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Biomaterials in the nano-era

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This article is a brief summary of my plenary talk at the World Biomaterials Congress in Chengdu, Sichuan, China, June 1–5, 2012. It highlights the trend to design and develop biomaterial implants and devices that are more compact and more efficient, as they "shrink" from the macro- to the micro- and down to the nano-scale.

biomaterials, nano-era

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Biomaterials are composed of many different types of materials and their combinations. The different types of materials include synthetic polymers, metals, ceramics, glasses and carbons. They also include natural materials, such as polymers of natural origin, and animal and human tissues and organs. Implants and devices may be constructed of one or a combination of such biomaterials. The recent trend in the past decade is to design and construct medical devices and instruments to be as compact and efficient as possible. This has led to the "shrinking" of numerous biomaterial devices and implants and their components from the macro- to the micro- to the nano-scale (Figure 1). This includes drug delivery systems, diagnostic assays, cell culture platforms and tissue engineering scaffolds, molecular separation systems, and imaging and imaging/therapeutic feed-back systems that may image or sense and respond with delivery of one or more therapeutic drugs. This article briefly highlights some nano-scale examples of these biomaterial applications, with several figures from my plenary talk.

1 Drug delivery systems (DDS)

The field of drug delivery systems (DDS) represents a good example of how such devices have shrunk from macroscopic to microscopic to the nano-scale. Figure 2 shows a list of examples of such DDS, descending from the macroscopic systems, such as skin patches and implanted tubes of contraceptive drugs, that were approved for clinical use in the 1980s, to the microscopic systems of degradable microparticles of PLGA approved in the 1990s, and down to the nano-carriers that are actively being pursued even today. As one of the earliest examples of micro-scale DDS, surface-coated DDS have been in the clinic since the 1960s. There are many nanocarriers that have been developed in the past 50 years, but most that are used clinically have only been approved in the past 15 years (an exception is PEGylation of drugs and drug carriers, which entered the clinic in the mid-1980s). A list of nanocarriers is given in Figure 3 along with schematic cartoons of some of them. Many of the nano-scale DDS have also been conjugated with targeting ligands to stimulate their uptake into target cells. Despite this long list of nanocarriers, there are only a limited number of polymer compositions that have been approved for use in nano-scale DDS ("approved" is meant to include clinical trials as well as approved for clinical use). The more recent polymeric nanocarriers are being designed to biodegrade in order to enhance their elimination from the body via the kidneys after the drug has been delivered [1–12].

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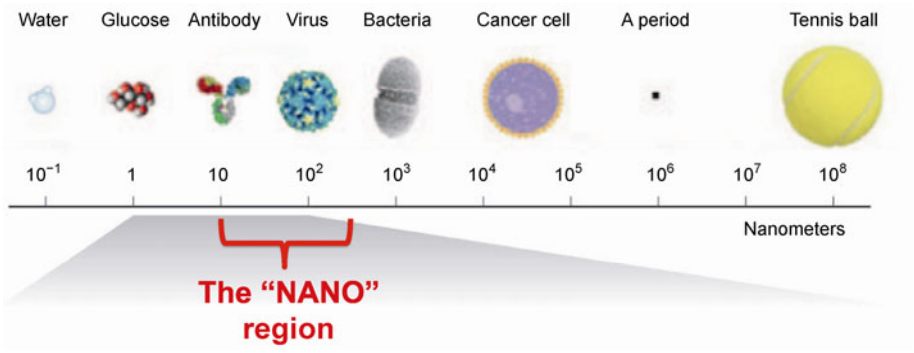

Figure 1 (Color online) Defining the "NANO" region.

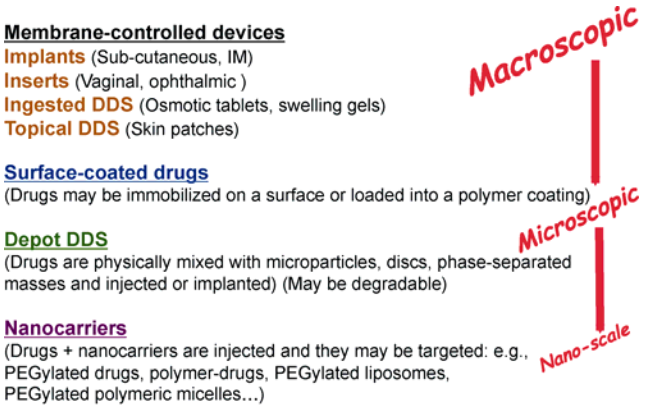

Figure 2 (Color online) Size evolution of controlled drug delivery systems (DDS) into the clinic from the 1960s to the present.

