05 Enabling translational nanomedicine and nanoMedical technology to overcome the valley of death in innovation

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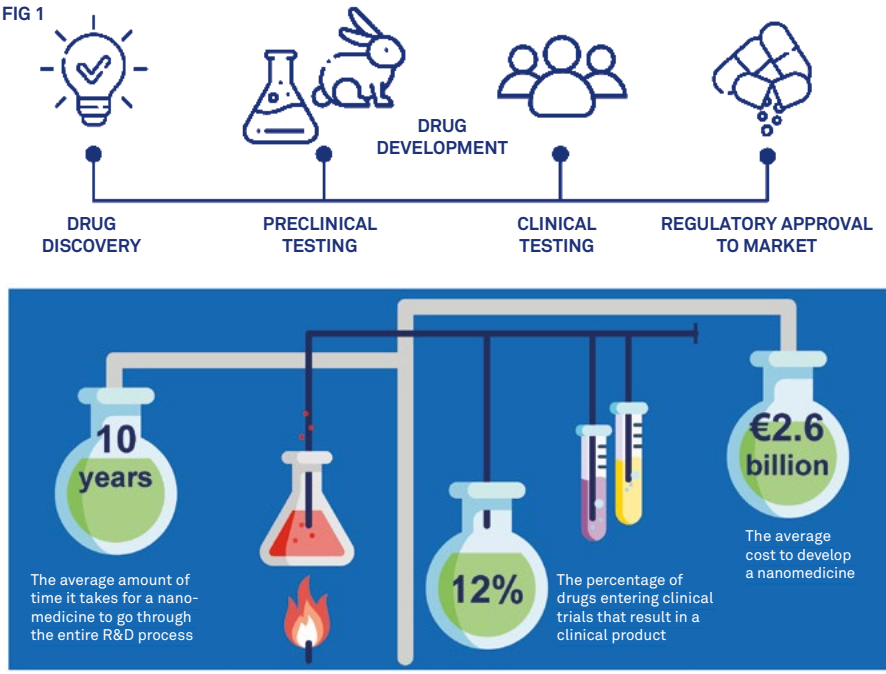
The translation of Nanomedicines or nano-medical-technologies, into clinically approved products is a complex and challenging process but one with unquestionable patient benefits and relatively minimal side effects. The improved survival prolongation and quality of life that these nanotechnology-enabled products contribute to justify the long and complex development from bench to bedside.

This development includes the 'valley of death', which in technology transfer is the metaphor often used to describe the gap between academic-based innovations and their commercial application in the marketplace (see Figure 1).

The most recent global success is the COVID-19 nanovaccine which is made of a lipid nanoparticle encapsulating the messenger RNA vaccine against SARS-CoV-2. These vaccines came about thanks to decades of nanotechnology-enabled drug development in cancer nanomedicine which have seen the approval of several very successful clinical products including: Ambisome®, Doxil®, Abraxane®, Onyvide®, Myocet®, and most recently the nucleic acid-based drug Onpattro®. Further contribution from nanotechnology, in the rapid testing against SARS-CoV-2 is evidenced by the development of rapid antigen based diagnostic assays, based on gold nanoparticles in a lateral flow assay.

My work over the past decade has contributed to the development of several methodologies such as standard operating procedures (SOPs) and quantitative techniques, aimed at understanding and quantifying the key "nano" properties of several potentially breakthrough nanomedicines or medical technologies. These methodologies are applied primarily to cancer, but also inflammatory and infectious diseases such as COVID-19.

FIG 1



3 Main Reasons

1. Preclinical research takes too long.
2. Failure rates are too high.
3. Drug discovery and development is too costly.

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FIG 1 – Translational Nanomedicine, schematic description of drug discovery from idea to regulatory approval, cost, attrition, and main reasons for translational failure. The valley of death in innovation is when the "idea" is not reaching sufficient scientific and financial support to make it into advanced clinical investigation or trials. (image courtesy of D. Movia, LBCAM, TCD)

Tackling the fingerprinting of the critical quality properties, or attributes, conferred to a nano-pharmaceutical or medical device, is one of the steps required during the translational process towards the clinical investigation. Building up reproducible, repeatable and transparent pre-clinical dataset is therefore a fundamental step towards the regulatory approval for a product.

