Uveal Melanoma Drug Delivery and Imaging using Nano-Technology

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Background

• Uveal melanoma is the most common type of ocular melanoma and typically presents as a small tumor near critical structures in the eye.

• Malignant “choroidal” melanoma arise from the blood-vessel layer “choroid” beneath the retina.

• Malignant choroidal melanomas can spread to other parts of the body.

• Most UM’s are detected during a routine ophthalmic examination, and ultrasonography. Diagnosed by dilated indirect ophthalmoscopy and

• Symptoms consist of mostly blurred vision, floaters, and visual field loss. However, about 30% of the patients have no symptoms at time of diagnosis.

• Causes and Risk factors of Uveal melanoma remain unknown.
Background

• The therapeutic modality of choice for melanoma will vary depending on the size, growth, and location of the lesion.

• Compared with other intraocular tumors, uveal melanoma has the highest rate of metastasis, with a 40% metastasis rate (median survival 2–7 months) and approximately 50% of mortal cases due to metastasis, most commonly to the liver.

• Approximately 30% of patients with successfully treated primary tumors will develop metastasis.

• Indirect ophthamoscopy through a dilated pupil provides a correct diagnosis in more than 95% of the cases (Char et al, 1980).
History

• Paul Ehrlich attempted to develop “magic bullets” to which drugs were added and which could be used to target diseases and would kill all pathogens after only a single treatment [12].

• At the end of the 1960s Peter Paul Speiser developed the first nanoparticles which can be used for targeted drug therapy [12], and in the 1970s Georges Jean Franz Köhler and César Milstein succeeded in producing monoclonal antibodies [13].

• At the start of the 1990s nanoparticles were modified for the first time for transport of DNA fragments and genes and were sluiced into cells with the aid of antibodies [12,14].

• Some studies have been varied out on the use of nanoparticles for tissue targeted and slow drug release in various structures of the ocular tissue.
Application

• Use of nano-materials as contrast media in diagnostic in vivo procedures enables imaging with an improved 3D view.

• Topical application is useful for treating disorders affecting the anterior segment of the eye.

• Nanomaterials are not filtered out of the blood and can circulate in the organism until they reach their target.

• Active substances can be encapsulated in their hollow interiors and their surface can be modified so that they overcome natural barriers such as cell membranes like “Trojan horses”, and with the aid of biosensors (for example antibodies) recognize particular cells and tissue, attach themselves to these and release the active substances to the target over a relatively long period of time.
What is a quantum dot?

- Nanocrystals
- 2-10 nm diameter
- Semiconductors
Results

• No toxicity to the retina was observed in another CCR3-targeting QD imaging mice experiment.

• Intravitreous injection of PNIPAM particles resulted in accumulation in the retina as shown in Figure 2. This could provide many useful clinical options as hydrogel nanoparticles have been shown to have good drug loading and release characteristics.

• Intravitreal injection of liposome-loaded tacrolimus for suppressing experimental autoimmune uveoretinitis (EAU) caused no side effects on retinal function or systemic cellular immunity.

• There is also data showing intravenously administered gold nanoparticles can penetrate the blood-retinal barrier without damaging the retina tissue[159].
Results

• Another study conducted by Takeda et al[126] showed that in vivo quantum dot imaging can be used to detect spontaneous CNV of age-related macular degeneration (AMD) before it invades the retina.

• Antibody-conjugated QD’s have also found to be a high-throughput screening system and effective strategy for detection of melanoma.

• Topically applied nanodevices have to overcome the conjunctival and scleral barriers.

• Use of liposomes via subconjunctival and subtenon routes were effective in delivering drugs and nanodevices to the posterior of the eye.
Limitation

• QD’s can specifically detect melanoma cells only.

• Lacks the important local and systematic toxicity data for the particles used for eye imaging, diagnosis and also drug delivery.

• Damage to ocular barriers which can affect patient’s vision.

• Allergic or hypersensitivity reactions have been reported from the use of titanium dioxide, dendrimers and polystyrene nanoparticles in certain animal models and even in humans.

• Nanotubes have the potential of disrupting and altering cell membrane.
Future

• Develop bi-functional nano-devices to diagnose and to treat cancer all at once.

• Contrast a nanoparticles that can detect circulating tumor cells, which play vital roles in the uveal melanoma metastasis to the liver.

• Nano-technology made up non-toxins and bio-degradable.
Reference


