### Background:
Age-related macular degeneration (AMD), a condition with progressive loss of central visual acuity creates blind spots on the retina with increasing age. Irregular angiogenesis characterized by weak and leaky blood vessels become prominent due to the over-expression of the vascular endothelial growth factor (VEGF). The currently available clinical regimens are commonly invasive, patient incompliant, along with numerous side effects and pharmacokinetic variations in individuals. For this reason, we tried to develop a multifunctional nanocarrier based system to effectively delivery the anti-VEGF siRNA.

### Methods:
Polyethyleneimine (PEI) modified large-pore mesoporous silica nanoparticles (MSNs) cargo systems have been developed for efficient siRNA loading. Rhodamine B loaded MSNs were first obtained to test the ability of PEI to cap the pores of the MSN system and control the release of its cargo. *In-vitro* release of rhodamine B from PEI-coated MSN was examined in the acidic lysosomal extract obtained from rabbit liver tissue. Additionally, the cytotoxicity of these MSNs was assessed in retinal cells of ARPE-19 cell line. Finally, the siRNA loading into the MSNs pores, its release and the silencing of VEGF was performed to confirm the effectiveness of the nanocarrier system.

### Results:
The shift in the zeta potential values confirmed the effective coating of the cationic PEI on MSNs surface with sufficient pore size and volume for nucleic acid loading. The triggered release of rhodamine B from MSNs was confirmed and hypothesized to be due to the proton sponge effect activated by the cationic PEI in the late endosomal/early lysosomal environment. The resultant nanocarrier system shows higher toxicity with increase in PEI concentration, and effective gene silencing of VEGF.

### Conclusions:
The developed porous silica nanocarrier system withholding huge potential as an effective gene delivery vehicle. The toxicity arising with PEI coating can be tackled with further functionalization steps with non-toxic and/ or biocompatible polymers. Thus, such a versatile platform technology has tremendous prospects for further scientific exploration and development.