iNANO lecture of the week
- open to all

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Title: Polymer Therapeutics as Nanomedicines: their design, preclinical development and medical use

Location: Auditorium 3rd floor, Dept. of Physics, Friday, January 12 at 10:15-11:00.
Coffee and bread will be served from 10:00

Abstract:
Nanomedicines
Recently the a Forward Look on Nanomedicine sponsored by the European Science Foundation defined the field in the following terms "Nanomedicine uses nano-sized tools for the diagnosis, prevention and treatment of disease and to gain increased understanding of the complex underlying pathophysiology of disease" (1). Within this framework 'nanomedicines or nanopharmaceuticals were defined as "the science and technology of nanometre size scale complex systems, consisting of at least two components, one of which being the active ingredient", and acknowledged that nanopharmaceuticals can be developed either as drug delivery systems or biologically active drug products. In this field the concept of nanoscale was seen to range from 1 to 1000 nm. Over the last three decades European R & D has been at the forefront of development of liposomes nanoparticles, antibodies and their conjugates, polymers conjugates, molecular medicine (including proteins), aspects of nanobiotechnology, and emerging technologies in the areas of tissue engineering and repair and stem cell research (2,3).

Polymer Therapeutics
The descriptor "polymer therapeutics" is an umbrella term that we coined to describe polymeric drugs, polymer-drug conjugates, polymer-protein conjugates, polymeric micelles to which drug is covalently bound, and multi-component polyplexes being developed as non-viral vectors (4). There is considerable hope that such bio-nanotechnologies, designed with an appreciation of the patho-physiology of normal and diseased tissue, using advanced polymer chemistry and precision engineering at a molecular level, will help realise the full therapeutic potential of the post-genomics era. From the industrial standpoint, these nanosized medicines are more like new chemical entities than conventional 'drug delivery systems or formulations' which simply entrap, solubilise or control drug release without resorting to chemical conjugation. Conceptually, polymer therapeutics share many features with other macromolecular drugs and the versatility of synthetic chemistry, which allows tailoring of molecular weight, addition of biomimetic features. Over the last decade we have seen the transfer of several polymer-protein conjugates to market (including PEG-asparaginase, and PEG-GCSF) (5) and > 11 polymer-anticancer drug conjugates into clinical development (6,7). Initially the anticancer drug conjugates incorporated well-known chemotherapeutic agents such as doxorubicin, paclitaxel and camptothecins, and the clinically most successful have been rationally designed in respect of their molecular weight, drug content and most importantly the polymer drug linker. Now that clinical proof of concept is established we are trying to develop more sophisticated second generation systems that will exploit either tumour, or tumour vasculature – specific targeting, improved delivery of novel natural product anticancer agents and also polymer-drug combinations (8). Novel polymer architectures (e.g. dendrimers) (9,10), biodegradable polymeric carriers incorporating the drug via pendant linkage or as a component of the polymer main-chain are being explored (11). Whilst the first generation polymer-drug conjugates have used lysosomotropic delivery as the route of intracellular delivery, bioreponsive, endosomolytic polymers provide an opportunity for intracytoplasmatic delivery of proteins (e.g. non permanent toxins) (12). Constructs are also being explored as a means to improve tissue repair (13). The characterisation of nanosized constructs requires development of new techniques and lately we have been developing SANS for this purpose (14).

Many classes of polymer therapeutic are now at the clinical stage of development or in the market. This is just the beginning ! (15)
1. European Science Foundation's Forward Look on Nanomedicine (2005) www.esf.org
2. Duncan R (2005) Targeting and intracellular delivery of drugs. In: Encyclopaedia of Molecular Cell Biology and Molecular Medicine, R. A. Meyers (Ed); WILEY-VCH Verlag, GmbH & Co. KGaA, Weinheim, Germany, pp 163-204