Have you ever approached a Claude Monet painting, stopping only when you are inches from the canvas? The whole becomes the sum of its parts: a brush stroke, minuscule touches of color, the interplay of shapes. Not unlike this, in medical diagnostic medicine, pathologists approach the patient in a similar way, zooming in and magnifying the infinitesimal details that make up the patient—a blood cell, the spiral of a DNA strand, a gene variant, a foreign bacteria or a virus.

Through these microscopic clues, pathology experts assist in the detection, diagnosis, treatment, and management of human diseases and conditions. Approximately 70 percent of patient-care decisions are based on in vitro diagnostic test results produced by a clinical laboratory.

*Magnify* focuses in on ARUP Laboratories’ current role in diagnostic medicine, as well as its drive for pushing knowledge and discoveries forward. As one of the country’s two largest nonprofit, national reference laboratories, ARUP has entrepreneurial roots and strong ties to academic medicine that guide its unique business approach. (It is a nonprofit enterprise of the University of Utah and its Department of Pathology.)

This approach includes emphasis on education, strict adherence to evidence-based knowledge, and an environment that promotes collaborations and thus accelerates innovations. The stories among these pages will allow readers to see for themselves, zooming in and back out, ARUP’s patient-focused and market-facing dynamics at work.
The Work Is Never Done

“In operations, we view solutions as a step forward. They may not be perfect, but they provide momentum in keeping us always moving toward ‘better.’ Waiting for the perfect solution can lead to stagnation or paralysis. It is a mindset of continual improvement that fuels our evolution.”

Martha J. Bale
Over the last two decades, I’ve witnessed an industry that has continually evolved, rigorously interacting with and reacting to advancements in science and technology. To excel, ARUP has had to adapt to keep up with this progress—at times even driving it.

We approach every operational challenge guided by our commitment to continuously improve without ever compromising quality or service. That’s how we find solutions.

What’s our advantage? As an academic medical reference laboratory, we have experts in the field constantly eyeing how we can improve existing tests and spot the need for new tests. This keeps our test-development pipeline robust. We are also always striving to improve the diagnostic value of current tests by improving sensitivity and specificity, as well as turnaround times.

Add in technology; that accelerates everything! More so than ever, we are constantly re-evaluating and adjusting to take advantage of technological advances. Consider, in the last 20 years, ARUP has gone from one lab using PCR (polymerase chain reaction) to 10 labs now employing this technique. This growth is also evident in development and use of mass spectrometry. We were one of the first major adopters of mass spectrometry for clinical testing and have now adopted versions of this technology across ARUP.

Right now, one of our key areas of focus is streamlining and standardizing instrumentation and processes. It is easier to support 10 of the same instrument than it is to support the same technology from 10 different types or suppliers of that instrument. We want to simplify to fewer platforms as long as the quality of our testing is not compromised.

Imagine using 12 different blenders and each one operates a bit differently, is built a bit differently, and whips up a different final product. This increases complexity; we are already a complex organization based on the nature of our industry. So standardizing instrumentation will allow us to continue driving high-quality diagnostics (i.e., consistent results) while also making practical sense (i.e., training, maintenance). We’ve already achieved this in mass spectrometry, where our own engineers maintain and service the instrumentation.

We’re applying this same standardization approach for liquid handling platforms. Currently, we have a lot of pipetting automation, but it consists of many different instruments all working toward the same purpose.

In addition, we are streamlining processes to meet increased demands in our labs using next-generation sequencing (NGS). The realm of NGS is taking off and is a key part of our laboratories, involving genetics, oncology, infectious disease, and immunology.

We want global solutions; it isn’t about each lab figuring out its own way of solving an issue—often the same issue might present itself in other labs as well. It is about developing and implementing the same solution across all labs. While there is separate testing in each lab, in many cases the processes are the same, and often there are similar pressure points.

In operations, we view solutions as a step forward. They may not be perfect, but they provide momentum in keeping us always moving toward “better.” Waiting for the perfect solution can lead to stagnation or paralysis. It is a mindset of continual improvement that fuels our evolution, and the fact that we know we are never done. It is this mentality among every single individual here that keeps us strong and moving forward.

Martha Bale, MS, MT(ASCP)
Vice President, Director, Technical Operations, ARUP Laboratories
Newly Arrived and Fighting for Life

A Newborn Genetic Test Searches for Answers
At 3 weeks old, the baby still had not gazed into his mother’s eyes or visually traced his father’s face. He could not open his eyes, nor could this tiny being move his arms or legs. He was trapped in a body that could not move. Each breath depended on a machine.

Doctors caring for him in the Primary Children’s Hospital’s Neonatal Intensive Care Unit (NICU) suspected a neurological issue, but without knowing specifically what was causing his catatonic state, they could not treat him.

The hope was that a new genetic test, developed by ARUP and in use in a pilot program with Primary Children’s Hospital (PCH), would provide an answer. Known as a NICU rapid-panel turnaround test, it uses next-generation sequencing (NGS) technology to analyze the baby’s genes. (NGS is a process used to analyze DNA and its many genetic variations.) Rather than analyzing the whole genome (24,000 genes), this test hones in on 4,500 known disease-causing genes.

Within five days of submitting a small sample of the baby’s blood and that of his parents, ARUP Medical Director Rong Mao, MD, saw something that might help the doctors. The baby had tested positive for a mutation located on his CHAT gene that was preventing him from producing a crucial enzyme called choline acetyltransferase that is responsible for making muscles move. The baby had congenital myasthenic syndrome. Chris Miller, one of ARUP’s 14 genetic counselors, immediately contacted the NICU with the news.

Back at the hospital, behind blinds drawn to protect babies’ eyes from the bright sunlight, a team of doctors and nurses from Intermountain Healthcare and the University of Utah gathered around the baby boy. Brandon Zielinski, MD, PhD, who was leading the Neurological Newborn Intensive Care team, injected a small vial of medicine into one of the tubes linked to the infant. It was a drug designed to compensate for his missing enzyme.

Within a few minutes, the baby boy began wriggling, and then his eyes fluttered open. Zielinski leaned in close, moving his own face from side to side to see if the baby tracked him with his eyes—the human face is a strong stimulus for babies. The boy’s eyes followed. Next, they turned off the ventilator, and the baby took his first full breath on his own. Zielinski quickly turned to a nurse. “Let’s get the parents in here.”

“It was profound; I had expected some response but not as strong as day and night,” recalls Zielinski, a University of Utah assistant professor in the Department of Pediatrics and Neurology. “It’s not often that you experience such a rush of emotion [as] this moment provided. It was impactful from both a medical and humanistic perspective.”

**Time Is Life**

Time is vital for these patients. The quicker the results, the sooner targeted treatment can begin. The NICU panel can provide preliminary results within five days, compared with the alternative test, exome sequencing, which takes approximately four to five weeks. At three weeks, a
comprehensive final report is provided that includes all test findings. “This sequencing technology is advancing so fast, along with bioinformatics, that the time it takes to get results is going to become less and less,” says Rong Mao, MD, medical director of the Molecular Genetics and Genomics labs at ARUP.

Another factor that can eat up precious time is when doctors start ordering one individual test after another or order tests that focus on a handful of suspected genes. The process of eliminating possible diagnoses can be slow. The cost isn’t just in time but in dollars too. Tens of thousands of dollars can be racked up in testing costs along with expenses for other diagnostic tools (i.e., MRIs, spinal fluid taps) during this period.

