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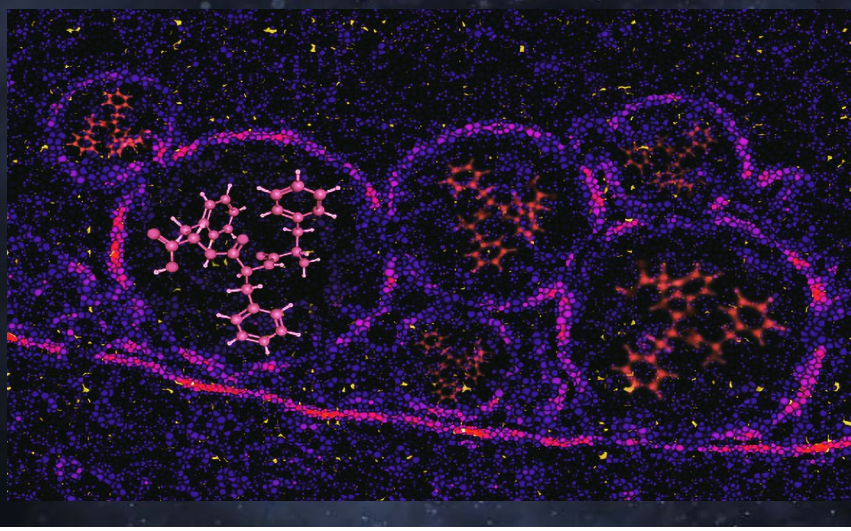


Magma bioharmonophores

"Spherism" rendition of triphenylalanine bioharmonophores captured by Transmission Electron Microscopy

Image © Konstantinos Kalyviotis

Bioharmonophores for biomedical precision imaging

Biodegradable, second-harmonic generating nanoprobes for targeted, high-resolution *in vivo* tumour imaging

The technology is a biodegradable optical imaging nanoprobe, termed bioharmonophore, that generates a strong second harmonic generating (SHG) signal which can be used for diagnostic and therapeutic purposes in biomedical imaging.

Proposed use

SHG is a non-linear optical process in which two photons directed at a non-centrosymmetrical media (i.e. material lacking a generalized mirror symmetry) combine to form a new photon with twice the energy. With its narrow signal profile, the SHG signal allows biomedical imaging with high signal-to-noise ratio and spatiotemporal resolution.

Thus, bioharmonophores can provide high resolution optical-signal for diagnostics and therapy of cancer. *In vivo* studies with zebrafish embryos proved high detection sensitivity of targeted cancer cells.

Problem addressed

Existing optical imaging probes such as bioluminescent and fluorescent probes have autofluorescence issues which often result in low signal-to-noise ratios and poor photostability.

Inorganic SHG nanoprobes were previously proposed as superior imaging probes for *in vivo* imaging. Unlike fluorescent probes, the SHG signal does not bleach or blink and the signal does not saturate with increasing illumination intensity. High probe sensitivity made SHG nanoprobes promising clinical and preclinical imaging probes, However high stability of inorganic SHG nanoprobes may cause long term toxicity concerns *in vivo.*

Benefits

- Achieves **outstanding signal contrast in tissue** due to absence of background signal
- Benefit from **superior photostability** than existing imaging probes
- Takes advantage of a **unique biocompatible and biodegradable nature** that does not elicit an immune response and is metabolised *in vivo*
- Utilises **great long-term stability and clinically relevant bioavailability** for *in vivo* imaging despite their biodegradability
- **Eliminates *in vivo* toxicity concerns** in long-term applications
- Ensures **cheap, reproducible, scalable production** of bioharmonophores
- Guarantees **highly efficient and straightforward functionalisation** of bioharmonophores for cancer targeting

