BeadChip Types Platelets For Better Transfusion Outcomes

BioArray Solutions
BloodCenter of Wisconsin

In a hospital birthing suite, a mother's labors are rewarded, and a new life enters the world. But the baby appears to be severely bruised, almost as if it had been beaten in the womb. How could this have happened?

In another hospital, a cancer patient who has received multiple transfusions shows a dangerously low platelet count. He receives yet another platelet transfusion. Hours later the platelet count remains seriously depleted, despite the transfusion. The new platelets seem to have mysteriously disappeared. Where did they go?

Both the newborn and the cancer patient are examples of immune-related platelet disorders. Almost everyone knows that humans have different ABO blood types and that, before transfusion, blood must be properly matched between donor and recipient to prevent serious complications. Few, however, are aware that platelets — the little disks in the blood that are essential for clotting — also have "types" that, when mismatched, can produce immune reactions such as those seen in the newborn and the cancer patient.

The newborn that appeared to be bruised is bleeding beneath the skin. That is caused by a low platelet count resulting from a mismatch between the platelet types of the mother and father. The medical term for this condition is neonatal alloimmune thrombocytopenia or NATP. According to the BloodCenter of Wisconsin, in the United States about 3,000 babies are born each year with NATP, which can result in bruising, intracranial bleeding and, in some cases, death.

In the case of the cancer patient, the newly transfused platelets are disappearing because the body's immune system is attacking them because of a mismatch of platelet types. About 10 million platelet transfusions are given each year in the United States. No one knows for sure how often immune problems resulting from transfusion mismatches may occur.

> *The good news is that both the newborn and the cancer patient can be helped with platelet transfusions that have been properly typed and matched to them.*

The Road to Finding out "Why"

When doctors first saw what happened to the 'bruised" newborn and the cancer patient with disappearing platelets, they were puzzled. "The antigens that cause blood types have been recognized for almost 100 years, but for many years nothing was known about platelet types," says Richard Aster, M.D., professor of medicine at the Medical College of Wisconsin and senior investigator at the BloodCenter of Wisconsin's Blood Research Institute. "Typing platelets didn't become important until people began transfusing platelets in the 1950s and 60s."

Over the years, a team of researchers at the Blood Research Institute would identify a number of platelet antigens critical to patient health. "I got involved at the very beginning," Aster says, "when we were defining platelet antigens using antibodies identified in individual patients."

Later, Aster and Peter J. Newman, Ph.D., now vice president for research at the BloodCenter of Wisconsin and associate director of the Blood Research Institute, would identify the molecular basis for various platelet antigens. "We were able to identify the single nucleotide polymorphism (SNP) that creates individual antigens. Knowing that opens the door to a fast, accurate test for platelet typing," Newman says. "It's a little like knowing which key opens which lock."

What was needed now was a fast, convenient way of executing such a test.

The Genesis of the BioArray BeadChip

In the early 1990s, researchers in New Jersey had the germ of a concept for such a test. The idea was to make a beadchip for complex nucleic acid and protein analysis. After some patents were filed on the concept and Small Business Innovation Research funding was secured, BioArray Solutions was formed. The company would eventually be acquired by Immucor in 2009, but much work had to be completed.

"To make the BeadChip work, many novel elements had to be developed in-house," says Sukanta Banerjee, senior director of research and development at BioArray. "This includes software for reading the chips, an associated microscope for examining the BeadChips and an entire system for manufacturing an array of BeadChips bonded to glass slides. None of these elements, with the exception of the microscope, which we heavily customize—can be bought off the shelf."

Banerjee adds that while they were developing the technology for the complete system that comprises the BioArray BeadChip, there was a question constantly in the back of their minds: "There are lots of things that the BeadChip could test for, but where is there a demand for a platform like this? The answer was in blood. Now we have separate

BeadChips for detailed analysis and typing of red blood cells, platelets and white blood cells."

To make their Human Platelet Antigen (HPA) BeadChip work, BioArray licensed the markers for human platelet antigens from the BloodCenter of Wisconsin.

Transferring the Technology

"In 2006, BioArray Solutions approached the BloodCenter of Wisconsin. We had a meeting in which BioArray explained what their base technology was and how it worked," says Laura Savatski, technology transfer officer for the BloodCenter of Wisconsin's Blood Research Institute. "They were interested in licensing our Human Platelet Antigens and in collaborating on samples that would give them access to positive controls to confirm that their system was working."

Savatski notes that while the agreement was executed in 2006, it took a couple of years to get the final product working and market-ready. "Now sales are growing, and we are getting royalties," she says, "which have actually taken off in the past two years."

Putting it All Together

At the heart of the BioArray BeadChip system are tiny silicon chips that measure just 300 micrometers by 300 micrometers, smaller than the period at the end of this sentence. Hard to see with the naked eye, 96 BeadChips fit on a glass slide, which means that 96 different samples can be tested at once. Each of the 96 BeadChips is seeded with 4,000 microparticle "probes" for detecting the various Human Platelet Antigens.

The sample to be tested is prepared by taking whole blood from the person to be analyzed, extracting genomic DNA from it and performing PCR (polymerase chain reaction) amplification for the target areas of interest. The sample is put onto an individual BeadChip, and when there is a match between the sample DNA and the BeadChip, there is a fluorescent reaction, which can be seen and analyzed using a special microscope and software that is part of the BeadChip system. The entire test, including sample preparation, takes place within a single work shift and shortens the process of typing platelets by more than two days.

According to Banerjee, the BeadChip is widely used in Europe and is considered the test of record there for platelet typing. The BeadChip currently is available for research use only in the United States.

Aster says, "From our viewpoint, the key benefit of the BioArray BeadChip is that it can be used to type large numbers of donors to create prescreened and typed platelet units.

"So when a baby with NATP or a cancer patient with the low platelet count needs a transfusion, we can give them platelets without fear of adverse reactions."

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