Mao’s laboratory had been providing exome sequencing for Primary’s Children’s Hospital for undiagnosed or rare diseases, but she felt it was taking too long (35 days) and started wondering how the process could be expedited while still keeping the cost down. The rapid-panel turnaround test sequences “the highest number of genes in any panel sequenced by NGS,” says Mao, an associate professor of pathology and co-director of the Clinical Medical Genetics Fellowship Program at the University of Utah School of Medicine. “We’re looking for disease-causing mutations and then we’re looking deep to see whether it is the cause of the baby’s illness.”

The test involves collecting and analyzing blood samples from each parent and the infant, known as a trio test. Such a test costs about $2,000 for each person (total $6,000 with both parents); this is less than half the cost of comparable tests, and results can be returned in a fraction of the time.

**Expertise Meets Collaboration**

“What makes this test so unique is the collaboration and real-time communication with the doctors,” says Mao. The test pilot draws on expertise from ARUP, Intermountain Healthcare, and the University of Utah.

“It’s allowing us to improve on and streamline the processes of the test before opening it up to others,” says Mao. She worked with Steven Bleyl, MD, PhD, who brought together a team of specialists to come up with a system to establish specific criteria to identify which patients would most benefit from such a test. Bleyl is the director of the Intermountain Healthcare’s Clinical Genetics Institute (part of Intermountain Pediatric Genetic Testing Stewardship).

“Reaching a consensus among our clinicians on criteria for when and how we use this test helps mitigate potential risks incurred when we depend on a rapid turnaround test like this,” says Bleyl, explaining those risks might be misdiagnosing a patient based on early test results, or ordering the test and waiting for results before pursuing the standard of care that might provide answers sooner and make the test unnecessary.

The pilot will involve measuring the test’s impact on cost savings and patient care and adjusting criteria as necessary. The pilot has been underway for less than a year, but Bleyl and his team view it as a work in progress until they are satisfied with established criteria.

While the test may allow some babies to leave the NICU more quickly with targeted treatment, for others it will determine whether their conditions can even be treated. “It allows us to stop the diagnostic odyssey earlier and give families a realistic idea of what the future might hold,” says Bleyl, adding that he could foresee using this test beyond the NICU.

**An Actionable Mutation: “We Can Do Something About It”**

“In neonatal intensive care, a major problem is when you have a critically ill infant, and there is no clear-cut diagnosis that can be made,” says neonatologist Luca Brunelli, MD, PhD. The most common conditions in the NICU for seeking out a next-generation sequencing panel include cardio-respiratory failure, central nervous system abnormalities, an anatomic anomaly, or a syndrome affecting multiple organs. “We’ll order this panel when we want to test whether a certain diagnosis is linked to underlying genetic makeup,” adds Brunelli, explaining neurological conditions are often genetically linked.

He recalls the boy with congenital myasthenic syndrome. “It gave us an answer so we could begin treating the baby,” says Brunelli, who is an associate professor in the Division of Neonatology at the University of Utah and works in the Primary Children’s Hospital NICU. “It is what we call an ‘actionable mutation’—we can do something about it. Unfortunately, for numerous mutations we cannot do anything to fix it.”
Why Test the Parents, Too?

“Overall, testing parents helps determine the clinical significance of the variants detected in the child,” explains ARUP Medical Director Rong Mao, MD. If a genetic variant is identified in a child, then scientists can look for this same variant in the parents. If neither parent has the variant, it is considered de novo; de novo variants found in the child have a higher chance of being disease causing than variants that are also found in a healthy parent.

When two mutations in the same gene are found in a child, it may cause an autosomal recessive disease such as cystic fibrosis or sickle cell anemia. Testing the child’s parents can confirm that the mutations are located on opposite chromosomes. (Each parent carries one of the two mutations.)

If a variant is detected in the child and also in one of the healthy parents, and mutations in that gene are inherited in an autosomal-dominant manner, then the variant is unlikely to be the cause of the disease. Because some dominantly inherited conditions have reduced penetrance (not everyone who inherits the mutation will show symptoms), one has to be careful before concluding the gene did not cause a child’s disorder.

The treatment was helpful, not curative, admits pediatric neurologist Betsy Ostrander, MD, an assistant professor of pediatrics at the University of Utah who is in the Division of Pediatric Neurology at PCH. “It allowed us to stop additional testing and that roller coaster of emotion that can be exhausting for the family when they don’t know what is going on and have to face one prospect after another with each test.”

Ostrander is excited about the transformation such a test can bring for neonatal intensive care, where use of genomics has been minimal. “There are really few things that can change outcomes of these babies, outside of antibiotics, surfactants (help protect the lungs), and echocardiography. This is a tool that can really enable us going forward.”

“"It was impactful from both a medical and humanistic perspective," says Dr. Brandon Zielinski, recalling the moment a baby boy opened his eyes after a genetic test helped identify what his body needed.
Sick of Being Sick
Six Families Help with Discovering Disorder

Discovery of a New Immune Disorder Leads to Answers and Earlier Treatment

Pneumonia has been an uninvited visitor throughout Roma Jean Ockler’s life, showing up every few years. Two years ago she almost died from a case so severe that it landed her in surgery. Sinus infections intruded even more frequently, hacking into her life every six weeks or so.

“Dealing with being sick becomes part of your life; you don’t ever seem able to stay away from the doctor’s office,” says Ockler, a mother and grandmother, whose original diagnosis in 1975 was a weak immune system. “It got incredibly frustrating.”

Harry Hill, MD, often sees this frustration in patients who visit the Clinical Immunology/Immunodeficiencies Clinic at the University Medical Center. By the time they arrive at his clinic, these patients have had one infection after another, often enduring a maddening diagnostic odyssey lasting years. Hill is medical director of the Cellular and Innate Immunology Laboratory at ARUP.

Many of these patients end up being diagnosed with common variable immune deficiency (CVID), a rare condition in which patients have dangerously low levels of infection-fighting antibodies. Hill estimates he’s diagnosed between 200 to 300 patients with CVID, a condition occurring in about 1 in 20,000 people, over his 42-year career.

When Ockler mentioned that her nephews were sick a lot too with similar symptoms, Hill, who is a professor of pathology, pediatrics, and medicine, wondered about a genetic cause. Only about 10 percent of CVID cases have been identified as having a genetic cause; Ockler didn’t have any of them.

Could There Be a New Genetic Marker Linked to CVID?
Collaborating with a number of Utah colleagues, including ARUP molecular pathologists Attila Kumánovics, MD, and Karl Voelkerding, MD, they delved into research, securing grants from the National Institutes of Health and the Utah Genome Project. They were able to test 30 of Ockler’s family members.
In the Labs: CVID Testing

“Our work here is to help diagnose patients, and genetic testing is one way to do that; once we know the cause of the disease, we can test more specifically, honing in on a specific gene, as is the case with common variable immune deficiency (CVID),” explains Attila Kumánovics, MD, assistant medical director of Immunology and co-director of Immunogenetics at ARUP. He adds that this is much quicker than testing to eliminate possibilities and means results get back to the patient faster. Genetic test results can also open the door for genetic counseling so families can better understand the condition and take steps to recognize and address their family’s health, which might entail preventative steps or earlier interventions.

Currently, ARUP Laboratories tests for 35 genes related to CVID by using sequencing. These 35 genes include more than those that are usually associated with CVID, so the test panel is called Primary Antibody Deficiency Panel. “The reason is that many of these diseases and diagnoses are hard to differentiate in practice,” explains Kumánovics. His team is working on developing testing for the gene encoding for IKAROS, a protein well known for its central role in immune cell development (see accompanying story).

Many ARUP labs are involved in the diagnosis of CVID involving non-genetic tests—for example, the serum immunoglobulin measurement tests in the Protein Immunology lab, the lymphocyte subset panels in Immunological Flow lab, and the vaccine response tests (e.g., Streptococcus pneumoniae antibodies, IgG) in the Autoimmune Immunology lab.

