COLLEGE of AMERICAN PATHOLOGISTS

Statement for the Record

College of American Pathologists

United States Senate Committee on the Judiciary
Subcommittee on Intellectual Property

Re: The Patent Eligibility Restoration Act – Restoring Clarity, Certainty, and Predictability to the U.S. Patent System

The College of America Pathologists (CAP) submits this statement for the record to share our serious concerns about the *Patent Eligibility Restoration Act (PERA)* in advance of the upcoming hearing. As the world's largest organization of board-certified pathologists and leading provider of laboratory accreditation and proficiency testing programs, the CAP serves patients, pathologists, and the public by fostering and advocating excellence in the practice of pathology and laboratory medicine worldwide. As physicians specializing in the diagnosis of disease through laboratory methods, pathologists have a long track record of delivering high quality diagnostic services to patients and other physicians.

The CAP firmly believes that abstract ideas, laws of nature, and natural phenomenon are fundamental tools of scientific and technological work, and that established Supreme Court precedent protecting these categories from patent eligibility has directly and positively fostered significant growth and innovation in the healthcare space. Clinical laboratory genomics is a rapidly growing field with numerous critical implications for patient care. The patenting of genes and the association between genes and diseases pose a serious threat to patient care, medical advancement, and medical education. Allowing commercial entities to patent genes – rather than diagnostic tools – will impede the provision of genetic-based clinical testing and patient care through exclusive licensing agreements, excessive licensing fees, and restrictive licensing conditions.

Increase Costs for Patients

The CAP is concerned that the bill would eliminate the judicially created exceptions to patent eligibility, thereby overturning the Mayo, Myriad, and Alice decisions. Prior to 2013, innumerable women were held captive to one company that held corporate ownership of diseases related to the BRCA1/2 genes through gene patents. A woman, and potentially impacted family members, could only learn if they had this specific increased cancer risk by taking a test provided exclusively by Myriad Genetics at a cost of more than $3,000[1]. The Supreme Court's unanimous decision against Myriad in 2013 created much needed academic and commercial freedom to create novel tests and

[1] https://ocrahope.org/news/supreme-court-strikes-down-brca-gene-patents/

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rapidly offer more competitive test options on previously patented genes. Now there are tests for *BRCA1*, *BRCA2*, for as little as for $249[2], and a litany of other pathologically significant genes.

In another example, the company Sequenome filed for patent-infringement against other companies claiming that it alone had §504 patent rights over cell free fetal DNA circulating in maternal blood. In fact, methods to isolate and utilize this material for diagnosis were well known. Fortunately for patients, the §504 patent was invalidated in litigation because it "violated" the judicially protected natural phenomenon exception. The use of cell-free fetal DNA represents a substantial testing area in clinical prenatal genetics. If the Sequenome patent-ineligible claims were reverted, the price of non-invasive prenatal testing (including for common chromosomal abnormalities like Downs Syndrome) would spike, and the other commercial and academic labs who had developed tests would encounter difficulties performing their tests at significant detriment to medical research and patient care.

Impede Patient Care

Further, the CAP is concerned that the legislation also cripples patient self-directed care, blocking patients' ability to seek second opinions on genetic or other clinical tests and interpretations. An independent second opinion on test-results protected by a gene patent would be unattainable because no laboratory would be able to offer such a test for confirmatory testing purposes.

Confirmatory tests are used for test result verification. Confirmatory testing is important for rare diseases, various conditions with difficult screening/diagnostic algorithms, and for tests that carry significant/life-altering implications (e.g., results would change the choice of chemotherapy). Cancer treatment highlights the vital importance of confirmatory tests; testing results frequently affect chemotherapy selection, may avert potentially devastating short and long-term drug toxicities, and may qualify a patient for life-saving targeted therapies.

If companies could patent genes, gene sequences and/or variations, and diseases, this would pose a significant roadblock to patient care. For example, if a condition can only be diagnosed using one proprietary test, and the development of newer/better testing for the same disease would be blocked, it would significantly harm patients with the disease that may test negative by the patented test, significantly stymieing scientific advancement in the care of that disease.

Threaten Treatment

Additionally, PERA would eliminate the prohibition against natural correlations. For example, reference intervals are important, as they allow healthcare providers to correlate clinical test results against an appropriate population. Pathologists are responsible for ensuring that reference ranges are established or verified to be applicable to their patient population, for every applicable analyte and specimen source proffered in the laboratory test menu. Multiple methods can be used to

[2] https://www.uclahealth.org/news/release/genetic-testing-all-women-for-breast-cancer-might-not-be-worth-the-cost

ascertain a physiologically meaningful reference interval, but this skill is an essential part of a pathologist's training and duty to patient care.

The Supreme Court's unanimous ruling in Mayo vs. Prometheus (2012) frees clinical pathologists to practice their medical specialty. In addition, the ruling clarified that ascertainment of a reference range simply describes the relationship between an analyte and a physical condition – "setting forth a natural law". This distinction helps to ensure that no entity can monopolize these natural correlations of the human body and thus impede improvement in medical knowledge and treatment.

Finally, as 'products of natural phenomena', gene sequence data is fundamental to the understanding of numerous diseases and should remain exempt from patent eligibility. No commercial entity should have 'exclusive ownership of a disease' through license agreements on gene-based tests. This practice has previously been used to prevent physicians and clinical laboratories from performing genetic tests as diagnostic medical procedures. In addition to BRCA, prior examples where testing has been halted due to patent enforcement include Alzheimer disease, Canavan disease, and Charcot-Marie-Tooth disease.