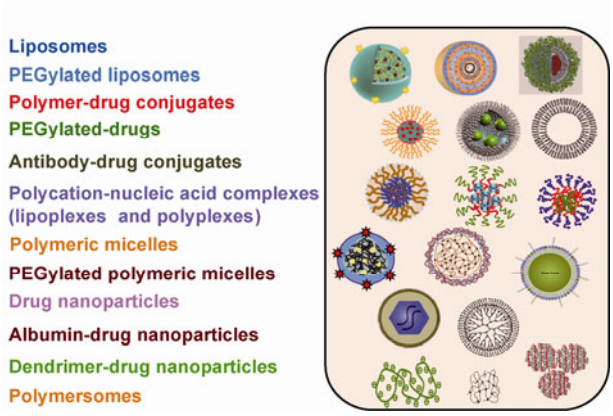

Figure 3 (Color online) Drug nanocarriers (1970s–today).

2 Diagnostic devices

There is much current activity to develop new micro-scale and nanoscale assay devices that are rapid, inexpensive, disposable, and also "semi-quantitative", i.e. able to quickly diagnose the probable cause of a fever, in order for treatment to begin right away. Many of the latest systems are paper-based, lateral flow strips that evolved from the original glucose dip-stick. Figure 4 shows one example of magnetic and gold "smart polymer" nanoparticles (NPs) that may be used in such devices. Much of the current work has been stimulated and supported by the Bill and Melinda Gates Foundation. Paper diagnostics have also been separately and individually promoted as "Diagnostics for All" by Whitesides and co-workers [14] of Harvard University. A very recently reported device is said to be able to sequence DNA by drawing the DNA through a nano-pore device; it is called the "Oxford Nano-Pore" device [13–19].

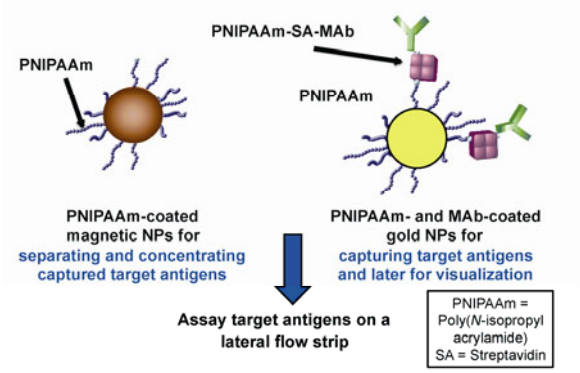

Figure 4 (Color online) Smart PNIPAAm-coated magnetic nanoparticles (NPs) and smart capture gold NPs for lateral flow strip diagnostic assays [13].

3 Cell culture platforms

Figure 5 shows schematically the evolution of cell culture platforms from the macroscopic to the microscopic and down to the nano-scale. Okano and co-workers [21,22] radiation-grafted the thermally-responsive polymer, PNIPAAm to cell culture surfaces, and they cultured confluent cell sheets on those surfaces at 37°C. They lifted the cell sheets off the surfaces by lowering the temperature to room temperature, and then successfully applied the cell sheets to repair of corneal and cardiac tissues. Nano-scale fibers are also being applied to the design of tissue engineering scaffolds, an exciting and rapidly expanding field [20–27].

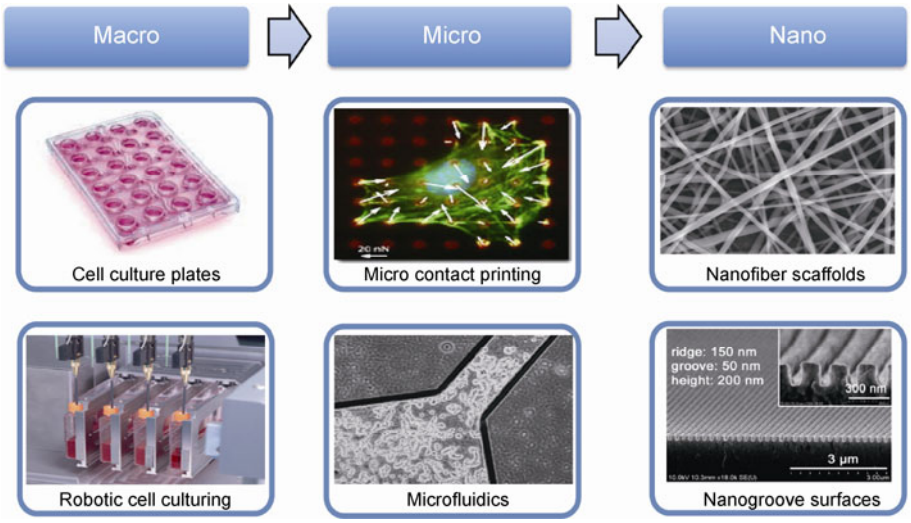

Figure 5 (Color online) Evolution down in size (and up in area) of cell culture platforms [20].