ARUP is one of 11 labs in the country offering exome sequencing and will soon be offering genome sequencing. Exome sequencing looks at only the parts of the genetic information that encodes for proteins, while genome sequencing looks at all of the gene’s DNA. Genomic sequencing holds huge promise for the estimated 30 million Americans living with an orphan disease, 80 percent of which are inherited. CVID is one such disease.

Infections are very much a part of life, but how many infections are too many before you suspect something else is at play? Unlike many other genetic diseases, there are no outward signs or symptoms that tip you off that genetics is at play here. That’s why it usually takes many years to diagnose these patients.”

Attila Kumánovics, MD, ARUP Assistant Medical Director, Immunology; Co-Director, Immunogenetics
They found that many of Ockler’s relatives were missing one of two copies of a gene that codes for IKAROS—a protein well known for its central role in immune cell development. Meanwhile, 2,000 miles away, Mary Ellen Conley, MD, from The Rockefeller University, independently came to the same conclusion with her own patients. She connected with the Utah team and coordinated what would become an international effort revealing a total of six unrelated families who share similar sets of symptoms and changes in the same gene, implicating IKAROS as the culprit behind their shared disorder. “Often research tries to answer a question that is brought up by the patients,” says Conley.

While some families had a change in just one DNA letter within the gene, others were missing a large piece, or all of it. Each of the mutations cripple a region required for IKAROS to function, a result confirmed by biochemical analysis, suggesting it cannot carry out its critical role in regulating immune B cell development. Indeed, as the experiments predicted, all six families have low B cell counts. In other words, their immune system is misconstructed, likely explaining why they also have low levels of infection-fighting antibodies (immunoglobulins), which are produced by B cells.

Yet one of the most surprising findings, says Kumánovics, assistant professor of pathology at the University of Utah, is that while some who carry the IKAROS mutations are prone to sickness, others appear to be healthy. He adds that understanding the biology that leads to this unexpected resilience could provide clues to overcoming the condition. “These rare patients don’t know how valuable they are. They are providing insights into how the immune system works,” adds Kumánovics.

The findings were published online in the New England Journal of Medicine last March; the Ocklers were the largest family included in the research. This finding makes it possible for doctors to make a definitive genetic diagnosis.
for this class of CVID, opening a door to precision medicine tailored to patients with the disorder.

In the near future, researchers have what they need to create definitive diagnostic criteria for this new class of CVID. “The diagnosis is rare but that makes it no less difficult for those who have it,” says Voelkerding, professor of pathology at the University of Utah and medical director of Genomics and Bioinformatics, at ARUP. “We think this discovery will help patients around the world,” he adds. “There is no good treatment if you don’t have a good diagnosis.”

Research collaborators also included Sarah South, PhD, Nancy Augustine, and Thomas Martins, MS, from the University of Utah School of Medicine and the ARUP Institute for Clinical and Experimental Pathology® at ARUP Laboratories, and 26 other scientists from institutions across the U.S. and Europe.

What Is Her Hope?
At 71, Roma Jean Ockler continues giving herself weekly gamma globulin shots, which help boost her immune system with disease-fighting antibodies. The mystery of all those infections fought throughout her life is now solved. Looking back, she wonders if her mother or father carried the genetic mutation; she suspects aunts and uncles may have had it—the ones who were sick a lot.

Mostly, Ockler focuses on now. She’s relieved that there are some answers, thus allowing for earlier intervention for her son and grandchildren who must contend with CVID. And her hope? “One day, and I know it will take a lot more research, I hope they treat the disorder so well that it is like a cure.”
It Must Be in the Cells

Three Generations of Histologists

“She told God, ‘If you get me walking, I’ll never lie down again,’” recalls Gina Anderson of her grandmother, Callie Cooling, whose battle with tuberculosis (TB) of the spine in the 1930s sparked a determination to make the most of her life.

It also ignited a fascination with the body and led her to pursue a career in histology that would ultimately inspire three generations of women—her daughter and three granddaughters—to pursue careers in histology. Gina Anderson, an ARUP histotechnician who works in the Histology Research Core Lab, is one of Callie’s granddaughters.

While in her 20s, Callie spent two years in a sanitorium in Michigan where doctors surgically removed a small bone in her leg and inserted it in her back for spine support. They told her that she would never walk again and advised her not to have any more children. “At night when everyone was asleep, she secretly did her own physical therapy,” says Gina. Callie would practice slowly sitting up to build core strength—first lifting her neck, then her chest, then from the waist up. One day, she told her family she wanted a glass of orange juice; she stood up and slowly walked over to pour one for herself, astounding her whole family. She also went on to have twins.

Callie eventually took a train west to Salt Lake City, laying on a flat board the entire trip, where she took advantage of a government-run education program for those rehabilitating from TB and pursued histology. She was trained by pathologist Dr. William Carnes at the University of Utah Department of Pathology and spent most of her 30-year career at the VA and the University of Utah hospitals. “She was an artist and a scientist at heart; histotechnology was a great fit for her,” says her daughter Margaret Carter (Gina’s mother).

Callie would go on to train dozens of future histotechnicians, including her daughter Margaret, her oldest granddaughter Callie (named after her), and Gina’s first supervisor. “The people she trained were grabbed up quickly, because everyone knew they would be good,” says Margaret, who became the fourth registered histotechnologist in the country in 1970 (at the time, this was a new certification and different from a histotechnician).

Callie would bring home unmarked and un-needed slides and tell her daughter Margaret about them, drawing her into the life of cells, talking about nucleus and cytoplasm and pathogens, and how they would appear beneath a microscope. Such conversations continued as Margaret’s own daughters grew up listening to histology banter when their grandmother would stop by the house.
Gina recalls visiting both her mother’s and grandmother’s labs. “I remember looking out over the valley from my grandmother’s lab at the university. It seems crazy now, but I also remember people eating, drinking, and smoking in the labs,” she says with a laugh.

Gina started at ARUP 19 years ago when she was in the midst of raising her daughters. “It was a good schedule for being a new mom, and ARUP works well with families,” she recalls. Gina started out in the Gross Room, which is the first stop for tissue after it is biopsied in surgery. It is measured, cut, and prepared for the histology process ahead, where it will be transformed into slides. Within six weeks, she had started doing work in the histology side of the lab.

**The Art and Science of Slide Prep**

“No one cuts tissue like Gina. It’s truly an art form,” says Dr. Mary Bronner, co-division chief of Anatomic and Molecular Oncologic Pathology and medical director of Biocomputing. “And every single patient who needs a tissue diagnosis goes through the hands of a histotechnician.”

Gina would agree, noting that her job is about a 60:40 percent art to science ratio. “The art is in the cutting and staining; the stains highlight clues that will tell us if a patient has a certain disease,” explains Gina.

It is the tissue cutting she likes best. “When you first sit down in front of a microtome cutting machine, it looks easy, but it is not,” Gina says, eyeing a tissue sample embedded in a wax cube while methodically turning the arm of the microtome machine. Crepe paper ribbons of wax, which she lays in a warm bath to ease out the crinkles, slip off the machine in front of her. She divides each tissue slice onto a slide. On average, she will slice hundreds of sections of tissue a day.

“I’m always aware of connecting a tissue sample to a patient,” says Gina. “I try to imagine that each biopsy belongs to one of my relatives, because I want it done so well that it will allow the pathologist to make an accurate diagnosis based on my work.”

Gina flips through a dog-eared histology textbook that used to belong to her grandmother, Callie. She stops on several...
What is Histology?

