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The therapeutic potential of polymersomes loaded with $^{225}$Ac evaluated in 2D and 3D in vitro glioma models

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Abstract

Alpha emitters have great potential in targeted tumour therapy, especially in destroying micrometastases, due to their high linear energy transfer (LET). To prevent toxicity caused by recoiled daughter atoms in healthy tissue, alpha emitters like $^{225}$Ac can be encapsulated in polymeric nanocarriers (polymersomes), which are capable of retaining the daughter atoms to a large degree. In the translation to a (pre-)clinical setting, it is essential to evaluate their therapeutic potential. As multicellular tumour spheroids mimic a tumour microenvironment more closely than a two-dimensional cellular monolayer, this study has focussed on the interaction of the polymersomes with U87 human glioma spheroids. We have found that polymersomes distribute themselves throughout the spheroid after 4 days which, considering the long half-life of $^{225}$Ac (9.9 d) [1], allows for irradiation of the entire spheroid. A decrease in spheroidal growth has been observed upon the addition of only 0.1 kBq $^{225}$Ac, an effect which was more pronounced for the $^{225}$Ac in polymersomes than when only coupled to DTPA. At higher activities (5 kBq), the spheroids have been found to be destroyed completely after two days. We have thus demonstrated that $^{225}$Ac containing polymersomes effectively inhibit tumour spheroid growth, making them very promising candidates for future in vivo testing.
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