at six months after the biological treatment were identified to be significant factors predicting destruction of the large joints at two years.
http://dx.doi.org/10.1016/j.jot.2016.06.098

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SYNTHESIS AND CHARACTERIZATION OF AN HSP27-TARGETED NANOPROBE FOR *IN VIVO* PHOTOACOUSTIC IMAGING OF EARLY NERVE INJURY

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Objective: Imaging is routinely used for clinical and diagnostic purposes, but techniques capable of high specificity and resolution for the early detection of nerve injury are still limited. Photoacoustic imaging (PAI), a novel imaging modality that combines the merits of laser and ultrasound, offers high contrast, high resolution, and satisfactory tissue penetration. So we aim to exploit the novel PAI with functionalized targeted probe for detection of early nerve injury.
Methods: After the sciatic nerve was crushed, Western blot observed that the expression level of heat shock protein 27 (HSP27) upregulated within 3 to 7 days of nerve injury. HSP27 was used as a specific marker for early nerve injury, we conjugated gold nanorods (GNRs) to HSP27-specific antibodies to generate a nanoprobe as GNR-HSP27Abs. The spectroscopy and zeta potential detected the characterization of GNR-HSP27Abs. The non-targeting GNRs or targeting GNR-HSP27Abs were injected into the site of nerve injury 3 and 7 days after surgery. The nanoprobe of GNR-HSP27Abs targeted to the nerve injury and detected by near-infrared PAI.
Results: HSP27 was weakly expressed in the intact sciatic nerves in uninjured animals. After nerve injury, HSP27 expression increased significantly in the injured nerve. The absorption spectroscopy, fluorescence spectroscopy, FTIR spectroscopy and zeta potential confirmed that the HSP27Abs was well-coupled to GNRs and was indicative of successful nanoprobe synthesis. *In vitro* and *in vivo* PAI acquired 12 hours after local administration of GNR-HSP27Abs demonstrated that the nanoprobe can distinguish between injured and uninjured nerves in rats. The toxicity assay results showed no cytotoxicity against human cell lines and no such inflammatory reactions occurred in these injection regions.
Discussion: High expression of HSP27 in early nerve injury was confirmed by our experiments. GNRs-HSP27Abs as molecular targeted probes possess a high absorption peak at the NIR wavelength, which allows for imaging with deeper penetration of laser light and lower intrinsic background noise. Due to the high optical absorption and targeting efficiency of GNRs-HSP27Abs, PAI was successful in detecting early nerve injury within 3—7 day. The toxicity test results revealed that a single imaging dose of GNRs or GNRs-HSP27Abs provided satisfactory biosafety for clinical application.
Conclusion: Taken together, these findings expand the application of nanoprobe-targeted PAI to the detection of injured nerves, and prompt further development of this novel imaging platform for clinical application.
Acknowledgements: This research was supported by the National Natural Science Foundation of China (81271619), the National High Technology Research and Development Program of China (2015AA020901), the Science and Technology Planning Project of Guangdong Province (2013B090500122), and the Guangdong Natural Science Foundation (S2013020012646).
http://dx.doi.org/10.1016/j.jot.2016.06.099