Histology is a science dealing with the structure of cells and their formation into tissues and organs. Histotechnology centers on the detection of tissue abnormalities and the treatment for the diseases causing the abnormalities. Members of a histology lab team are called histotechnicians and histotechnologists; the latter typically performs more complex techniques and can teach or supervise. Because of a histotechnologist’s skillful application of sophisticated laboratory techniques, the seemingly invisible world of tissue structure becomes visible under a microscope.

Source: National Society for Histotechnology
black and white photos of lab equipment. “It was all very manual then. It didn’t allow us to move near as quickly or with as much accuracy as we can now.” Gina recalls how her grandmother used to strop a knife on a swath of leather in her lab to keep it sharp for tissue cutting, noting just one seemingly archaic example of how technologies have advanced her field.

On a less technical note, Gina recalls the bright whites her grandmother Callie and her mother Margaret used to wear to work each day. “They would polish and polish their shoes to an ultra-white sheen,” reminisces Gina. “My mom practically gleamed when she left for work each morning.”

ARUP has two laboratories located in the Huntsman Cancer Institute: the Histology Research Core Lab and the Division of Anatomic Pathology Lab, which includes Surgical Pathology, Autopsy, and Cytopathology. Gina works in the former, where slides are made for clinical trials and research purposes. The other Histology Lab at ARUP is open 24/7 to expedite slide results to thousands of physicians countrywide intent on providing vital treatment for their patients. “Doctors usually want to start seeing slides first thing in the morning,” says Gina. “These labs are always under the gun.”

“Traditionally, research labs are stuck trying to figure out how to provide histologic sections for their research. Here, we have a core facility of experts providing us with high-quality tissues and stains,” says Allie Grossmann, MD, PhD, an ARUP medical director in Anatomic Pathology and Molecular Oncology. “Histology is a skill—even an art—developed over time, and having incredibly proficient people like Gina and her colleagues frees us up to focus on our research.”

Gina’s final step in processing her slides ends at the microscope, where she slips one slide, then another and another underneath the scope. “That’s kidney; this one is large intestine; this one, liver,” she says, showing them off like a proud mother … or artist. The tissues are all paisleys and swirls and ruffles of pink and purple around islands of white. It feels as though you are viewing something from a great distance, like astronauts looking down at the topography of Earth, rather than the microclose topography within the human body. “You see,” says Gina, “There’s never a dull moment in histotechnology.”

“I try to imagine that each biopsy belongs to one of my relatives, because I want it done so well that it will allow the pathologist to make an accurate diagnosis based on my work.”

Gina Anderson, ARUP Histologist
Robert Schlaberg, MD, Dr Med, MPH, pulls up a colorful pie chart on his laptop. “This shows us a very high-level view of what microbes are present in this patient’s sample,” says Schlaberg, who specializes in molecular infectious disease testing at ARUP.

He clicks on a slice of the pie labeled “Viruses” and what look like purple tree rings appear, instantly revealing virus subcategories. Click. Now the “Bacteria” slice of the pie presents a set of orange tree rings.

Behind this interactive display is the processing work of Taxonomer, a new analysis software that sifts and sorts through millions of bits of information representing all known pathogens—those normally in our bodies and those that can make us sick— including viruses, bacteria, fungi, and parasites.

Taxonomer can identify an infection without the physician having to decide what to test for, something a PCR-based test cannot do. In other words, a doctor doesn’t have to suspect the cause of a patient’s infection, but can instead simply ask, “What does my patient have?” and Taxonomer will identify the pathogens. This means the patient is diagnosed more quickly, likely decreasing testing and hospitalization costs.

Taxonomer is an ultra-fast, metagenomic analysis software tool, meaning it can mine information from the vast amounts of genomic information extracted from
microbial DNA. This DNA is found in the pathogens located in a patient specimen (i.e., blood, saliva). The amount of data that Taxonomer is extracting information from is immense; it must sift through millions of DNA sequences (fragments) to hunt for any known pathogen DNA.

To understand the enormity of this information, imagine finding the novel Moby Dick shredded, then being given the task of locating the third letter in the 10th word, in the 23rd paragraph, in the 15th chapter. Now, find the equivalent letter in every other chapter. Now, patch together each letter and see if it forms a word—an identifiable known pathogen.

“While light microscopes allowed us to see what constitutes the blood and eventually what causes infections, Taxonomer is like a genomic microscope, allowing us a very detailed view of the processes going on in infected tissue,” says Schlaberg. The software’s analysis provides vital clues for detecting and treating infectious diseases.

Infectious diseases are one of the biggest killers in the world. Almost 2 million children under age 5 die each year from infectious diseases worldwide, yet many infections are treatable if the pathogen culprit can be quickly and accurately identified.

Take community-acquired pneumonia, for example. As one of the most common infections, it hospitalizes thousands annually, but no discernible responsible pathogen is identified in 20 percent of children and 60 percent of adults with pneumonia, according to findings published by Schlaberg’s collaborators in the New England Journal of Medicine last year.

“Taxonomer can identify an infection without the physician having to decide what to test for. In other words, a doctor doesn’t have to suspect the cause of a patient’s infection, but can instead simply ask, ‘What does my patient have?’”

Robert Schlaberg, MD, Dr Med, MPH
Medical Director, ARUP Laboratories
“This technology can be applied whenever we don’t know the cause of the disease, including when there are sudden outbreaks,” says medical epidemiologist Seema Jain, MD, with the Centers for Disease Control and Prevention. “We urgently need more accurate diagnostics to greatly enhance the ability of public health response and clinical care.”

“Not only can you interrogate a sample without knowing what you are looking for, but you can study the relationship of pathogens,” explains Andrew Pavia, chief of the Division of Pediatric Infectious Diseases at the University of Utah. “This can be helpful for hospital outbreaks in which the origin of infection might be an IV or specific drug. We’re able to fingerprint the organisms, which can help show that the pathogens came from a single source.”

“In the realm of infectious diseases, this type of technology could be as significant as sequencing the human genome,” says Taxonomer co-developer Mark Yandell, PhD, a professor of human genetics at the University of Utah and co-director of the USTAR Center for Genetic Discovery. “Very few people have inherited genetic disease. At some point, everyone gets sick from infections.”

The combination of speed, accuracy, and ease of use are Taxonomer’s stand-out characteristics against the backdrop of this rapidly evolving area of metagenomic technology. After a patient’s sample is sequenced, the data is uploaded via the internet to Taxonomer. In less than one minute, the tool displays a thumbnail inventory of all pathogens in the sample, including viruses, bacteria, and fungi.

“It’s tens to hundreds of times faster than similarly accurate tools,” adds Schlaberg. He points out that current diagnostic testing still relies heavily on growing pathogens in the laboratory, which may not provide accurate results and can be time consuming. While advanced PCR-based tests are much faster, they are only available for a limited number of pathogens. PCR stands for polymerase chain reaction, a method used to amplify sections of DNA for analysis.

While similar “catch-all” tests have been used in the past to study infectious disease outbreaks, the data analysis was not suitable for use in a diagnostic laboratory. Analyzing millions of DNA sequences took days or weeks; results were often difficult to interpret or not sufficiently accurate.

Taxonomer technology is currently being applied to developing universal pathogen-detection tests at ARUP Laboratories and by the start-up IDbyDNA based in Silicon Valley and Salt Lake City; the first ARUP test using this technology will go live this year.