Impact on Medical Diagnosis

DNA as it exists in the body is not, by itself, useful to determine whether a patient has a genetic condition or mutation or whether the condition will respond to certain drugs. DNA must be extracted from the human body, isolated/purified to ensure the appropriate amount of DNA is present for testing, reduce contaminants, enable gene sequencing, and reduce errors in testing, and in some cases manipulated (i.e., modified from its original state) before even rudimentary testing can occur.

These initial alterations/modifications of cellular components represent decades-old routinely performed methods of scientific inquiry that must be performed for the vast majority of genetic analysis. PERA would drastically alter the patent eligibility status of these natural materials within all living things. These conventional alterations are necessary for nearly all genetic diagnosis of medical conditions; from evaluation of tumor tissue for targeted cancer therapy to identification of hereditary conditions like Canavan's disease (a fatal degenerative disorder that causes progressive damage to nerve cells and loss of white matter in the brain) or Marfan syndrome (a genetic condition that affects the body's connective tissues and can also be life threatening).

While we all recognize that the nucleic acid molecules themselves are vitally important, we must again emphasize that the genetic sequences encoded by the molecules are of equal or greater importance to our members. The DNA molecule can be viewed as a book or text, with the nucleic acids representing the letters of the unique genetic-alphabet (A, C, G, and T). The information being conveyed by the "genetic language" is just, if not more, important than the chemical structure of the DNA itself.

Clinically, when pathologists look for mutations in a gene, they are looking for typos in the original text. Certain typos are benign and don't really change the meaning of what you're reading. Other

typos are harmful, like deleting big portions of text or changing words, such that it changes the context and meaning of what you're reading. But these typos (mutations) can't be discerned from looking at unmodified DNA as it exists in the human body; pathologists need to look at the translated, or modified, text to diagnose disease.

Similarly, one can view DNA in its natural state as a book in an ancient language that no one can read anymore. For the text to be useful, it must be translated. Different people might use different means of translation (a computer program or a translation dictionary) and it may even be translated into different languages depending on the reader who needs it, but it must be translated to be read, and all the translations should ultimately be the same because they are based on the same initial book. This is one reason why PERA fails to protect patients and pathologists and will impede the practice of medicine. It short, it fails to protect the basic tools of scientific and technological work needed to diagnose diseases and treat patients.

Stifle Innovation

Another clinically important point is that a genetic disease can outwardly manifest in one way but may be caused by mutations in a variety of different genes (and vice versa), thus comprehensive multi-gene tests have become the current standard of care. This type of testing would not be possible if PERA were to be passed. To meet current standard of care practices, a child with developmental delay and facial malformations and a woman with a family history of early-onset breast/ovarian cancers would both need comprehensive gene sequencing studies performed to clarify their diagnoses. However, the gene content of their testing panels would be quite different, and hundreds of genes would need to be tested between them with very little content overlap. If companies were to become the sole purveyors of individual genes and their sequences, clinical laboratories would not be able practically to manage multiple royalty payments, and patient's access to timely diagnosis would be severely limited. PERA would return us to a similar, scientifically problematic, pre-judicial exemption state.

As you may recall, before the Supreme Court cases that created judicial exceptions, biotech companies attempted to patent the SARS virus. The CDC stepped in and forcibly obtained patent rights over SARS so that multiple entities could collaborate on the necessary research to understand the disease, develop diagnostics, and create treatments. While PERA prevents the patenting of unmodified material as it exists in nature, the material needed to develop diagnostics and treatments for a virus, for example, does not typically exist in nature in a form that is immediately clinically applicable. The elementary manipulation needed to render these basic materials into a useful state should not be considered sufficiently transformative as to warrant patent eligibility.

The RNA in the coronavirus (or other viruses) is not often free-floating in nature. When it is, it's not useful because it doesn't survive in nature long enough to be studied. It needs to be converted, through basic non-proprietary methods, to cDNA for basic study of its sequence. PERA might not allow patenting of COVID-19, but it could allow for patenting COVID-19 RNA once it has been removed from the virus. Subsequently, the study, manipulation, and development of diagnostics and

vaccines could therefore be blocked. The first step in development is to pop or disrupt intact viral particles and release their nucleic acid. Through an extremely basic manipulation, the viral particle is no longer generally how it exists in nature, and this modification drastically changes its patentability under PERA.

Responding to a pandemic in a situation where the exchange of critical genetic/genomic information was restricted would be disastrous. It is not in the public's interest for any single entity to hold ownership over the means to diagnose a disease or serve as the sole gatekeeper for targeted therapeutics. This approach would be bad for patient care, for public health, and for the U.S.' standing as a global leader in the provision and quality of health care.

Enacting PERA would represent a large step backwards, limiting the exchange of basic scientific knowledge and stifling innovation. This legislation would also immediately erect barriers to quality healthcare. In short, while patenting new and innovative techniques and testing methods may be fine, **the patenting of natural materials and rules of nature will stifle innovation, increase costs for patients, exacerbate disparities, and harm patient care.**

The CAP appreciates your diligence and attention to our concerns. Please contact Darren Fenwick at dfenwic@cap.org if you have questions or comments.

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