To realize these exciting applications, many challenges have to be overcome, such as the development of even smaller lasers with lower threshold, higher brightness and higher stability in the biological environment. The tasks include the search for more efficient rare-earth doped nanomaterials as the gain medium, high refractive index materials to enhance Q-factor in biological samples, and the development of materials fabrication procedures to make smaller and integrated resonators. For example, the large variation in lasing threshold among 22 demonstrated microsphere lasers, reported by Fernandez-Bravo et al., suggests that alternative fabrication approaches have to be explored for better control of nanoparticle concentration and coating. With many advances being made in the design and fabrication of a variety of micro- and nanoscale cavities[2], for example, disks, tubes and rings, that accommodate WGM with high Q-factors, the challenge broadly lies in the seamless integration of a cavity with a gain medium.

With the landmark work reported by Fernandez-Bravo et al., we expect a new wave of technology integration and interdisciplinary collaborations between material science, photonics, nanotechnology and device engineering to develop a new set of cell biology methods and analytical devices. ❐

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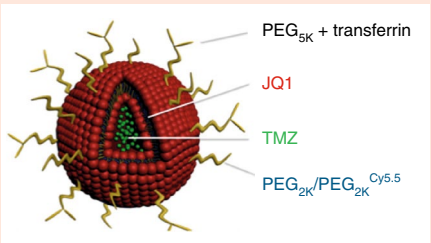
CANCER NANOTECHNOLOGY

Getting to the brain

Glioblastomas are the most frequent and most highly malignant tumours of the brain, with the current survival rate 5 years after diagnosis reported to be lower than 5%. The heterogeneity of the tumours, which makes them poorly responsive to single therapeutic agents, and the limited drug permeability across the blood–brain barrier (BBB) contribute to the low efficacy of the current therapies. Use of drug carriers for targeted delivery could improve therapeutic efficacy by increasing the drug concentration within the tumour and simultaneously reducing the toxic systemic effects, but such carriers are often too big to efficiently cross the BBB.

In a recently published paper (*Nat. Commun.* **9**, 1991; 2018), Lam et al. develop a transferrin-functionalized poly(ethylene glycol) (PEG)ylated liposomal nanoparticle for glioma therapy. Transferrin ligands have previously been shown to help nanomedicine cross the BBB, and in this study the authors leverage on this property to effectively co-deliver a combination of two drugs to tumours in two orthotopic mouse models of glioma.

First, the authors use multiphoton intravital live imaging to demonstrate that fluorescently labelled, transferrin-functionalized nanocarriers injected intravenously in healthy mice can successfully cross an intact BBB, supporting a transferrin receptor-mediated transcytosis across the endothelium. The authors confirm these results in tumour-bearing mice and, using immunochemistry on tissue slices, also show that in these animals functionalized nanoparticles accumulate in tumours at a higher concentration than non-functionalized ones. This result is explained not only by an efficient transferrin-mediated crossing of the BBB, but also by experiments indicating that glioma cells express transferrin receptors on their surfaces, therefore enabling targeting and cellular uptake of the functionalized nanoparticles. The researchers then test the possibility of using the carrier for simultaneous delivery of temozolomide (TMZ), a gold-standard drug for the treatment of gliomas, and JQ1, a bromodomain inhibitor with anticancer activity. As shown in the picture, their therapeutic nanoparticles consist of a TMZ core, a JQ1 hydrophilic coat, PEG-polymers that impart stealth properties for long circulation lifetime, and transferrin receptors for tumour targeting across the BBB. The researchers show that these nanoparticles deliver drugs concomitantly, resulting in increased cancer cell toxicity, reduced systemic drug toxicity and extended survival when compared to free drugs combination or non-functionalized PEG particles, highlighting the potential use of such delivery systems in the clinic. ❐



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