Genes Have Expressions Too
Another unique feature of Taxonomer is its ability to analyze the patient’s own genetic material, in this case mRNA that shows which genes are turned on, providing information on how or whether the patient’s body is reacting to an infection. “As a clinician, this gives you a better idea, when we identify a pathogen, whether it is really the cause of the disease,” says Carrie L. Byington, MD, professor of pediatrics of the University of Utah and co-director of the Center for Clinical and Translational Science. Finding an infectious pathogen does not always mean that it causes...
As a clinician, this gives you a better idea, when we identify a pathogen, whether it is really the cause of the disease ... Seeing how a patient reacts is extremely valuable; I believe this is a paradigm shift in how we diagnose people. It is why I wanted to be involved.

Carrie L. Byington, MD, Co-Director, Center for Clinical and Translational Science, University of Utah

Sometimes discovering the absence of a pathogen is critical information. Consider the case of a transplant patient whose body may appear to be fighting an infection. Should the doctor prescribe a high dose of antibiotics, which could put the patient at risk for other types of infection if "good" bacteria are killed off, or should the doctor refrain from antibiotics and risk the patient developing sepsis, which can be deadly? Taxonomer’s pathogen-detection capabilities could reveal that there are actually no infection-causing pathogens present; the body sometimes mimics infection-like symptoms.

According to Schlaberg, the possibilities with Taxonomer extend beyond diagnostics. The tool has already uncovered a previously unknown virus from one patient sample. There’s likely much more where that came from, meaning Taxonomer could accelerate discovery of never-before documented causes of illness, including emerging infectious diseases set off by rapidly evolving pathogens that seed new outbreaks.

"We don’t know the diversity that exists within those pathogenic organisms, within a given species, but we’re generating that information very quickly now," adds Schlaberg, pointing out that the genomes of viruses and bacteria are much smaller than the genome of humans, so it is more feasible and faster to generate and analyze this data.

Such information could set forth new diagnostic tests, preventions, and treatments. "The implications for discovery are what makes this so exciting," says Yandell. "The potential is huge."
Most of these deaths are preventable; it’s a tragedy. To prevent them, you first need to know what is causing the disease. With this technology, we have the methods to make a huge difference.

Robert Schlaberg, MD, Dr Med, MPH
Medical Director, ARUP Laboratories
In May, ARUP Medical Director Robert Schlaberg, MD, Dr Med, MPH, was one of 43 individuals globally to receive a prestigious grant from the Bill and Melinda Gates Foundation for a project to help decrease the high mortality rate of children with infectious diseases in resource-limited settings.

The $100,000 grant is part of the foundation's Grand Challenges Explorations, which fosters innovation to solve global health and development problems. More than 1,400 applications were received.

His proposal, titled *Universal Pathogen Detection in Post Mortem Tissues*, will use universal pathogen detection based on next-generation DNA sequencing to identify fatal infections. Using RNA sequencing and Taxonomer, a new analysis tool co-developed by Schlaberg, scientists will be able to identify the cause of death by detecting all known pathogens, including viruses, bacteria, fungi, and parasites, in postmortem tissues. Scientists will also differentiate infectious from noninfectious causes of death by immune profiling.

"The diagnostic tests that pick up on what is causing the child's infection are often lacking, and children may not be seen by a healthcare provider in time," says Schlaberg, who notes that some 2 million children under age 5 die each year from infectious diseases. Most of the fatalities stem from different types of pneumonia and diarrhea-causing infections, but hepatitis, meningitis/encephalitis, and sepsis are also culprits.

Schlaberg's findings could ultimately help plan vaccine and prevention efforts and provide recommendations on treatments. "While we know the cause of many severe infections, such as malaria, in resource-limited settings, things become much more difficult when routine treatments for these common causes fail," explains Schlaberg, pointing out that doctors may cast a wide net and base guesses on the most common known causes, which often happens with pneumonia. "Knowing the less common or unexpected causes will help design better preventative measures and treatment programs," explains Schlaberg, who is also an assistant professor of clinical pathology at the University of Utah School of Medicine.
The Wow Factor

Since 1984, ARUP has worked quietly behind the scenes to support patient care—so quietly, in fact, that people don’t realize the extensive role ARUP plays in diagnostic medicine. So we’ve decided to speak up and share some extraordinary facts with you.

More than 50 percent of the nation’s university medical centers, pediatric hospitals, and teaching hospitals choose to send their testing to ARUP.

To propel research, **12 open-source databases**, all focused on inherited diseases, are provided free to the public through ARUP’s educational website. The most visited is the *BRCA1* and *BRCA2* database—the two genes identified and linked to hereditary breast cancer.

ARUP has averaged more than **208 new tests** over the last three years while further honing the precision of hundreds of existing tests.
As one of the most automated laboratories in the United States, ARUP’s track system zips specimen-filled pucks along at up to two meters per second. Sixty mini motors are in every meter of the track, and the system also includes ten high-speed sorters and seven pick-and-place binders, all built in house.

More than 90 ARUP medical experts help our clients understand test results, expediting vital treatment for patients. These experts are faculty at the University of Utah School of Medicine, and many participate in care teams at the Huntsman Cancer Hospital and Primary Children’s Hospital.

ARUP is home to more than 60 individual labs specializing in all aspects of clinical and anatomical pathology.

In a six-month period, ARUP identified more than $200,000 of duplicate genetic testing for all clients combined. Catching these unnecessary tests saved patients money.
It woke me up in the middle of the night.

It left me gasping and sobbing. Screaming.

Someone was sticking a knife in me and slowly turning it.

Kidney Stones
Very Scary True Stories and Entombed Mysteries.
Is this a nightmare? PTSD from an especially contentious election year? Or are they descriptions of the pain involved in passing a kidney stone? “It’s like giving birth to a watermelon,” expressed one man, sheepishly admitting he had never passed an 8 lb. baby. One in eleven Americans will experience kidney stones at least once in their lifetime, and if preventative measures aren’t taken, at least half of those will have another episode within ten years.

Kidney stones form when certain chemicals become concentrated enough in the urine to create crystals. These crystals grow into larger masses (stones), which can make their way through the urinary tract. “It is when they grow larger, get stuck, and cause obstruction that they begin causing pain,” says Blake Hamilton, MD, a University of Utah urologist.

Stones develop when calcium combines with either oxalate or phosphorous; they can also form from uric acid, which is produced as the body metabolizes animal protein.

Food That Helps Stones Grow
“There are a lot of myths about what causes or prevents kidney stones, but what is good for one person may have no benefit in another,” adds Hamilton. “If you want to make changes, you have to know what changes will be helpful, especially when it has become a recurring problem.” Typically, urologists will analyze the chemical concentrations in their patients’ urine to determine specific causes.

Stones can be caused by a variety of conditions, including diet, poor hydration, infections, medications, and genetic disorders (e.g., cystinuria and hyperoxaluria). “Some people just excrete more calcium into their urine, and it crystalizes,” adds Hamilton.

For those prone to stones, staying well hydrated—particularly in the summer when the formation of stones is more likely—can decrease incidences. While caffeine, sodas, and alcohol all contribute to dehydration, there are conflicting studies on whether they really cause stones. But

The five-year recurrence rate is reported to be as high as 50 percent after the first episode.

50%

Medical providers order testing to determine the chemical composition of the patient’s stone. Knowing the components of the stone helps guide treatment to decrease the likelihood of stones forming again and allows providers to educate their patients on factors that may be contributing to the stones.

Elizabeth Frank, PhD, DABCC, ARUP Medical Director
all agree water is best, though the citrate in some citrus beverages, like lemonade and orange juice, can help block stone formation. Drinking two and a half liters of fluid daily is recommended for those susceptible to stones.

Foods rich in oxalate, such as spinach, berries, nuts, quinoa, beets, black teas, and chocolate (the darker the more oxalate), can contribute to stone formation. Eating too much animal protein, such as red meat, poultry, eggs, and seafood, boosts the level of uric acid and could lead to kidney stones. A high-protein diet also reduces urinary citrate, a component that helps prevent stones from forming.

