



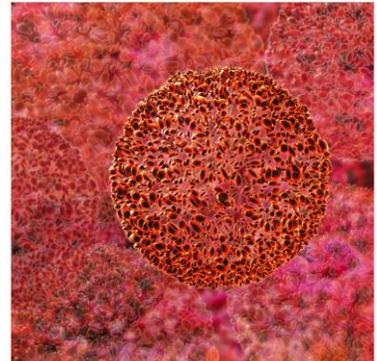
Dear Friends,

Last month we reported on promising research being conducted on a new drug that will target Progressive MS. The Australian scientists doing the research are using blood samples from ACP's Repository. In this issue, we review the history of how this important resource was created over a decade ago, and the ways in which it is being distributed around the world today. If you are one of the original participants who donated blood, we think you'll find these accounts gratifying. And if you were not, but you now wish to accelerate the pace of research, we hope you'll visit www.iConquerMS.org and register to contribute data and samples, intelligence and ideas to influence research on MS topics you care about. Currently numbering 2900 people, iConquerMS™ is led by a majority of patients and provides a structure and framework for people with MS to participate in research from design to dissemination.

Whatever Happened to that Blood I Donated . . . or How the ACP Repository Was Built

By Katina Leodas

About a month ago, we had lunch with a man we were recruiting to join the ACP Board. He mentioned that soon after he was diagnosed with MS in 2006, he donated blood to the ACP Repository. He asked how his blood donation was “converted” into usable biosamples and how many samples were created from the multiple tubes of blood he gave that day. The answer, provided by our CEO Robert McBurney, was detailed and interesting (particularly to those of us not familiar with research laboratory procedures) so we decided to capture the conversation and share it with you.



In telling the story of how the Repository was built, Robert highlighted the important role played by the Study Coordinators, a group of skilled professionals employed in the clinics where samples were collected. This information led us to Jan Weaver, Study Coordinator at UMass Medical Center in Worcester, Massachusetts, a “soldier” on the front lines during those exciting years of building the Repository. We have woven our separate conversation with Jan into this account as well.

Leodas: When and how was the Repository created?

McBurney: In 2006, after running an initial 6-month pilot, ACP sought and received IRB approval¹ and contracted with 10 leading MS clinics around the United States to gather blood samples from people with MS. Key to the success of this effort was ACP's decision to fund a Study Coordinator – a paid professional -- at each site, whose role was to spread the word about the opportunity to participate in MS research and to recruit people to donate blood and assist them in filling out a lengthy questionnaire. The answers to the questionnaires constituted an enormous trove of data that, like the biosamples, is still being used today. For example, at UMass Medical Center in Worcester, Massachusetts, Jan Weaver worked with the clinic's doctors to enroll over 700 people as Repository participants!

Leodas: How did the enrollment process actually work?

McBurney: When a person with MS came into the clinic to see their neurologist, either the doctor or the Study Coordinator told them about the opportunity to participate in the creation of a Repository.

Jan Weaver: I am a scientist who started out working in laboratories and then developed an interest in clinical work because it combined my love of science with my interest in people. I had been employed as a Research Coordinator in the Neurology Department at UMass Medical Center for about a year when ACP approached us about working together to build a new Repository. I loved the idea and so set about making it as easy as possible for people to donate blood.

Each week I looked ahead in the schedule of appointments to see which patients were coming in to see their neurologists in 2 or 3 weeks. I then called those individuals, told them about the opportunity to participate and, if they were interested, I sent them the 38-page questionnaire. That way, they had plenty of time to complete it. Sending the document in advance dramatically increased the likelihood that patients arrived with the form completed and, in instances where they didn't, I sat down with them on the day of their visit and helped them finish it. In addition to the patient provided information, there is also a critical section of the Case Report that is filled out by the neurologist, so I would corral their doctor while the patient was in the clinic to ensure that the clinical information section was fully filled in. In this way, I ensured that the people who provided blood samples to the Repository also completed 100% of the questions on the Case Report Form.

Leodas: What motivated you to do the work in this way?

Weaver: Well, in the process of helping people with MS fill out these lengthy forms, I wound up making friends and learning a lot about them. I was humbled by the people I met at that clinic; inspired by their resilience, courage and great spirit. The work became much more than a job but rather a mission to help people with MS. I miss them!

