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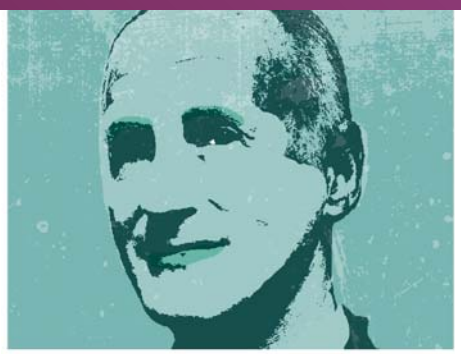

Confessions of a Live Surgeon

The intriguing world of live surgery, as told by those who know it best




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The Secret is the Secretions

Stem cells hold great promise, but is it the cells we really need?

By Nicolas Sohl, CEO and co-founder of Cell Care Therapeutics, Los Angeles, California.

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Ophthalmology is full of advances, but sometimes the field is very conservative. Look at the extended-release drug delivery systems that have made it to market: Vitrasert, Ozurdex, Retisert, Iluvien. New drug delivery technology, but really old drugs (ganciclovir, dexamethasone, and fluocinolone acetonide). I think it's clear that the use of steroids for the treatment of retinal disease will diminish – their drawbacks and side-effects are well-known, and there's (hopefully) better therapeutic approaches on the horizon.

Many companies are focusing on cell therapies to treat retinal diseases. They look like an attractive option; they've been heralded as being able to "regenerate" or "rebuild" the retina. There are a number of companies that are currently developing and even trialing intravitreal stem cells clinically for retinopathies, in particular for retinitis pigmentosa,

Stargardt disease and AMD. If they can deliver on their promise, that's wonderful. But there are aspects of this approach that still need to be resolved.

Adult bone marrow or adipose tissue-derived mesenchymal stem cells (MSCs) and CD34+/hematopoietic stem cells (HSCs) – look like they have beneficial paracrine effects on ischemic and/ or degenerating retina. Placing them into the vitreous, or on a scaffold, subretinally to replace damaged tissue are all potential ways of treating currently untreatable diseases. But what is really happening to MSCs or differentiated retinal progenitor cells (RPCs) once they've been implanted? What happens to their phenotype and their therapeutic capacity over time? Some incredible work has been put in to ensuring that implanted cells behave well but, over time, growing evidence suggests that they can become problematic when they abnormally turn towards an epithelial-like phenotype.

Nevertheless, there are a number of companies developing treatments that use MSCs. Other stumbling blocks ahead? If they're allogenic, and the goal is transplantation, they will need to express MHC – and the immune system will seek and destroy them. So if they're being used for their immunoregulatory properties, they won't persist for too long. Essentially, the transformative effect is only that of the initial dose, so it truly is an initial benefit, not a prolonged one. How frequently and how often, then, would you need to continue administering stem cells for?

What if the main benefit of MSCs is the secretion of a potent mix of anti-inflammatory mediators and pro-regenerating growth factors and extracellular vesicles? And if you can harvest those and administer them, why do you need the stem cells?

We are doing exactly that. We can – on an industrial scale – grow engineered MSCs, harvest their secretions, and process them into a cell-free biologic (at high concentrations – essential for intraocular drug formulations – and stable at room temperatures) that can be administered by traditional intravitreal injection. We've implemented robust manufacturing controls and use a panel of analytics to ensure comprehensive product identity and batch-to-batch consistency. We're still at a pre-clinical stage, but animal studies have shown that for chronic inflammatory diseases in the retina, such as wet AMD and DME, you can get very robust protection from inflammation, oxidative stress and fibrosis, thereby protecting vision – which, at a minimum, should provide a treatment option for patients refractory to anti-VEGF therapy.

We're still working on dosing frequency. Clearly, treating a chronic disease with a single injection won't have a permanent effect, but we believe our offering will be comparable with the latest biologics administered intravitreally to the eye. Furthermore, unlike cell therapy, this approach allows you to tightly control the dose administered – something that "conservative" ophthalmologists will both appreciate and be comfortable with. Perhaps the future of retinal stem cell therapy isn't a single application of stem cells, but rather one that looks much like it does today: intravitreal injections, but with far better outcomes.

About the author

Nicolas Sohl

Nicolas Sohl is CEO and co-Founder of Cell Care Therapeutics