A Descent into Utah’s Miniature Stone Quarry

ARUP was one of the first reference laboratories in the country to start offering stone analysis, just a year after the young start-up began in 1984. And for the last 25 years, those in the Calculi and Manual Chemistry section have collected the most unusual of kidney, bladder, and gallbladder stones sent for analysis. In this collection, known as the “Stone Quarry,” some stones defy logic, some sparkle, and some weigh a pound. Others have stories buried within them, like the pearl or the rhinestones each entombed in a kidney stone. Another contains a bullet.

Teri Wojcik, a recently retired senior medical technologist and the collection’s unofficial muse, has educated and entertained people over the last 20 years about kidneys, calculi, and the hands-on process and technology involved in stone analysis. The resulting information helps physicians determine the cause and best treatments for the stones.

Wojcik pulls out a delicate transparent box, seemingly arranged with perfect, mini seashells: a snail, a spiny sea urchin, a spiraling conch—all from the body, not the sea. These are a mix of kidney and bladder stones, a few from dogs submitted when ARUP had an animal reference pathology lab.

Another container harbors a bent suture needle, stitching threads, staples—all items found in stones and left in the body from some previous operation. “The body being the wonderful thing that it is coats those things with either protein or calcium phosphate to help them travel more smoothly as they journey through,” says an upbeat Wojcik.

**WARNING: ROCKY ROAD AHEAD**

Tests for Avoiding Stones

When a stone is not available for analysis or if patients want to know if they are at risk of forming stones, three ARUP-designed urinary analysis panels are available to help assess and monitor the likelihood of stone formation. This is also a preventative approach when a patient is known to be at higher risk due to family history.

Each panel includes measurement of the concentrations of certain compounds in the urine (i.e., calcium, oxalate, uric acid, citrate, etc.) that promote or inhibit stone formation. The largest of the three panels, Urine Supersaturation Profile, tests for more than a dozen components. “After measuring the panel components, we use the results to calculate risk for particular types of stones,” explains Golden Welch, ARUP clinical product manager. The varying degrees of risk are presented in a colorful bar graph showing the range of risk for each stone type. “This relative risk is communicated in an enhanced report we provide with the purpose of making it easy for the medical provider to read and, in turn, share the information with the patient.”

A smaller panel assesses stone risk but does not include risk calculations, and the smallest panel, the Kidney Stone Risk Panel, can be used to monitor patients with the more common calcium oxalate and uric acid stones. This targeted approach saves the patient money (the larger panels cost more), maximizes efficiency, and avoids unnecessary testing.

**$5.3B**

Incidence of this disease is rising and estimated to cost $5.3 billion per year in healthcare dollars.
There’s the “gravel in the urine” stones made of uric acid, often caused by gout; the “stag horns” and “coral” stones (kidney stones); and the “river rocks” (bladder stones), smoothed by the ebb and flow of “water” in the bladder.

As Wojcik holds up different stones, Marlene Thaitumu, senior technologist specialist, identifies what comprises each one: “Uric acid, calcium oxalate, calcium phosphate, magnesium ammonium phosphate.” A crystalline gallstone is composed of “pure cholesterol.”

“A two millimeter stone is tiny, but passing a stone that size is still painful to the individual,” says Thaitumu. “Anything larger than 8 millimeters usually needs surgery or lithotripsy.” An alternative to surgery, lithotripsy uses shock waves to break down stones into smaller fragments that can be passed through the body.

When stones arrive in the lab, they are first analyzed externally for shape, color, size, then weighed and cut in half to reveal the core; this center is the genesis of what led to stone formation (i.e., calcium, oxalate, uric acid). The stone is then ground using the Stone Crusher, developed by ARUP’s bioengineers, and finally subjected to FTIR—Fourier transform infrared spectroscopy—a technique that analyzes the composition.

“Determination of chemical composition is the main reason medical providers order stone testing,” explains Elizabeth Frank, PhD, medical director of ARUP’s Calculi and Manual Chemistry Lab. “Knowing what is present in the stone can help determine the best treatment to decrease the likelihood of stones forming again and helps providers educate their patients on how their diet and lifestyle may be contributing to the stones.” When a doctor expressed how impactful it would be to show his patient the stone, Frank’s lab added a test that includes a photo in the report and is one of only a few labs to do so.

Surgery to remove stones is a last resort; most people don’t require surgery. “It really depends on the size of the stone, the patient’s pain level, and if the obstruction could cause damage,” explains urologist Hamilton. “We usually give people a chance to pass them, which could range from two days to two months.” Proof that even nightmares—and elections—come to an end.

In ARUP’s Stone Quarry, some stones defy logic, some sparkle, and some weigh a pound. Others have stories buried within them, like the pearl or the rhinestones each entombed in a kidney stone. Another contains a bullet.

11% Approximately 11 percent of adults in the United States will develop kidney stones in their lifetime. These rates double in patients with a family history.

3Xs Men are two to three times more likely than women to experience kidney stones.
Advancing Precision Medicine through Pharmacogenetics
Test Prevents Adverse Drug Reactions
Her patient was suffering from severe depression, and despite prescribing an anti-depressant, University of Utah psychiatrist Anne Lin, MD, was not seeing any improvements. She switched the patient over to several other types of anti-depressants, but the depression didn’t budge. Further aggravating the patient’s wellbeing were side effects, including insomnia and nausea.

Lin ordered a gene panel test to gain insight into how her patient's body reacted to certain drug categories, in this case anti-depressants. She found that her patient was a poor metabolizer of an enzyme (CYP2D6) integral to metabolizing anti-depressant drugs. Her patient also had a mutation on her MTHFR gene, which plays a key role in the body's chemistry. (MTHFR activates folate, which is used to make various proteins required for physiological health; the inability to activate folate adversely affects production of neurotransmitters in the brain).

Such genetic tests, like ARUP’s updated Cytochrome P450 Genotype Panel test (CYP), offer care providers with information key to personalizing therapy for their patients. According to the Centers for Disease Control and Prevention, adverse drug reactions cause more than 700,000 ER visits each year, with some 120,000 patients needing to be hospitalized for further treatment. When not metabolized properly, drugs can be lethal or completely ineffective.

Pharmacogenetic tests are proving especially helpful for patients within the psychiatric and elderly populations, who may be on multiple medications, as well as for treating children, who often have no personal history with medications.

Many children’s hospitals test all their young patients undergoing a tonsillectomy or adenoidectomy for CYP2D6 variants before surgery. (The CYP2D6 enzyme is involved in the metabolism and activation of certain drugs.) These relatively common procedures have resulted in deaths across the United States because some children who received codeine post-surgery as a pain reliever were genetically ultra-rapid metabolizers of codeine, which resulted in fatal amounts of morphine being produced by their bodies. CYP2D6 catalyzes the activation of codeine by converting it to morphine. The body’s inherited ability to convert codeine to morphine by CYP2D6 can be determined with a genetic test before the drug is administered.

Addressing elderly patient populations, a recent observational study conducted in part by the University of Utah’s College of Pharmacy and Program in Personalized Health Care, focused on people who were over 65 and taking at least three different medications. For those who received guidance based on the results of their genetic drug test, clinic and emergency room visits declined significantly.

Adverse drug reactions cause more than 700,000 ER visits each year, with some 120,000 patients needing to be hospitalized for further treatment. When not metabolized properly, drugs can be lethal or completely ineffective.