McBurney: While the clinics were integrally involved in building the Repository, the resource that was created – a collection of samples and data that was unprecedented at the time – has been stewarded

¹ An institutional review board (IRB) is a type of committee used in research in the United States that has been formally designated to approve, monitor, and review biomedical and behavioral research involving humans. The purpose of the IRB is to assure that appropriate steps are taken to protect the rights and welfare of humans participating as subjects in a research study.

by ACP. By agreeing that the Repository would be managed by a centralized, independent entity (ACP), clinicians and participants ensured that the samples and data would remain open and accessible to anyone. In this way, the creators of the Repository provided for its contents to be broadly distributed. (In recognition of the enormous role they played in creating the resource, the 10 participating clinics were granted priority access to the samples and data for later MS research).

Leodas: Why did ACP choose to build a Repository, rather than selecting promising neuroscientists and investing in their work?

McBurney: The reasons go to the heart of ACP's understanding of MS. The organization's founder believed, as we still do today, that MS is a complex multi-factorial disease. It is not likely to be fully understood or cured by researchers in a single discipline. (For example, a geneticist working in isolation is not likely to cure MS.) Instead, ACP believes the greatest value is created by encouraging researchers from different institutions, different disciplines, and with different disease foci, to work together towards better treatments and a cure. In the 10 years since building the Repository, ACP fostered dozens of *virtual* collaborations among scientists and researchers around the globe, whose individual use of our samples and data overlap with one another.

Leodas: So what happened to the blood and data once they were collected at the clinics?

McBurney: Typically, researchers need a number of "products" derived from blood, including plasma, white blood cells, which are the cells of the immune system, DNA, RNA and serum. Different processes yield different blood products. Blood plasma is the pale yellow liquid component of blood that normally holds the blood cells in suspension and makes up about 55% of the body's total blood volume. It is prepared by spinning a tube of fresh blood containing an anticoagulant in a centrifuge until the blood cells are forced to the bottom of the tube. The plasma is then drawn off leaving a thin layer of white blood cells on top of the red blood cells. The white blood cells are carefully drawn off. In the laboratory, the white blood cell fraction is treated in different ways to extract DNA and RNA. Serum is prepared by causing blood to clot, and removing the clear pale yellow fluid that remains. It is similar to plasma but does not include certain components that are removed when it is allowed to clot.

ACP contracted with Precision Bioservices, a Maryland-based company that houses a number of leading biobanks, to help collect, transport, prepare, organize, store and distribute the blood samples and the blood products that make up the ACP Repository. Blood is collected in different types of tubes depending upon the product to be harvested, for example, some tubes promote clotting, some *prevent* clotting and some preserve RNA. Precision Bioservices sent to the MS clinics kits that included the necessary tubes and packaging for safe transport of the samples. The tubes were then collected and sent overnight to Precision, where the various products were extracted from the samples.

Meanwhile, data gleaned from the Case Report Forms was entered into a database that is housed at Document Solutions Group, a leading provider of clinical data management services based in Malvern, Pennsylvania.

Leodas: Most donors gave about 67 milliliters of blood, or about 9 test tubes. How many actual samples are produced from that size donation?

McBurney: The blood and the products derived from the collected tubes is divided into much smaller portions, referred to as “aliquots.” Typically, a samples collected from an individual yielded 20 aliquots of serum; 4 aliquots of white blood cells; 3 aliquots of RNA; 10 aliquots of DNA; and 4 aliquots of plasma. So in all, somewhere around 40 different samples were created from each donation. More than 3,200 people with MS and related demyelinating diseases, and some healthy control subjects participated, and about 700 of them returned to provide new samples and update data at a second time point.

In all, approximately a quarter of a million usable samples were created. As we’ve reported in previous issues of this newsletter, they have been used in about 90 studies on MS conducted by scientists from different disciplines and institutions around the globe, thus far. Some of the scientists work in academia while others are employed by private companies, both large and small. They include small, scrappy biotech start-ups, established industry giants like Biogen and Pfizer, and top research institutions like Brigham and Women’s Hospital, the Broad Institute and Mayo Clinic.

