genetic Testing – Market size, market growth and the practical challenges of the clinical workflow." 2016. http://concertgx.wpengine.com/wp-content/uploads/2017/02/ConcertGenetics_TheCurrentLandscapeOfGeneticTesting_March2016.pdf Accessed August 31, 2021.
[41] Concert Genetics, "The Current Landscape of Genetic Testing: Market Growth, Reimbursement Trends, Challenges and Opportunities – 2018 Edition." 2018. http://www.concertgenetics.com/wp-content/uploads/2018/04/12_ConcertGenetics_CurrentLandscapeOfGeneticTesting2018.pdf Accessed August 19, 2021.
[42] Concert Genetics, "The Current Landscape of Genetic Testing: Market Growth, Reimbursement Trends, Challenges and Opportunities – 2018 Edition." 2018. http://www.concertgenetics.com/wp-content/uploads/2018/04/12_ConcertGenetics_CurrentLandscapeOfGeneticTesting2018.pdf Accessed August 19, 2021.
[43] American Society of Human Genetics, "The Economic Impact and Functional Applications of Human Genetics and Genomics." May 2021 https://www.ashg.org/wp-content/uploads/2021/05/ASHG-TEConomy-Impact-Report-Final.pdf. Accessed August 19, 2021

counselors, as well as many workers in adjacent, corporate, or operational roles in firms developing lab equipment and software, performing clinical genetics and genomics testing, or manufacturing pharmacogenomic drugs. Moreover, the analysis determined that the US human genetics and genomics domain supported an additional 684,000 jobs (indirect and induced effects) within the US economy for a total employment impact of more than 850,000 workers. Nearly 63,000 of those jobs were at medical testing/diagnostics companies. While these talented scientists and professionals cannot patent naturally occurring entities and associations, many patents applying to novel innovations and approaches are filed on a regular basis, protecting the critical IP that was developed with hard work and insight.

The benefits of the *Myriad, Mayo, and Alice* decisions is not specific to just diagnostic medicine. One only needs to look toward the recent authorizations from the Food and Drug Administration for novel gene therapy and CRISPR therapy treatments for rare inherited diseases like sickle cell disease[44] and beta thalassemia[45] as evidence of the incredible advances in scientific understanding in the etiology of diseases that has resulted since these pivotal Supreme Court decisions. In fact, had there been patents on the sequence of the genes or the association of the pathogenic mutations with disease status, this would have restricted the ability of companies like Bluebird Bio or Vertex Pharmaceuticals to conduct the research that led to these innovative therapies and would likely have greatly increased the cost of the development and access to the treatments due to exorbitant licensing fees.

Taken together, we find that the current state of patent eligibility jurisprudence in the United States has had an extremely positive impact on the state of innovation, research, and the US economy, especially since the relatively recent decisions made in *Myriad*, *Mayo*, and *Alice*. The ability of our members to develop and offer these groundbreaking tests for patients is built upon the current patent eligibility jurisprudence, and we fear that attempts to widen patent eligibility to include laws of nature and natural phenomena would have drastic repercussions, both for our members and the patients they serve.

AMP members, who were recently described as "invisible" heroes at the front lines of pandemic response[46], continue to be inspired and eager to make a difference. AMP is confident that their work will continue to significantly impact the economy, but more importantly, the lives of patients, provided their work is not blocked by drastic changes to patent eligibility.

Sincerely,

Maria E. Arcila, M.D.
President, Association for Molecular Pathology

[44] https://www.fda.gov/news-events/press-announcements/fda-approves-first-gene-therapies-treat-patients-sickle-cell-disease
[45] https://www.cnn.com/2024/01/16/health/crispr-casgevy-beta-thalassemia/index.html
[46] https://www.nytimes.com/2020/12/03/health/coronavirus-testing-labs-workers.html