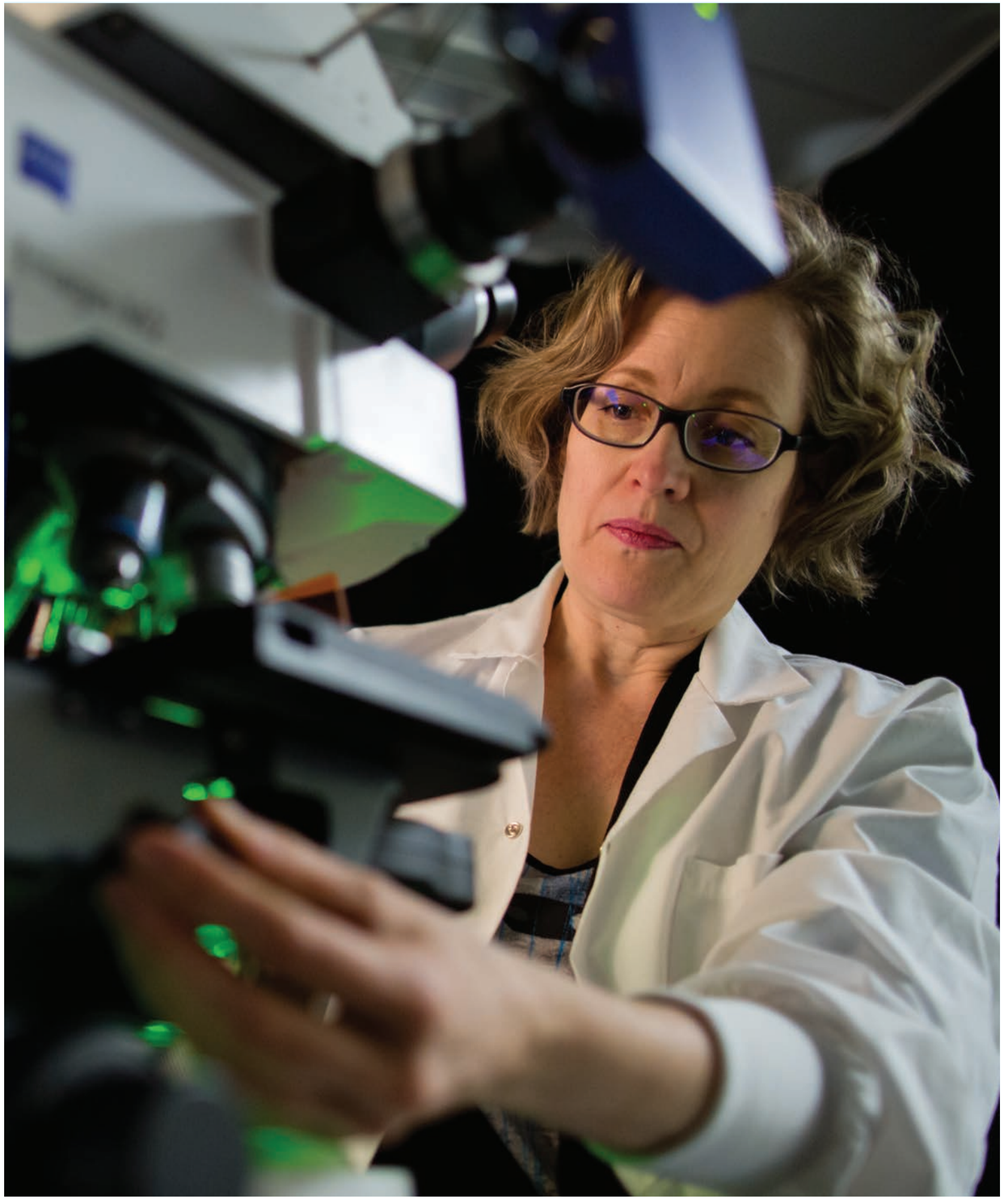

Searching for a way to bring back the light

Through research, Dr. Valerie Wallace hopes to show that cell transplants can help restore vision for those with retinal disease

Renee Sylvestre-Williams

When the photoreceptor cells in your retina die, the light vanishes. For good. But recent exciting work by Krembil's Dr. Valerie Wallace, when studying cone photoreceptor transplants to the eye, has uncovered a novel and surprising property of material exchange between cells.

