What Gets Across

A goal of doctors and prospective parents is to protect the health of a growing fetus. Pregnant parents are often given a list of drugs and substances to avoid because they can pass through the placenta and harm the developing fetus, for example. But some molecules, even helpful ones like antibodies, don't pass through easily. Researchers, including me, work on ways to improve the health of newborn babies by acting during pregnancy to give them a stronger immune system. Because vaccinating pregnant people has been effective in improving the health of babies, scientists knew that it was possible for antibodies to cross the placenta, but we noticed that antibodies to some diseases were transferred in greater quantities than others. I was curious about these differences and wondered whether the placenta was somehow controlling which antibodies could get across and in what quantities?

To answer these questions, I looked at the antibodies collected from infants and their pregnant parent. By comparing the kinds of antibodies in an infant's blood to the parent's blood we could see whether certain kinds of antibodies were either getting blocked from transfer across the placenta or getting selected for transfer. We thought about many different characteristics of antibodies, such as, what pathogen they bound to, how strongly they bound, and how effectively they served as a beacon, signaling the presence of a pathogen to the rest of the immune system.

I compared almost a hundred characteristics of the antibodies in each participant. Because this was so much data to sift through, and there were many differences, instead of looking at each variable separately, we used computational biology to figure out what was really important. **Computational biology** uses mathematical models to turn lots and lots of data into simpler models that are easier to understand. We gave the model all of the hundreds of data points we had collected and asked it to identify what distinguished antibodies in the parent from those in the child. For each person we had collected close to 50 individual measures! And across all of our pairs of parent and child, that's a lot of data! Our results are shown in **Figure 1**.

Out of all of this data, I saw that the antibodies in the cord blood differed in a specific way. Cord blood is found in the umbilical cord, part of the placenta which provides a passage from the parent's blood to the developing fetus' blood. All antibodies have some number of sugar molecules attached to them that are involved in cell signaling. There are lots of different sugars, but almost all of the antibodies in the cord blood had one specific sugar structure. This suggested to me that the placenta was in a sense, a **selectively permeable** filter, only letting in certain kinds of antibodies. One of those antibodies signals to a specific kind of white blood cell, called a natural killer cell. Natural killer cells are the only mature immune cell a developing young baby has, so they are super important to that baby in terms of being able to fight off illness! So the placenta was letting in a very important antibody, one that gives the eventual newborn its first working immune cells.

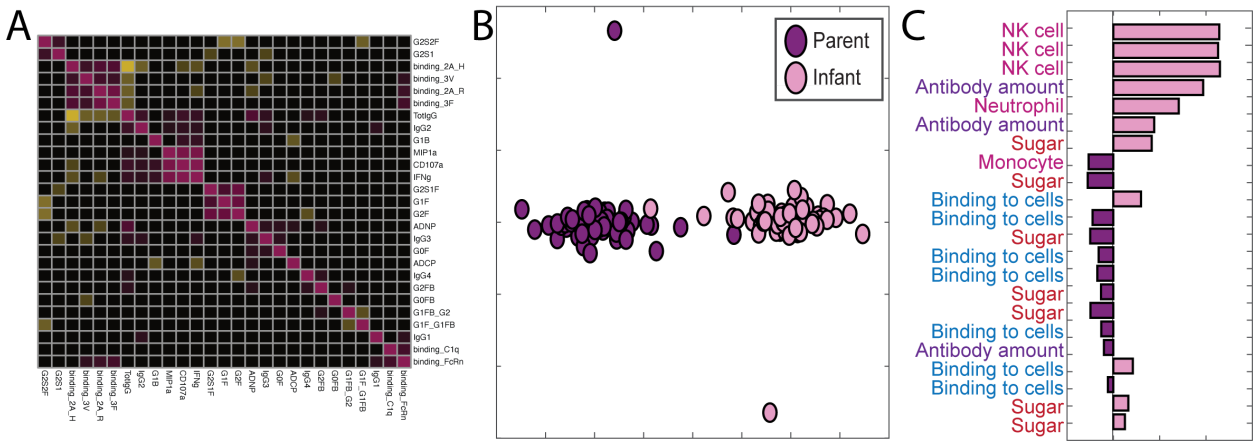

Figure 1. Computational Analysis. Because so many data points were measured (**A.** Shows all of the data measured), computer analysis was used to understand what was different between the parent and the child's blood. **B.** Each participant (parent or infant) is represented as a single point on a plot that combines all of the data measured into one plot. **C.** The individual measurements taken were ranked based on how much they helped distinguish the parent and the child's blood. You can see that the top factors are related to natural killer cells (NK cells)**.** That means that if you looked at just the substances related to NK cells in a given sample, it'd be a huge clue as to whether the sample you're looking at is from a parent of an infant. Samples with a higher density of NK "stuff" were most likely infant samples. *Source:* Data provided by M. Jennewein.

The data was really interesting, but it *of course* led to more questions, that's what science is all about! I now knew that antibodies were actively transported across the placenta, but I didn't know exactly *how* it was happening. I thought that maybe the receptor that grabs on to antibodies and pulls them across the placenta was somehow favoring antibodies that had the particular sugar structure I had identified.

To test this idea, I modeled a placenta in the lab by looking at the interactions among antibodies, and the antibody receptors found on the placenta. My hypothesis was supported by the data! The placental receptor (called FcRn) bound more strongly to the same kind of antibodies that were found in the infant!! The receptor specifically recognized antibodies based on a certain sugar structure and transferred them more efficiently across the placenta!

Beyond just understanding the mechanism of how antibodies are transferred, this research is really exciting for showing what kinds of antibodies successfully transfer across the placenta. While this might seem like a really tiny discovery, it actually has implications for designing vaccines that could really help infants. If we know what kinds of antibodies successfully cross the placenta, we can design vaccines specific for pregnancy that teach the body how to make these antibodies, and hopefully, these vaccines would be able to increase the quantity of antibodies transferred across the placenta, and improve the immunity of babies. When we think about developing new vaccines, such as one for coronavirus, making vaccines that will help babies before the babies can be vaccinated themselves will be very important!

References

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BiteScientist Profiles

Maddy Jennewein completed their PhD at Harvard and a postdoc at the Fred Hutchinson Cancer research center. They currently work as a scientist at the Infectious Disease Research Center in Seattle working on vaccine development. Outside of the lab, Maddy likes to read and sew, they were active in their school's LGBTQ group and in their graduate student union.

Bonnie Nieves loves hiking, writing, and teaching science. She teaches Biology and Anatomy and Physiology to high school students in Massachusetts. Outside of the classroom, Bonnie likes hiking with her dog and traveling with her family.