Diabetic retinopathy is one of the leading causes of vision loss in adults. It develops when prolonged high blood sugar levels damage the small blood vessels in the retina—the light-sensitive tissue at the back of the eye. As the disease progresses, damaged blood vessels leak fluid, trigger inflammation, and can even cause abnormal blood vessel growth, eventually impairing vision.

In recent years, scientists have learned that a specific type of cell stress known as cellular senescence plays a key role in this process. Senescent cells no longer divide but remain active and secrete harmful substances that damage neighbouring tissues and worsen inflammation. In the retina, senescence affects the endothelial cells, which form the inner lining of blood vessels and help regulate blood flow and barrier integrity. Additionally, other retinal cells, like Müller glia, also contribute to inflammation by releasing pro-inflammatory signals and growth factors such as vascular endothelial growth factor (VEGF).

Current treatments, such as injections that block VEGF, only target the consequences of the disease rather than its root causes. This project proposes a different approach: using smart nanoparticles to deliver a drug (rapamycin) directly to senescent and inflamed cells in the retina. These nanoparticles are based on hyaluronic acid (HA) and bind to a surface molecule called CD44, which is more abundant in senescent cells. Once bound, the nanoparticles release rapamycin to reduce inflammation and improve vascular function.

The study will begin by testing these nanoparticles in laboratory models using human cells. The research team will mimic diabetic stress in endothelial cells and measure how well the nanoparticles are taken up, whether they reduce harmful signals, and how they influence protein production. The results will help determine whether the treatment works at a molecular level.

Next, the therapy will be tested in diabetic mice, which naturally develop symptoms similar to diabetic retinopathy in humans. The team will assess whether the nanoparticles reach the retina after injection, and whether they improve vessel health and reduce inflammation and cellular damage. Advanced techniques like RNA sequencing and proteomics will help researchers understand how the treatment changes cell behaviour.

By combining modern drug delivery methods with the investigation of molecular mechanisms involved in diabetic retinopathy, this project aims to improve our understanding of endothelial and glial contributions to disease progression. The outcomes may help assess the potential of targeted nanoparticle-based treatments. The insights gained could lay the groundwork for future research into early-stage therapeutic strategies for diabetic retinopathy.