Centers for Disease Control and Prevention

As a psychiatrist who specializes in working with children and adolescents, Dr. Anne Lin has used genetic drug tests to help determine the most effective medications for her clients.
“Considering that in just over four months we were already seeing cost savings suggests that such testing certainly makes sense in elderly patients who are taking multiple drugs,” says Joseph E. Biskupiak, PhD, MBA, director of the University of Utah’s Pharmacotherapy Outcomes Research Center (PORC).

ARUP’s Genetic Test Focuses on Four Genes
For more than 15 years, ARUP has been providing CYP2D6 genotyping and other pharmacogenetic tests, currently more than 30, which are continually improved to reflect new scientific and medical findings. The most updated CYP test (Cytochrome P450 Genotype Panel) includes a comprehensive medication-recommendation report. The report also includes access to GeneDose LIVE, an interactive (real-time) risk-management tool offered through Coriell Life Sciences (CLS). While blood specimens are the most common specimen for genetic tests, this test can also be done using saliva, which is often preferred by patients (no needles!) and doesn’t require a phlebotomist.

The panel test focuses on four genes that predict drug-metabolizing enzyme activity for many commonly administered drugs. “I chose them based on the range of gene-based dosing guidelines published for these four genes and commonly prescribed drugs, many of which involve more than one gene,” says Gwen McMillin, PhD, a medical director of Toxicology and Pharmacogenetics at ARUP.

Test results inform physicians as to whether a patient will metabolize certain drugs quickly or slowly, providing a guide to selecting certain drugs and dosages tailored to that patient and preventing adverse reactions, including therapeutic failure.

CLS has the technology to interpret the results ARUP’s genetic test provides and to produce an easy-to-view, comprehensive report that lists medications that are standard, low-risk, or high-risk for a specific patient. “We’re increasingly focused on providing our clients with a deep, information-rich context for the test results they receive,” says Brian Jackson, MD, MS VP, chief informatics officer. “This knowledge allows clinicians quick access to comprehensive information, including references to evidence-based research, to guide them in patient care.”

Metabolizing Drugs: Is Everyone Different?
All patients who require drug therapy could potentially benefit from this personalized approach to drug and dose selection. The medication-recommendation report is particularly relevant to drugs used in treating pain and psychiatric conditions, but many classes of medications are represented in the report. GeneDose LIVE allows for further personalization of therapy by including co-medications, lifestyle factors, and clinical factors that could contribute to risk of adverse events.

“Everyone’s metabolism is unique. This test will help identify those people who are at increased risk for therapeutic failure or toxicity from certain drugs.”

Gwen McMillin, PhD, ARUP Medical Director of Toxicology and Pharmacogenetics

Gwen McMillin, PhD, developed a test panel that focuses on four genes that predict drug-metabolizing enzyme activity for many commonly administered drugs. McMillin oversees the Toxicology Laboratory and Pharmacogenetics at ARUP.
The recommendations provided by the CYP panel report are based on well-vetted guidelines, including those published by the Clinical Pharmacogenetics Implementation Consortium, for gene-based drug and dose selection.

"Drugs may be activated or inactivated by metabolism. There may be multiple routes of metabolism, involving several enzymes," explains McMillin. Drug metabolism is also influenced by non-genetic factors, including drug-to-drug interactions, food-drug interactions, kidney and liver function, age, and body size. "Everyone's metabolism is unique. This test will help identify those people who are at increased risk for therapeutic failure or toxicity from certain drugs," adds McMillin.

In poor metabolizers, a drug that is inactivated by metabolism can build up to potentially toxic concentrations of active drug in the blood, as is the case with many antidepressants. A drug that is activated by the affected enzyme may not work at all in a poor metabolizer because the drug would not be activated as expected. Generally, accumulation of an active drug suggests dose-related toxicity, while accumulation of an inactive drug suggests therapeutic failure. Based on the results, a doctor may want to select an alternate drug or adjust the dosage.

Intermediate metabolizers have impaired metabolism with specific drugs, which may or may not impact drug and dose selection. In a rapid or ultra-rapid metabolizer, a drug can be metabolized too fast, leading to higher than expected blood concentrations of an active drug that could become toxic. A drug inactivated by the affected enzyme may not work at all if it's metabolized too quickly. As with poor metabolizers, such cases of extreme metabolic activity may prompt a doctor to select an alternate drug or adjust the dose.

The results of pharmacogenetic tests reinforce the fact that everybody is different and treatments need to be individualized to be most effective. The CYP panel is one example of how precision diagnostics are sharpening the "precision" in personalized medicine.

The test results for Lin's patient, who was suffering from depression, prompted her to prescribe an antidepressant that was not metabolized through the CYPD26 enzyme. She also gave her a supplement, l-methylfolate, to provide her body with activated folate to help with the depression.

"These tests really help me figure out which medications we have to use and at what doses, especially for my hard-to-treat patients," says Lin, who often refers back to these lab reports when major medication changes are required.

And the patient? Lin says, "She is much better, closer to her old self and functioning well on less medication."
Diagnostic testing isn’t the only service ARUP provides worldwide; for the last three years, it has built a growing educational resource specifically designed for students in the medical laboratory sciences. It’s free, quickly digested by the brain (short and simple), and uses technology accessible on any visual platform.

Faculty and students in medical laboratory science (MLS) programs are using ARUP’s MLS Student Resource Center, which is a segment of ARUP’s Institute for Learning (IFL). More than half of the site’s visits last year came from an international audience. Unlike other educational outreach through IFL, this center is designed primarily for beginners, focusing on the basics.

“Walk the Talk”

The online center includes a series of short (three to six minute) how-to videos showing a variety of procedures, such as how to perform an Acetest, make a blood smear, or what a bone marrow biopsy entails. Although demonstrations may be done in class, the video provides an unobstructed view of the procedure. “Everyone gets a front-row seat,” quips McRae, pointing out that all ARUP-produced videos meet high standards of accuracy, standing out from other videos on the internet dealing with these topics.

University of Utah Department of Pathology Professor Karen Brown, MS, MLS (ASCP), regularly uses the bone marrow video in her clinical hematology laboratory class, since it is not something easily accessible to demonstrate. “In the past, I’ve shown some photos in PowerPoint presentations, but it doesn’t capture the procedure as well.”

She advises her students to view the “how-to” videos in between labs or prior to a test. “These videos are short, right-to-the-point, quick refreshers on technique for students,” says Brown, whose feedback has been instrumental in helping ARUP create useful videos.

“There was a blood bank lecture I wasn’t quite sure I understood during the real-time lecture, so I went back and listened to the parts that were unclear and also to the parts that reiterated the things that I didn’t catch in class,” says Sue Cummings, an MLS student and a senior technologist in the Cellular and Innate Immunology Lab. “It’s great to have this as a second resource.”

The site also provides more in-depth topics—video lectures presented by experts on topics ranging from the role of the clinical laboratory in pain management to the history of syphilis, invention of penicillin, and research on vulnerable populations; the topics include laboratory tests and clinical algorithms for diagnosing.
Professors might assign these videos as homework or extra credit to reinforce what they are teaching in class and/or to enrich their students’ learning experiences. Some videos provide an exciting trajectory of what newcomers to the field can look forward to learning and doing with their MLS degree.

“We collaborate with faculty to create the content they need, often targeting what students have a hard time grasping or remembering,” says McRae, who has a master’s degree in biomedical laboratory science with an emphasis in instructional technology. The site provides material ideal for a flipped classroom experience, where the students will watch a video and then go to class more prepared to discuss and/or participate in a related activity.

“[MLS] programs are always looking for inexpensive and quality ways to enhance education,” says MLS Professor Brown. “And this online resource fits that criteria.”