Continue reading this issue to know how pioneering scientists learn about the ACP Repository and make use of this important resource.

Accelerating MS Research by Sharing Samples and Data from ACP’s Repository

By Katina Leodas

Since its inception in 2006, ACP has aimed to distribute samples and data from its Repository as broadly as possible within the multiple sclerosis research community. To date, we’ve supported over 90 studies conducted by scientists around the world. In 2014, we realized that while Repository samples and data had been used by dozens of researchers over the preceding 8 years, much more research into MS could be done with this resource if more researchers knew of its existence.



That realization prompted us to adopt a highly pro-active approach to publicizing its existence and to distributing the samples, all of which remain vital and useful to this day. If scientists weren’t coming to us of their own accord in the numbers we desired, we needed to reach out to understand their needs, make them aware of this valuable resource, and help them identify ways the Repository could advance their research. In years past, this task fell to long-time ACP staff members, Hollie Schmidt and Sara Loud. Just over one year ago David Gwynne, was recruited to ACP as its Director of Alliances and Collaborations, to coordinate this activity, working closely with Sara and Hollie.

An experienced scientist and business development executive, David develops and maintains relationships with investigators who could or already do have interest in the Repository biosamples and data. Born in the United Kingdom and educated in Canada, David studied molecular genetics and obtained a B.Sc. and M.Sc. from the University of Toronto, followed by a Ph.D. from McGill and post-

doctoral studies at the University of California, Davis. Before coming to ACP, he led research and drug discovery teams in biotechnology companies in Toronto, Canada and Cambridge, MA, the latter involving him in the leadership of a multiple sclerosis drug discovery effort. David's career eventually included leading business development and licensing activities for several companies, something he has also pursued as an independent consultant, with a focus on neurology.

By training and temperament, David is perfectly suited to the work. His scientific background gives him unique insights into the technology underpinning licensing opportunities. And conforming to a positive stereotype we Americans hold of our neighbors to the North, he is one of the friendliest people we know. David says, "I've got a great job! I love talking to people, I love talking about science, and I like solving problems, which is what business development is all about."

Many of the commercial clients of the ACP Repository are early-stage biotechnology companies. It's difficult, costly and time-consuming to build a successful biotechnology company. Having a novel idea is really just the first step. After raising seed capital, scientist/entrepreneurs must advance the technology consistently through successive tests and value-increasing product development milestones. All investors like to hear about companies making steady progress along a planned development pathway and this, in turn, puts scientists under pressure—some times huge pressure—to demonstrate consistent progress by meeting the milestones. By achieving that in a timely and consistent manner, entrepreneurs increase the value of their companies, decrease the investment risk and increase the likelihood of securing subsequent funding from investors.

David knows the science and he understands these pressures and cycles of growth, which makes him very good at identifying the "pain points" of biotech companies and suggesting areas where their use of samples from the ACP Repository will advance their work towards short- and long-range goals. He reads the relevant scientific journals, stays current on work being done in the field, and tracks the progress of new companies or of established firms with new products in development. Then he picks up the phone and makes cold calls to scientists and company R&D executives whom he believes can use our samples. By demonstrating his knowledge and understanding, he gets scientists' attention and effectively spreads the word on the ACP tissue repository and data assets.

David has described one area where the ACP Repository can make the biggest contribution to the growth of new therapeutics ventures. "Our sweet spot," he says, is after companies have studied the effect of their molecule on mice. "They've gathered some positive pre-clinical efficacy data and they're planning to test their drug candidate on humans. Within a matter of weeks, we can send them samples, which enables them to test and generate human disease data." That, in turn can help them acquire investor and other funding sufficient to complete the demonstration of clinical efficacy in humans. This is particularly important in MS, given the limited applicability and relevance of animal models to the treatment of MS in humans.

There are several ways in which our samples are most commonly used. Some companies use them to discover biomarkers that can reveal or predict disease as well as determine how a patient may respond to a particular drug. Biomarkers can also be useful to drug discovery companies to identify drug targets. A second way to use patients' samples is a drug challenge to blood cells. Some of the most useful samples in the Repository contain live cells, the white blood cells, known technically as peripheral blood mononuclear cells (PBMCs). These are blood cells, which include some key components of our immune system (lymphocytes, and monocytes). They are a critical component in the

body's fight against infection. Because the PBMCs in the Repository are from individuals with MS whose immune systems are regulated differently, they can be used to reveal the biological differences between cells from MS patients and those from donors who do not have MS. Scientists developing drugs that they hope will affect MS can expose these cells to their molecules to see whether their drugs can generate the appropriate biochemical response.

