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CORIELL INSTITUTE FOR MEDICAL RESEARCH

Dr. Michael Christman, *President and CEO*

The Coriell Institute for Medical Research houses one of the world's most diverse and widely utilized biorepositories, connecting academic and commercial research organizations with high-quality biomaterials required to pursue human health improvements. As part of the Institute's mission to enable discovery using cell lines, Coriell is leveraging its expertise and infrastructure to provide an essential service offering: cell line authentication.

Dr. Michael Christman, President and CEO, has been at the helm of the organization for a decade and continues to pursue innovative research programs in stem cell biology and personalized medicine. Dr. Christman earned his Ph.D. in biochemistry from the University of California, Berkeley, was a postdoctoral researcher at MIT and chaired the Genetics and Genomics Department at Boston University prior to joining Coriell.

Q. Why have researchers been paying more attention to cell line integrity?
Cell line misidentification has been a problem in the research community for decades, dating back almost to the establishment of the first human cell line. Over time, the persistent use of these misidentified or contaminated cells has essentially nullified more than 4 billion dollars of NIH funding and resulted in wasted research hours generating irrelevant and irreproducible data. Now, researchers seeking NIH funding are required to provide a cell line authentication plan to ensure cell lines are correctly identified and not contaminated. This has also spurred many journals to request the same information about cell line identity as determined by morphology and analysis of Short Tandem Repeats, in addition to confirmation that they are free from microbial contamination. These policies are helping the NIH and many journals raise awareness of this issue, while introducing optimized practices.

Q. What led the NIH to implement new rules around cell line integrity?
It's been a long time coming. Stanley Gartler first discovered cross-contamination and misidentification of several cancer cell lines with HeLa cells through Isoenzyme profiling. Currently there are over 480 cell lines listed as misidentified in the International Cell Line Authentication (ICLAC) database, and the prevalence of the issue is only growing. About 15% of cell lines are contaminated by HeLa cells and about 30% of cell lines are misidentified. Even more staggering is that only 43% of cell lines can be uniquely identified. This is a growing problem that can have a profound effect on the integrity of research and discovery in the scientific community. I'm encouraged to see the NIH and journals, such as *Nature*, implementing these regulations in an effort to ensure a high-standard of scientific integrity.

Q. Is cell line identity the only potential problem?
Several parameters contribute to cell line authentication; cell morphology, sterility and identity. With each specific cell type, you expect the cells to represent a particular tissue or disease state, otherwise cell line misidentification might be suspected. Another contributing factor is microbial contamination. Bacterial, mold and yeast contaminations are easily uncovered, as they can be visually detected. Viral and mycoplasma contaminations are more insidious and easily evade detection unless they cause pathogenic effects. Mycoplasma contamination rates in the US are estimated at 11 to 15% and remain largely unknown, as mycoplasma are smaller than bacteria, have no cell wall and are easily aerosolized in tissue culture hoods, yet these contaminations can lead to alteration in many cell functions. Coriell evaluates all cell lines for morphology, cell line identity, species identity, sterility, mycoplasma contamination and contamination with blood borne pathogens such as HIV-1, HIV-2, HBV and HCV.

Q. What type of measures is Coriell implementing to ensure cell line integrity?
As a pioneering biobank, Coriell is uniquely qualified to operate in this space. We set the standard for quality, employ proven best practices and have performed nearly 45,000 cell line authentications to date. When establishing a line submitted by an outside researcher, we take a small portion of the blood or tissue sample and set it aside before doing anything else. Then, when we make or regrow cell lines, we compare our DNA profiles with the original sample. We quarantine external cell lines, making sure they are not in contact with any of our other lines and we test for contamination. When we freeze our cells, we authenticate one more time. When we accept outside lines, the researchers can choose from a list of potential tests. We think identity checks by STR analysis and mycoplasma tests are key and are a pretty cost-effective way for most labs. Coriell will also maintain an authenticated stock for those lines we test in case a researcher needs to return to it in the future.

Q. Does this issue pertain exclusively to academic and research institutions?
Absolutely not. Pharma and biotech utilize cell lines for a sizeable amount of discovery work, whether it be for new therapeutics or for developing diagnostic tests. It is important for them to have accurate starting material for which to make these discoveries because their products are being utilized by doctors and labs, which in turn impacts potential therapeutics and health care outcomes. Over $114 billion is spent in the US on research by pharma and biotech alone. Another $28.2 billion is spent on research that cannot be repeated. If we could reduce the amount of cell line misidentifications from 20% to 10%, we could save roughly $14 billion per year.

Q. What other scientific areas are of interest to Coriell?
The Coriell Personalized Medicine Collaborative (CPMC) research study has been a fixture of the organization and has returned meaningful and insightful findings, including a recent publication identifying six new targets related to human sleep duration. We started this project a decade ago in order to try and understand how individuals would use personal genetic information in clinical care, and have since expanded to engage a network of influential research partners, including the United States Air Force. The longevity of our study is now permitting our research team to discover new gene targets and promote the adoption of genomics in everyday life.