Many of the longer videos involve ARUP’s own medical directors, all faculty in the University of Utah’s Department of Pathology. Other experienced professionals provide insight into areas such as finance, human resources, and customer service in the center’s management and professionalism video series. “It’s about teaching students how to be the leaders of tomorrow in this field,” adds McRae.

Keeping the perspective of the student and teachers in mind, material is designed to meet multiple learning styles, so varied visual and auditory elements are incorporated, including the use of different voices, colorful animation, and graphics.

MLS student Jeff Clifford agrees. “I had my professor’s version of how to do a blood smear but it’s nice to see other professionals doing it and explaining how they do it and why it works.” Clifford is a technologist in ARUP’s Microbial Amplified Detection Lab.

“In creating our content, we are focused on how people learn best. What can we do to help this learning curve? What can we do to help students retain info? Recall it? Find it?” says McRae. “All this, plus keeping people up-to-date in a fast-moving field.”

Karen McRae, MS, MT(ASCP)
Education Coordinator, IFL

Karen McRae, ARUP education coordinator, depends on input from faculty like Karen Brown, a pathology professor, to ensure a well-vetted, academic resource for students.
Advancing Education
with ARUP’s Tuition Reimbursement Program

Terms such as return-on-investment, portfolio, appreciation, and equity are all associated with investments of one sort or another—stocks, bonds, CDs. *Things.* For more than 20 years, ARUP has invested in *people,* speculating that the payoff, both personally for the individual and for the company, is worth it.

Through the tuition reimbursement program, ARUP has contributed millions of dollars to the education of employees and their family members. Over the last four years, more than 500 people have taken advantage of this benefit annually.

“The amount of tuition reimbursement has fluctuated over the years as the number of employees has increased and changes have been made to the benefit” says James McVey, supervisor of Education. “Last year, we provided more than $930,000; this amount has been fairly consistent.” Employees can be reimbursed up to $2,000/year, or a lifetime total of $8,000 for classes.

One hundred percent reimbursement is provided for those employees pursuing medical laboratory science (MLS) or medical laboratory technician (MLT) degrees. Qualifying participants must have worked at ARUP for six months and agree to stay for at least two years once they have completed the degree (or pay back the cost of the tuition).

“I have to admit, it was an amazing feeling to graduate from college debt free,” says Ashley Morris, a medical technologist in the Genomics Lab who graduated this spring from the University of Utah’s MLS program. “For the most part, I think people here really want to see you be successful and get more education.”

“It’s a strong incentive,” adds Eleri Paul, who took advantage of the tuition program to complete her MLS degree this spring at the University of Utah as well. She advises participants to be aware of at what point tuition reimbursement is taxed by the government. “I’ll definitely be going back for more education eventually and when I do, I’ll be using ARUP’s tuition reimbursement program,” adds Paul.

“Investing in the education of our employees creates an atmosphere where employees want to continue to learn and grow,” says McVey. “Plus, it plays into our mission to continually improve patient care; we know that an educated workforce improves processes and the work being done on behalf of patients.”

Employees outside the labs are also taking advantage of the tuition reimbursement. Hollie Banks, an education event coordinator and a single mother, is earning her bachelor’s degree. “They really walk the talk here; education is part of the mission, and I’m just one example of that mission in action.”
Build It and They Will Come

Joint Test Directory Strengthens Test Ordering & Business

“We were absolutely buried in phone calls,” recalls Jason Anderson, marketing and sales director for Intermountain Laboratory Services, part of the Intermountain Healthcare system. “A few years ago, our client service reps were constantly fielding questions about specimen requirements and other basic information.” Anderson estimates that the incoming phone calls have now decreased by 15 percent and continue to decline each month.

What was the catalyst for this change? Anderson attributed it to their new Gateway™ website. This web-based, joint test directory allows ARUP clients to house all their laboratory test information—whether that testing is performed in house or sent out to other laboratories—in one centralized online location.

ARUP hosts Gateway and provides clients with the infrastructure to customize the site to their needs. Client administrators can add, edit, or delete a test; insert images to help convey information and avoid errors (i.e., a test tube with a red cap versus a green one); and incorporate sidebar menu items on their launch page linking users to specific topics such as specimen-collection guidelines, general forms, and industry updates.

As of last December, ARUP Gateway surpassed 4 million views. “We attribute this growth to the value clients find in Gateway and to our account executives who are connecting our clients with it,” says Julie Turner, Gateway product manager.

Intermountain’s Gateway site alone receives upwards of 50,000 hits a month. “It has really educated our clients about what we offer in terms of lab testing as well as other services,” says Anderson. In addition to providing test information, Intermountain uses the site as a way to alert Gateway users about news and developments at Intermountain, as well as educational opportunities within the laboratory industry.

Apart from a small icon at the bottom of the screen that reads “powered by ARUP Gateway,” the test directory identically matches the branding of the client’s main website. “It’s convenient to have control over the look and

“It’s very convenient to have control over the look and feel of the site; we can make updates to it in conjunction with changes to the main website and branding.”

Jason Anderson, Marketing and Sales Director, Intermountain Laboratory Services
We attribute this growth (4 million plus views) to the value clients find in Gateway and to our account executives who are connecting our clients with it.

Julie Turner, ARUP Gateway Product Manager

Gateway, ARUP’s web-based joint test directory for clients, nearly doubled its number of users last year, surpassing four million client views. The hard work of the LTD/Gateway Development team and the effort of ARUP account executives is helping drive its popularity among clients.

Wahl points out how Strong Memorial Hospital leadership supported the creation of a test-tier system on Gateway to guide test-ordering patterns, resulting in significant institutional savings. She explains that tier 1 tests have no ordering restrictions, tier 2 tests are restricted to board-certified subspecialists, and tier 3 tests are restricted and require review and authorization.

“[Gateway] guides people toward proper ordering ultimately resulting in better patient care,” says Turner, adding that all clients who purchase Gateway services receive training on how to customize and manage the site and are provided ongoing technical support.

“Using Gateway to implement our tier levels has been key in the success of our program, ensuring the right test is ordered with appropriate clinical utility while also controlling costs,” says Vicki VanDeWalle, a process improvement and projects manager at University of Rochester’s Strong Memorial Hospital. “Gateway has made it easy.”

Tailoring Improvements Based on Client Feedback

Client feedback informs ARUP how to continuously improve the product. When Intermountain said it needed a more efficient way to export the URLs of individual test pages from within the test directory—wanting to make it more accessible and avoid the tedium of copying and pasting—ARUP responded by including URLs as one of the fields in the test report export.

The test directory has attracted new clients and interested parties to Intermountain. “We didn’t expect this,” says Anderson. Gateway’s mobile functionality is also a big boost for the Intermountain sales team, who can conveniently display Intermountain’s test directory to potential and current clients on their mobile devices.

Intermountain Healthcare is one of 135 organizations using Gateway. “For us, Gateway has made huge differences both internally and externally,” says Jessica Wahl, outreach lab services account manager and analyst at Strong Memorial Hospital, who finds using and updating the Gateway site to be easy and user friendly. It was up to nearly 15,000 views in January 2016. “We used to have a test index that wasn’t reliable, but now we have this awesome tool,” adds Wahl.

Feel of the site; we can make updates to it in conjunction with changes to the main website and branding,” says Anderson.

Left to right: Adam Harmon, Developer; Janice Banks, Business Analyst; Julie Turner, Product Manager; Rielly Maxfield, Developer; Debra Wright, SQA; Michael Bode, Scrum Master.

Jason Anderson, marketing and sales director for Intermountain Laboratory Services, part of Intermountain Healthcare, says Gateway’s mobile functionality provides a big boost for the Intermountain sales team, who can display Intermountain’s test directory to potential and current clients conveniently on their mobile devices.
Your Experts
A–Z

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