^{19}F MOLECULAR IMAGING AGENTS RESPONSIVE TO IN VIVO SIGNALS

Andrew K. Whittaker, Kewei Wang, Cheng Zhang, Hui Peng, Kristofer J. Thurecht

Australian Institute for Bioengineering and Nanotechnology, and Centre for Advanced Imaging, The University of Queensland, St. Lucia, Queensland 4072, Australia. Email: a.whittaker@uq.edu.au

ABSTRACT

Recently there has been intense interest in the development of fluorinated molecules to allow tracking of therapeutic particles and cells in vivo. The motivation for this is the very high selectivity of the ^{19}F imaging experiment, since unlike in ^{1}H NMR imaging, the body does not contain a confounding fluorine background signal. In principle therefore, if doubly-tuned MRI coils are available, highly-selective ^{19}F images can be superimposed on high-resolution anatomical 1H images, thus allowing tracking of suitably-labelled cells or biomarker molecules. In this presentation I will describe the current status of magnetic resonance imaging agents with a focus on polymeric agents. This will define the motivation for the development of new partly-fluorinated copolymers which have outstanding potential as ^{19}F MRI imaging agents.[1-5]

In this paper we describe the development of several new classes of polymeric ^{19}F MRI agents with precisely controlled architecture and functionality. In the first generation of materials, amphiphilic copolymers PAA-b-p(nBA-stat-TFE(M)A) were prepared by ATRP of trifluoroethyl (meth)acrylate and n-butyl acrylate using PtBA as macroinitiator, followed by acidolysis in TFA/DCM. The block copolymers were micellized by slow addition of water from various solvents. MRI properties were measured for all systems and the relationship between structure and performance determined.[1,3] The second generation materials[2] arising from these studies are hyperbranched analogues constructed from similar monomers and made highly branched by incorporation of a crosslinking monomer during RAFT (or ATRP) synthesis. Excellent imaging performance was observed. More recently we have developed a series of linear, branched and star molecules incorporating the monomers N,N-dimethylaminoethyl methacrylate and poly(ethylene glycol) methacrylate which are responsive to external stimuli, for example local temperature, pH or ionic strength.[4,5] The ultimate aim of this work is to develop non-invasive methods for determination of the biology of tissue. Examples of application of these systems to a range of important diseases, such as melanoma, prostate cancer, malignant glioma and Alzheimer's disease will be presented.

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References:

[1]Peng, H.; Blakey, I.; Dargaville, B.; Rasoul, F.; Rose, S.; Whittaker, A.K. *Biomacromolecules* **2009**, 10, 374.
[2]Thurecht, K.J.; Blakey, I.; Peng, H.; Squires, O.; Hsu, S.; Alexander, C.; Whittaker. A.K. *J. Am. Chem. Soc.* **2010**, 132, 5336.
[3]Peng, H.; Thurecht, K.J.; Blakey, I.; Taran, E.; Whittaker, A.K. *Macromolecules* **2012**, 45, 8681.
[4]Wang, K.; Peng, H.; Thurecht, K.J.; Puttick S.; Whittaker, A.K. *Polym. Chem.* **2013**, 4, 4480.
[5]Wang, K.; Peng, H.; Thurecht, K.J.; Puttick S.; Whittaker, A.K. *Polym. Chem.* **2014**, Advance Article DOI: 10.1039/C3PY01311A.