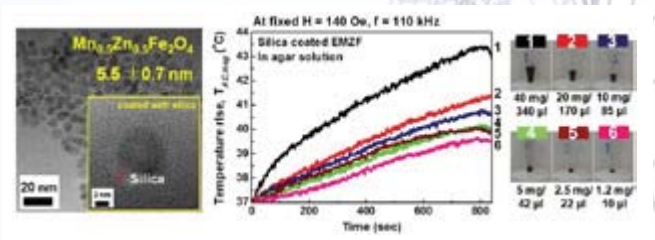
OCULAR NEUROPROTECTION IN GLAUCOMA
(A NANOMEDICINE APPROACH)

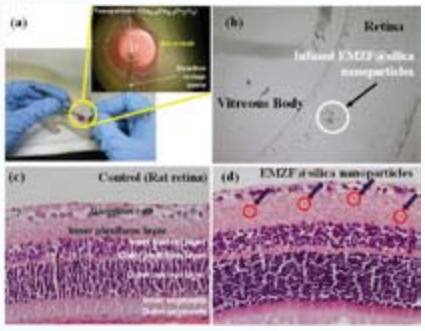
Glaucoma is an optic neuropathy disease wherein the optic nerve is damaged with loss of retina ganglion cells (RGC), mainly due to an increase in intraocular pressure, leading to progressive and irreversible loss of vision.

For the past few decades, vast research activities have been undertaken to develop biotechnical approaches that will protect the damaged optic nerve. Eventually, it was discovered that neuroprotection of the optic nerve or RGCs is effectively made by heat-shock proteins (HSPs), or stress proteins. These proteins exist in all living creatures from bacteria to human beings and are induced by hyperthermia, metabolic stress, or oxygen deprivation. In particular, it was clinically confirmed that the induction of HSP 70 families is powerfully efficacious for the protection of damaged optic nerve or RGC resulting from glaucoma. To date however, all attempted methods, to induce HSPs from optic nerve or RGC, have proven ineffective. This has been due to undesirable chemical and physical side effects caused by difficulty in inducing HSPs and controlling heating temperature in the localised RGCs (or optic nerve).



Left: 2 nm thick silica coated engineered superparamagnetic $Mn_{0.5}Zn_{0.5}Fe_2O_4$ nanoparticles (EMZF@silica, 5.5 nm in diameter).

Right: Successful demonstration of AC magnetically induced heating characteristics of EMZF@silica for localised heat shock proteins (HSPs) in an agar solution with the same viscosity of cytoplasm (retinal ganglion cells).



A new infusion technique to introduce nanoparticles to the retina: (a) Injection of nanoparticles into the rat eyeball; (b) image of successfully infused nanoparticles in the retina.

Histological exam results of infused EMZF@silica in in-vivo: (c) Control rat retina (RGCs); (d) Infused EMZF@silica nanoparticles in RGCs

For a more effective and safer method, Asst Prof Seongtae Bae, together with his research team in Biomagnetics Laboratory (BML), ECE, has recently developed a new biotechnical approach that induces localised HSPs in the optic nerve or RGCs by local magnetic hyperthermia using engineered superparamagnetic $Mn_{0.5}Zn_{0.5}Fe_2O_4$ nanoparticle agents with a 5.5 nm mean particle size. Their scientific achievement, published in "Biomaterials in Sep. 2010 on-line issue", can be summarised in to three main areas:

1) Developed a very small size of nanoparticles with 5.5 nm mean diameter as a localised HSPs inducing agent. The nanoparticles were coated with a very thin (~ 2 nm) silica layer and showed a higher SAR (specific absorption rate) as well as higher heat generation in a short time.

2) Developed a new infusion technique of nanoparticles into the retina layer through the vitreous body. Most of the current technologies regarding infusion are through intravenous injection via blood vessels. However, the eye does not have any blood vessels, excepting the choroid that consists of reticular structures located in the back side of the eye. For this reason, a new technique through the vitreous body was developed as part of this research, wherein the nanoparticles were injected into the eyeball and diffused through the vitreous body to the surface of the retina.

3) Successfully demonstrated the heating temperature in a similar environment to RGC for inducing HSPs (in the range of 39 – 41°C) particularly in the biologically and physiologically safe range of AC magnetic field (<140 Oe) and frequency (<110 kHz).

This work was also featured in "Nanowerk spotlight, USA online": *http://www.nanowerk.com/spotlight/spotid=18646.php* on 25 October 2010. In the article, Dr Bae said: "All the experimental results shown in our study strongly suggest that the ocular neuroprotection, based on the HSPs induction by local magnetic hyperthermia using silica coated superparamagnetic $Mn_{0.5}Zn_{0.5}Fe_2O_4$ nanoparticle agents, can be an innovative approach for the efficacious treatment of glaucoma. Furthermore, it emphasises that our new nano-bio technology can be extended to treating other neural diseases such as Parkinson's disease, Alzheimer's, epilepsy, and other bioelectric transmitting-related diseases as well as immunology-related diseases".