Dr Marika Reay

Senior Executive

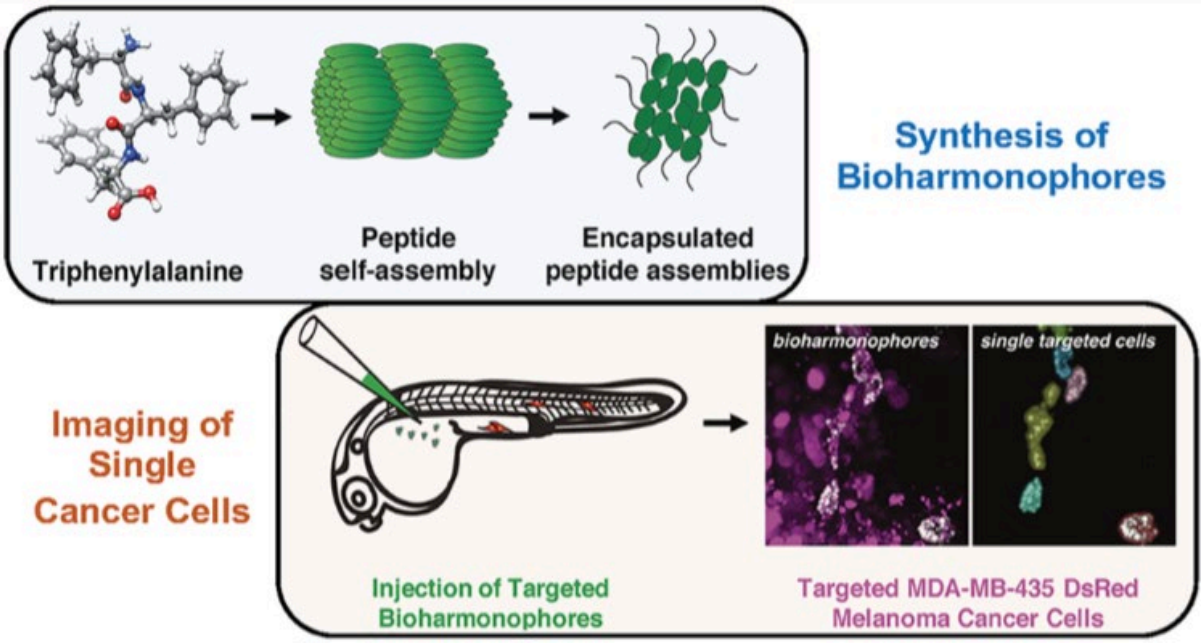
Industry Partnerships and Commercialisation - Engineering

e: m.reay@imperial.ac.uk

t: +44 (0)20 759 46867

Technology reference: 10443

Imperial College London



Technology overview

This technology covers biodegradable nanoprobes, second harmonic generating bioharmonophores. Bioharmonophores are composed of both biodegradable and biocompatible components, self-assembling triphenylalanine peptides that are coated with poly(L-lactic acid) (PLLA) polymer. They can be readily surface functionalised with tumour targeting peptides to target cancer cells with high specificity. Optical properties and targetability of bioharmonophores make them ideal diagnostic imaging tools. Despite their biodegradable nature, bioharmonophores have high *in vivo* stability to perform their function.

Intellectual property information

EP3518986 A1 – BIODEGRADABLE, SECOND-HARMONIC GENERATING NANOPROBES FOR BIOMEDICAL IMAGING APPLICATIONS

Link to published paper(s)

Sonay, A. Y. *et al.* (2021) 'Biodegradable Harmonophores for Targeted High-Resolution In Vivo Tumor Imaging', *ACS Nano.* doi: 10.1021/acsnano.0c10634.

Inventor information

Dr Periklis Pantazis

Reader in Advanced Optical Precision Imaging, Imperial College London, UK

Dr Ali Yasin Sonay

Research Scholar, Memorial Sloan Kettering Cancer Center, USA

Assoc. Prof. Dr. Daniel Crespy

Head of Colloid Organic Materials Laboratory, Department of Materials Science and Engineering, Vidyasirimedhi Institute of Science and Technology, Thailand

Prof Dr Katharina Landfester

Director, Department of Physical Chemistry of Polymers, Max Planck Institute for Polymer Research, Germany