Now, she and her dedicated team are evaluating whether this exchange process could help restore vision.

Dr. Wallace, co-director of the Donald K. Johnson Eye Institute within the Krembil Research Institute and holder of the Donald K. Johnson Chair in Vision Research, is primarily interested in blindness as a result of retinal disease. "My lab in particular is focused on diseases that impair the function or cause the death of the photoreceptors," she says. "The photoreceptors are the cells in the retina that you need to sense light. If you lose them, your retina does not work," says Dr. Wallace.

"Because there are no treatments to restore vision after photoreceptors die, we are taking this very conceptually simple approach, and that is: 'Can we circumvent all of this cell loss by just putting in healthy photoreceptors, and would they behave like normal photoreceptors and hook up to the rest of the retina and restore the ability to respond to light?' It's really, really simple." Dr. Wallace laughs, "Well, the idea is simple."

We still do not have a deep understanding of why photoreceptors die, even in inherited diseases such as retinitis pigmentosa. Dr. Wallace says that there is a huge body of research over the last 25 years that has discovered many genetic mutations that cause photoreceptor disease, but there is significant variability in how vision loss manifests in these conditions. In some instances, the problem manifests at birth but can also emerge in adulthood. Furthermore, there are other conditions, such as age-related macular degeneration (AMD), which cause the death of cone photoreceptors. The cause of AMD is multifactorial and includes inflammation, genetic susceptibility and other age-related components that can lead to blindness. Currently, there is no cure for retina-related blindness.

Dr. Wallace's lab has been targeting cone photoreceptors for transplantation, due to their high clinical relevance. Cone cells die when a patient has AMD or in late-stage retinitis pigmentosa, robbing patients of central vision. Ultimately, this means that these people can't read, see fine detail or discriminate colours. People, says Dr. Wallace, have been transplanting cells to replace bone marrow and skin for years, and those two procedures are relatively common. Everything else related to cell transplantation is still experimental. "Years ago, people started transplanting photoreceptor cells to the eye and used a green fluorescent protein, which comes from jellyfish, to track the cells. When you transplanted those cells, what people found was that they got these really beautiful green photoreceptor cells in the eyes of recipients. Photoreceptor cells are a very complicated cell type and are structurally very specific to the retina," says Dr. Wallace. "Detecting green photoreceptors was very exciting, because what people thought at the time was that their immature cells were going in and setting up shop in the recipient retina."

Except the cells weren't setting up shop. Instead, they were transferring material. Specifically, they were donating their green fluorescent protein to the remaining photoreceptors, and in some cases, also the missing proteins that were lost due to retina-related diseases. Researchers were finding that this material exchange could create modest improvements in vision. "It has to be really formally proven, but it raises the possibility that just transferring the missing proteins may be enough. Somehow [the recipients] were acquiring the normal proteins from the normal donor cells that were transplanted – at least that is what the interpretation is now," says Dr. Wallace.

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>
> – Dr. Valerie Wallace

It's too early to tell whether material exchange could be a treatment or a cure for blindness. But it is deeply interesting and has raised even more questions such as: "How do the donor proteins know where to go? What happens to the donor cells after the material exchange? How long after donor cells die can you still detect this exchange? How long can you keep donor cells alive to mediate this transfer? Do the donor proteins integrate fully within the recipient's retina with the photoreceptors?" The short answer? There are no definite answers.

"It's just so impossible to say how this will all pan out," says Dr. Wallace. "It may be that we can harvest material from photoreceptors and use that to repair retinas, like a drug therapy, which is speculation at this point." Adds Dr. Wallace: "We're really asking these fundamental questions, but we would really need to have enough answers [in order] to support any kind of cell transplantation to the eye." ■