IMMUNOTHERAPY AN ATTRACTIVE CELL- THERAPY APPROACH

Cell-based immunotherapies hold promise in the treatment of cancer, but delivering immune cells to tumours is challenging: local injection is often not feasible whereas systemic injection results in most cells becoming sequestered within nontarget tissues. Previously, Munnitha Muthana *et al.* showed that super-paramagnetic iron-oxide nanoparticle (SPIO)-loaded macrophages could be guided into superficial tumours in mice using external magnets. Now, they have used this approach to target cell-based virotherapy to deeper tumours by exploiting MRI scanners to generate localized magnetic-field gradients internally.

“We used the magnetic-field-gradient coils inherent to all MRI systems to direct macrophages carrying an oncolytic herpes virus, seprexvir (HSV1716), into orthotopic prostate tumours or related lung metastases in mice,” Muthana explains. The SPIO-labelled human macrophages were injected intravenously before pulsed magnetic-field gradients were applied for 1 h in the direction of target tumours; this approach was termed magnetic resonance targeting (MRT). “MRI was then used for its conventional purpose to see if the magnetic cells had reached their destination, and to track tumour growth over time.”

Flow cytometric, histological, and immunofluorescence analyses confirmed that MRT, compared with exposure to the static magnetic field of the scanner only, increased tumour-infiltration of the human macrophages. Importantly, MRT of virus-loaded macrophages to the primary tumours resulted in significantly decreased tumour growth and lung metastases for the entire duration of assessment (21 days) after a single dose of cells, compared with the rates in animals treated in the same way but exposed to only a static magnetic field, as well as those in animals injected with either untreated macrophages or cell-free seprexvir. “The speed at which the tumours shrunk (within 7 days) was quite remarkable, and we have not seen this previously with our cell-based therapies.”

Muthana concludes, “we would like to establish whether we can reduce the duration of MRT and still achieve the same therapeutic effect. We would also like to perform modelling to scale up and make predictions about possible use of this approach in humans.”

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