An example of this "PBMC challenge" approach was detailed in our [April 2016 issue](#). Innate Therapeutics, a New Zealand company, is using ACP samples to develop a drug that modifies the function of the immune system, in order to interrupt a recognized pathological process that occurs in progressive multiple sclerosis (MS). The hope is that their therapy will halt and, ideally reverse that process.

Increasingly our samples are used by companies seeking to reposition a drug that has already been approved to treat another disease, as a treatment for MS. Known in the industry as "repurposing," this approach can be the fastest and least costly path to getting a new drug on the market. In fact, the majority of drugs submitted for approval to the FDA today are repurposed. Along these lines, ACP was recently approached by a company whose drug was approved a number of years ago for treating high blood pressure. Its scientists wanted to test the drug on ACP samples to see whether any impact could be detected on MS. Since the blood pressure medicine was commonly prescribed about 10 years ago (when most of the samples in our Repository were drawn), David wondered whether samples of people with MS who had taken the blood pressure medicine might already exist in the Repository. By just looking at those samples and comparing them with other samples of people with MS who did *not* take the blood pressure medicine, it seemed plausible that something valuable could be learned. Indeed, we had samples in the Repository that met this criterion (the donors had taken the blood pressure medicine) and the company is currently considering a research project that would include a comparison of samples from MS patients taking the blood pressure medicine with those who were not on the drug.

If you're wondering, as I did, about the numbers of samples that we distribute to each company, the answer is, it's all over the map (literally and figuratively!). Numbers of samples sent have ranged from less than 10 to over one thousand. Once a researcher expresses interest in receiving samples, David, Sara and Hollie work with them to understand the nature and scope of their research and the particular project they are undertaking. They then assist the researcher to develop and refine a clear proposal to the Repository for samples. The proposal is reviewed for scientific merit, research quality and likelihood of success by an Oversight Committee composed of many of the people who were involved in the Repository's creation. They include the Principal Investigators from the 10 original MS clinics that gathered the blood samples; representatives from two non-profit organizations with which we partnered on creating the Repository; and ACP staff. This is followed by selection of the actual samples that meet the scientists' criteria. ACP then notifies Precision Bioservices, the Maryland-based company that houses the Biorepository, to "pull" the samples we have selected, and within several days they are sent to points around the world.

Over the following year and a half, we maintain close contact with the researcher, tracking their progress and checking to make sure their needs are met. Sometimes, they request follow-up samples to confirm their original "pilot study" results in a larger experiment. Just as often, during the course of their work they identify other factors they need to test and this necessitates additional samples. Regardless of the outcomes, under the terms of our agreements, within 18 months of completing their

studies, all researchers are required to return to ACP all data generated by the work done with ACP samples. In this manner, and as envisioned by ACP at the time we created the Repository, we are steadily building one of the largest collections of data about people with MS anywhere in the world. We are currently seeking funding to organize and analyze the data, in order to determine the most promising fruitful directions for future MS research.

More than 3,200 people contributed samples and data to the ACP Repository. It is important for them to know that their contributions are still working hard to generate new insights. While we are no longer enrolling new participants in the Repository, our online patient-powered research network, iConquerMS (www.iConquerMS.org) provides everyone with MS an opportunity to power research in a similar fashion. For more information on that initiative, we encourage you to visit <http://www.iConquerms.org>.

Interested in learning what scientists regard as the latest frontiers in MS research?

On June 28, the New York Academy of Science is holding an all-day seminar titled "Multiple Sclerosis: Diagnostic and Treatment Frontiers," which will convene academic and clinical researchers with industry leaders to discuss:

- Current therapeutics,
- Diagnostic, prognostic, and predictive biomarkers,
- MRI usage in diagnosis and monitoring, and
- Novel and emerging treatments

For more information and to register to attend, visit [this site](#).