For the past five years, I have been part of a large joint effort between the European Nanomedicine Characterisation Laboratory (EUNCL) and the U.S. Nanotechnology Characterisation Laboratory (USNCL) which established a preclinical testing cascade with validated SOPs supporting the preclinical assessment of promising nanotechnology-enabled products. Such effort has been recently expanded in the medical technology research area, in a very large collaborative effort, supported by the European Union programme Horizon2020, under the creation of an Open Innovation Test Beds (OITB) aimed at supporting early developing or high-risk high-gain nano-medical technologies.

Bridging the valley of death – Within the Trinity Translational Medicine Institute (TTMI), I am leading the academic and industrial research in the Laboratory for Biological Characterisation of Advanced Materials (LBCAM), providing pre-clinical characterisation, translational and regulatory guidance to national and international collaborators and customers. This involves assisting both SMEs and multinationals as technical R&DI infrastructure or OITB.

Such exposure has brought me to the conceptualisation of a preclinical toolbox for the assessment of complex nanotechnology-enable medicine and medical technology. The development of orthogonal physicochemical characterisation techniques and 3-dimensional in vitro models has brought my research to be widely recognised and followed in bridging, the so-called translational valley of death in innovation.

My lab has recently assisted, after a nine-year pan-European fruitful collaborative work under two EU programme projects, the translation of first clinical investigation for superparamagnetic nanoparticles used for hyperthermia treatment against pancreatic cancer (see Figure 2). More recently, we are assisting the development of new therapeutics based on extracellular vesicles.

FIG 2

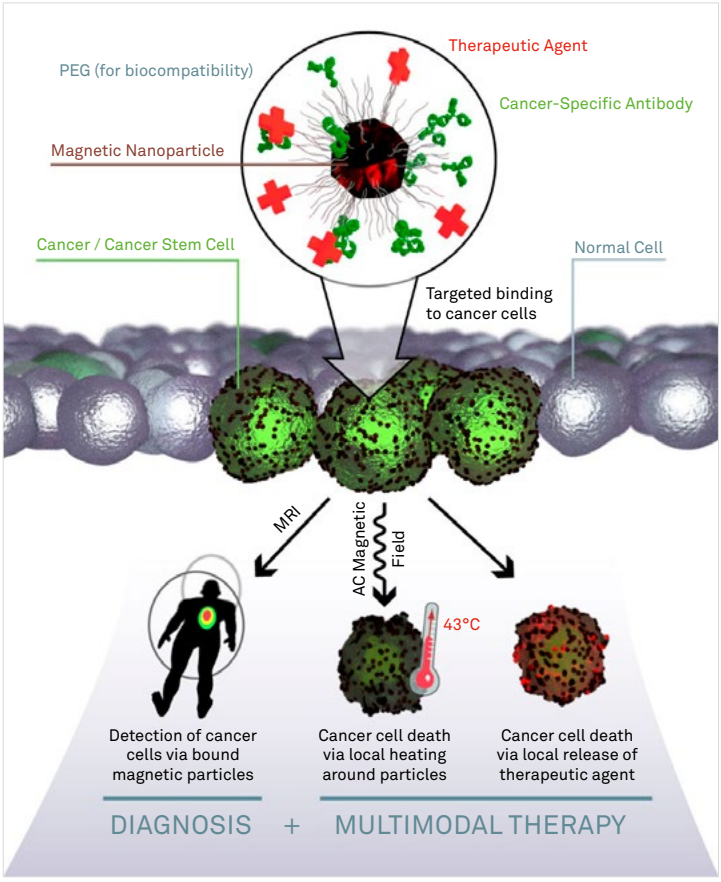

FIG 2 – Schematic description of minimally invasive multimodal treatment approach using nanoparticles and therapeutic agent for the treatment of advanced pancreatic cancer. Magnetic nanoparticles are injected in the tumor (also acting as diagnostics probes), followed by the application of an alternating magnetic field to enhance the therapeutic effect of the existing agents. The locally increased temperature combined with the action of the therapeutic agent will lead to the selective cancer cell death. (image courtesy of D. Crotty, LBCAM, TCD)