4 Molecular separation systems

Separation of small toxins (e.g. urea, uric acid and creatinine) from blood is essential for patients undergoing dialysis for kidney failure (http://en.wikipedia.org/wiki/Artificial_kidney). Figure 6 shows the hollow fiber separation system that evolved from the rotary dialyser and the coil dialyser.

Figure 6 (Color online) Evolution of the rotary and coil dialysers to the "nm thin skin" hollow fiber artificial kidney.

This system is known as the hollow fiber artificial kidney (HFAK) dialyser. The "thin skin" hollow fiber membrane evolved from water desalination research and development, and it has a nm scale thin skin on the inside of the hollow fiber. Nano-porous membranes have also been developed for rapid dialysis, and the pore sizes in those membranes are only a few nm in diameter [28].

5 Imaging and imaging + therapeutics ("the-ranostics") systems

These interesting combination diagnostic and delivery systems are described in Figure 7. It is clear that applications of many different NPs are involved in such systems, especially quantum dot fluorescence emitters and their nano-technologies. There is much work going on to develop useful "feed-back" systems combining imaging and delivery systems with NPs such as Quantum Dots [29–46].

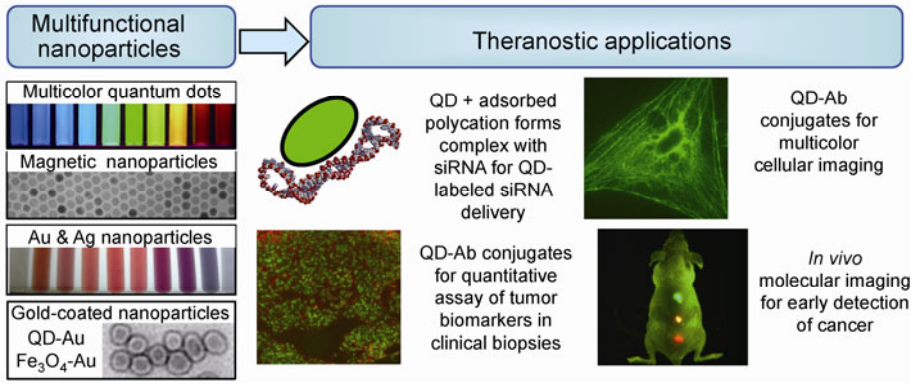

Figure 7 (Color online) Quantum dots (QDs), magnetic NPs, gold and silver NPs & gold-coated QDs have many diagnostic & therapeutic uses [38–45].

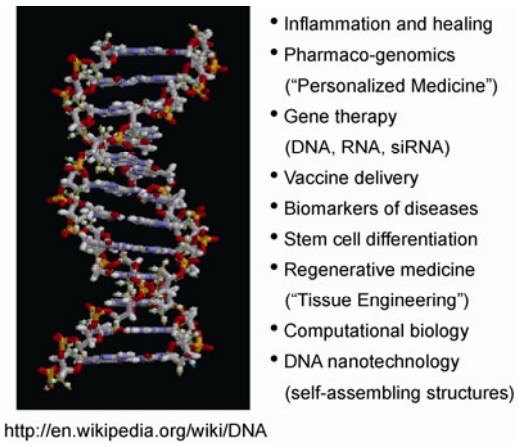

Figure 8 (Color online) DNA will be even more involved in the future in biomaterial "pico-technology".

6 DNA will be critical to future nano- and pico-scale applications

DNA is likely to be the key molecule in the future nano-scale applications. This is presented in Figure 8. Useful medical predictions will be applied to individual genomic assays and will be based on computer analysis of DNA data from large populations. This rapidly expanding and important field is called pharmacogenomics, or "personalized medicine" (http://en.wikipedia.org/wiki/Pharmacogenetics; http://www.pharmacogenomicsforum.org/files/2P17AlexParker.pdf:2010).

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