Novel 3-D cell culture model shows selective tumour uptake of nanoparticles

August 31 2007

A nanoparticle drug delivery system designed for brain tumour therapy has shown promising tumour cell selectivity in a novel cell culture model devised by scientists at The University of Nottingham. The project, conducted jointly by the Schools of Pharmacy, Biomedical Sciences and Human Development, will be featured in the September issue of the *Experimental Biology and Medicine*.

Therapy for brain cancers is particularly difficult for a number of reasons, including getting sufficient drug to the tumour and selectivity of drug action. Dr Martin Garnett, Associate Professor of drug delivery at the School of Pharmacy said: “We are working on a number of new therapeutic approaches using nanoparticle drug delivery systems. However, understanding and developing these systems requires suitable models for their evaluation.”

The nanoparticles used in this study were prepared from a novel biodegradable polymer poly (glycerol adipate). The polymer has been further modified to enhance incorporation of drugs and make the nanoparticles more effective.

Dr Terence Parker, Associate Professor in the School of Biomedical Sciences explained: “The interaction of tumour cells with brain cells varies between different tumours and different locations within the brain. Using 3-dimensional culture models is therefore important in ensuring that the behaviour of cells in culture is similar to that seen in real life”.

The work was mainly carried out by graduate student Weina Meng who formulated the fluorescently labelled nanoparticles and studied them in a variety of tumour and brain cell cultures. Her early studies showed faster uptake of nanoparticles into tumour cell cultures than normal brain cell cultures grown separately. This selectivity was only seen in 3-dimensional cultures and was the driving force to develop a more complex and representative model.

Tumour cell aggregates have been used as cell culture models of cancer cells for many years. Similarly thin brain slices from newborn rats can be cultured for weeks and are an important tool in brain biology. In the cell co-culture model now reported, these two techniques have been brought together for the first time.

Brain tumour cell aggregates were labelled with fluorescent iron microparticles and grown on normal newborn rat-brain tissue slices. The double cell labelling technique allowed investigation of tumour cell invasion into brain tissue by either fluorescence or electron microscopy from the same samples. Using these techniques the tumour aggregates were found to invade the brain slices in a similar manner to tumours in the body. Having developed the model then the tumour selective uptake of nanoparticles was demonstrated in the co-culture.

The collaboration on this project has been nurtured by Professor David Walker of the School of Human Development who co-founded the Children's Brain Tumour Research Group at Nottingham. Professor Walker said: "Understanding the biology of tumours is important if we are to develop effective new treatments. This work demonstrates how close co-operation between disciplines can help to push forward ideas which could lead to new clinical therapies".

Dr. Steven R. Goodman, Editor-in-Chief of Experimental Biology and Medicine, agrees with Professor Walker. Dr. Goodman stated: "The

convergence of cancer cell biology and nanoscience, exemplified by this study, holds great promise for the future of brain tumour therapy."

Source: University of Nottingham