Development of an *In Vivo* Screening Platform for Polymeric Drug Delivery Libraries

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Background: Polymeric nanoparticles are useful tools to address the challenge encountered in delivering drugs to targets without toxicity to non-diseased tissues. This is because the pharmacokinetics of drug delivery is more controlled, whilst allowing targeting of organs or tissues. However, due to the current high-throughput screening methods in drug discovery and the complex biology of humans many of the new polymeric drug delivery systems are poorly soluble in water and exhibit low bioavailability. Therefore, in this work, we sought to synthesize nanoparticles (NPs) of Poly (glycerol adipate) (PGA) and its novel derivatives as biocompatible drug delivery systems while developing a drug screening platform with *Caenorhabditis elegans,* one of the most completely understood animals on the planet.

Glycerol-based polymers are promising drug delivery systems, due to their enhanced self-assembly and a readily functionable pendant hydroxyl group. Drug-like molecules have been added to the backbone of the Poly (glycerol adipate) (PGA), a glycerol-based polymer and formulated into polymeric pro-drugs that have shown good efficacy. Nanoparticles produced using these polymers are biodegradable to prevent bioaccumulation.

C. elegans, a free-living nematode, is a model organism, that has been used to study many human processes and diseases due to high genetic homology with humans. Nematodes allow fast and efficient screening of drug leads at low costs before progression to later development stages. *C. elegans,* therefore present as a useful tool for replacing, reducing and refining the use of animals in research while addressing challenges encountered in translating new pharmaceutically active compounds into therapeutics such as understanding of their pharmacokinetics and bioavailability.

Methods: NPs were synthesized by nanoprecipitation. Synchronised adult worms were challenged to PGA and its derivatives at concentrations of 0.5 mg/mL with M9 buffer and ethanol (20 %) as viable and non-viable controls.

Results: The polymers self-assembled under aqueous conditions without surfactants or additives. When *C. elegans* was challenged to the polymeric nanoparticles of PGA and its derivatives, the worms showed viability, evidenced by motility and production of progeny after 48 hours. The results are indicative of *in vivo* biocompatibility as no statistically significant differences were found between the polymers and viable control.

Conclusions: We have shown the nanoparticles of PGA and its derivatives are biocompatible and promising drug delivery systems. This work has the potential to develop various polymeric drug delivery systems by modifying functionalities. Whereas *C. elegans* will be developed as a comprehensive screening platform to study not only biocompatibility, but also bioactivity and bioavailability of the polymeric nanoparticles before and after loading with model drugs. This work is expected to culminate in a library of polymeric nanoparticles some of which may be useful drug delivery systems as well as a simple and inexpensive biological screening platform that helps translate leads into therapeutics.