

Nanotechnology and the differentiated medicine

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Pharmaceutical nanotechnology involves the formation of drug loaded nanoparticles from polymers, lipids and surface active agents¹. Such nanoparticles have been used to formulate approved drugs, which target a particular clinical problem, such as: avoiding cardiotoxicity in the case of Doxil and avoiding hypersensitivity reactions in the case of the excipient used in Abraxane^{2,3}. To gain approval, provide real patient benefit and encourage prescribing, it is essential that nanomedicines are sufficiently differentiated from a clinical perspective and preclinical data should support such potential differentiation, prior to proceeding to expensive clinical testing. An increase in bioavailability, for example, is often an insufficient driver for clinical development.

Over the last two decades, we have designed a large variety of self assembling polymers⁴⁻⁶ and peptides^{7,8} and used these to develop nanomedicines, which may be administered via the intravenous⁷⁻⁹ oral¹⁰⁻¹² and intranasal¹³ routes. Some of these preclinical stage nanomedicines have already demonstrated that they are well differentiated in a manner that is relevant to their clinical use. These nanomedicines show advantageous alterations in drug biodistribution and additional studies have illuminated some interesting mechanisms^{7,12,14}. These nanomedicines will be discussed in the talk. Additionally diagnostic platforms are now being investigated within our laboratory¹⁵.

References

- 1 Uchegbu, I. F., Schätzlein, A. G., Chen, W. P. & Lalatsa, A. *Fundamentals of pharmaceutical nanoscience*. (Springer, 2013).
- 2 Sleep, D. Albumin and its application in drug delivery. *Expert Opin Drug Deliv* **12**, 793-812, doi:10.1517/17425247.2015.993313 (2015).
- 3 Gabizon, A., Shmeeda, H. & Barenholz, Y. Pharmacokinetics of pegylated liposomal doxorubicin - Review of animal and human studies. *Clin. Pharmacokinet.* **42**, 419-436 (2003).
- 4 Wang, W., McConaghy, A. M., Tetley, L. & Uchegbu, I. F. Controls on polymer molecular weight may be used to control the size of palmitoyl glycol chitosan polymeric vesicles. *Langmuir* **17**, 631-636 (2001).
- 5 Brown, M. D. *et al.* Preliminary characterization of novel amino acid based polymeric vesicles as gene and drug delivery agents. *Bioconjug. Chem.* **11**, 880-891 (2000).
- 6 Cheng, W. P. *et al.* Polyelectrolyte nanoparticles with high drug loading enhance the oral uptake of hydrophobic compounds. *Biomacromolecules* **7**, 1509-1520 (2006).
- 7 Mazza, M. *et al.* Nanofiber-based delivery of therapeutic peptides to the brain. *Acs Nano* **7**, 1016-1026, doi:10.1021/nn305193d (2013).
- 8 Lalatsa, A. *et al.* Chitosan amphiphile coating of peptide nanofibres reduces liver uptake and delivers the peptide to the brain on intravenous administration. *J Control Release* **197**, 87-96, doi:10.1016/j.jconrel.2014.10.028 (2015).
- 9 Fisusi, F. A. *et al.* Lomustine Nanoparticles Enable Both Bone Marrow Sparing and High Brain Drug Levels - A Strategy for Brain Cancer Treatments. *Pharm Res* **33**, 1289-1303, doi:10.1007/s11095-016-1872-x (2016).
- 10 Serrano, D. R. *et al.* Oral particle uptake and organ targeting drives the activity of amphotericin B nanoparticles. *Mol Pharm* **12**, 420-431, doi:10.1021/mp500527x (2015).
- 11 Siew, A. *et al.* Enhanced oral absorption of hydrophobic and hydrophilic drugs using quaternary ammonium palmitoyl glycol chitosan nanoparticles. *Molecular Pharmaceutics* **9**, 14-28, doi:10.1021/mp200469a (2012).
- 12 Soundararajan, R. *et al.* Direct in vivo evidence on the mechanism by which nanoparticles facilitate the absorption of a water insoluble, P-gp substrate. *Int J Pharm* **514**, 121-132, doi:10.1016/j.ijpharm.2016.08.013 (2016).
- 13 Godfrey, L. *et al.* Nanoparticulate peptide delivery exclusively to the brain produces tolerance free analgesia. *J Control Release* **270**, 135-144, doi:10.1016/j.jconrel.2017.11.041 (2017).
- 14 Garrett, N. L., Lalatsa, A., Uchegbu, I., Schätzlein, A. & Moger, J. Exploring uptake mechanisms of oral nanomedicines using multimodal nonlinear optical microscopy. *J Biophotonics* **5**, 458-468, doi:10.1002/jbio.201200006 (2012).
- 15 Hobson, N. J. *et al.* Clustering superparamagnetic iron oxide nanoparticles produces organ-targeted high-contrast magnetic resonance images. *Nanomedicine (Lond)* **14**, 1135-1152, doi:10.2217/nmm-2018-0370 (2019).