Monocytes as “Trojan horses” for chemo-drug delivery in brain tumor

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Abstract:
Ineffective drug delivery due to the blood-brain barrier (BBB) and poor tumor vascular distribution are major causes for poor glioblastoma response to chemotherapy. Accumulation of monocytes/macrophages (MC) into the brain tumor is a prominent characteristic of the brain tumor. Tumor recruited monocytes are thus proposed as a “Trojan horse”-like carrier to sneak chemodrugs across the BBB to the brain tumor. A nano chemodrug (Nano-DOX) was first fabricated based on doxorubicin and polyglycerol-functionalized nano-diamonds with a RGD targeting moiety. In vitro cell experiments were carried out and showed that MC were able to take up Nano-DOX and carry the drug across an artificial BBB. Mixed culture experiments next demonstrated that brain tumor cells promoted Nano-DOX-loaded MC to release the nano drug back into them. Brain tumor cells that accepted MC-released Nano-DOX increased expression of damage-associated molecular patterns (DAMPs) which are danger signals indicative of cell damage. Further, Nano-DOX-loaded MC were found to be able to infiltrate brain cancer cell spheroid and release drug. Finally, mice bearing orthotopic brain tumor xenograft were intravenously injected with Nano-DOX-loaded monocytes which in 24 hours were found in the brain tumor tissue and released drug. Conclusion: MC could be exploited to deliver Nano-DOX across the BBB into brain tumor.