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What's up in Nanomedicine?

From now on, this column will appear in each issue of the *European Journal of Nanomedicine* that I have been recently appointed to as Assistant Managing Editor. The column's purpose is to present novel and significant developments within Nanomedicine excerpted from recent publications, introducing new relevant books, informing our readers about upcoming conferences and other related issues. We very much appreciate your feedback on our column or other related issues and to receive proposals of a topic to be argued about by using the email address below. Please keep in mind that the publications discussed here are selected exemplarily among many other excellent publications. This also applies for the mentioned books and conferences or events.

Let me begin by briefly introducing myself. My professional life started in the fields of clinical genetics; DNA research and diagnostics at the Academic Medical Centre in Amsterdam (the Netherlands) in 1996. In 2005, I changed my professional field into the microfluidic and nanofluidic world at the University of Twente in Enschede (the Netherlands) and investigated the electrokinetic transport behavior of single DNA molecules in nanoslits on chips. For this I received my PhD in 2009, and continued the next 2 years at the Korean Institute of Science and Technology (Saarbrücken, Germany) with nanodroplet pseudocrystals in microfluidic chips. Meanwhile, I also worked for the Mesa Institute for Nanotechnology (Twente University), who were then setting up their BioNano Laboratory. In November 2012, I joined the multidisciplinary NanoMedicine Group of Prof. Patrick Hunziker, working for the DiscoGnosis project (www. discognosis.eu).

Publications digest

Novel peptide nanomedicine for diabetes and the use of PEG

Banerjee and coworkers (1) presented a novel peptide nanomedicine for the treatment of pancreatogenic diabetes. This type of diabetes is the result of pancreatic diseases and accounts for about 8% of all diabetic patients. It is known that the hormone pancreatic polypeptide increases the expression of the insulin receptors in the liver, however, the biological half-life of the peptide is rather short and it has the property to form aggregates in aqueous media. In this investigation sterically stabilized micelles (SSM) were used. The micelles used were polyethylene glycolated (PEGylated) posholipid micelles, which have already been proven to increase the half-life of several peptides in vivo. In addition, these micelles are capable to prevent aggregation in aqueous media and to deliver at desired sites. The investigators already demonstrated the capabilities in vitro and with this publication they presented the effectiveness of the pancreatic peptide-SSM in improving glucose tolerance and insulin sensitivity compared to free peptide. They demonstrate that pancreatic peptide-SSM has an equivalent therapeutic efficacy as metformin, which is a commonly used medicine for diabetes. They postulate that the pancreatic peptide-SSM is due to its size, passively targeted to its site of action and that the pancreatic peptide in SSM is well protected against proteolytic degradation in vivo. The authors note that the use of this nanomedicine can be considered as safe as both the pancreatic polypeptide as PEGylated phospholipids, are approved by the Food and Drug Administration for the use in humans.

At this point, I would like to mention the editorial of Garay and coworkers (2). It is generally assumed that PEG is non-immunogenic and non-antigenic, however, animal studies clearly showed that PEGylated agents are capable of eliciting the formation of antibodies against PEG. When this occurs in humans, it might limit the therapeutic efficacy of several currently used drugs. Of even more concern might be the recent finding of anti-PEG antibodies in healthy blood donors, which had been found in greater numbers when compared to the 0.2% of two decades earlier. Garay and coworkers suggested that the cross-reactivity between anti-PEG and the different PEGylated proteins should be investigated in vitro and evaluated in animal models and the approved compounds should be carefully examined in humans.

Alternative methods are also mentioned. For example the half-life extension technology (XTEN), which is based on the substitution of a polypeptide chain of varying length. These are composed of alanine, glutamic acid, glycine, proline, serine and threonine and are proven to be safe and poorly immunogenic in a number of animal species. Other available methods are in the early phase of their development. To conclude, the use of PEG might not be as harmless as was assumed earlier, as discussed in the publication of Gary and coworkers. Therefore, it should not be considered as safe and the side effects should be carefully investigated in both animal models and in a later stage in patients. Note that immunogenic and antigenic reactions might also depend on the type of PEG-complex.

New imaging method

Imaging nanoparticles or nanocarriers loaded with drugs from the start to the site of delivery is highly important when developing nanomedicines. El-Sayed and coworkers (3) presented a novel method for in vivo imaging of the biodistribution of single wall carbon nanotubes (SWNTs), labeled with a recombinant thermo-stable Japanese firefly luciferase protein (LcL). LcL is coupled in two different ways to the SWNTs with no intermediate linker entities such as phospholipids. The primary amine groups present on the N-terminus of the polypeptide chain or on the lysine side chain of the LcL and the oxygen-containing functional groups on the surface of the SWNTs are used for the coupling. The first method is the conjugation of the LcL to the oxidated SWNTs using carbodiimide chemistry and the second method was the physical adsorption process. The two different species of SWNTs were investigated on the effect of the mode of attachment by using an in vitro imaging system. The fluorescent signal of the chemically coupled LcL-SWNT is quenched when comparing to the physically coupled LcL-SWNT, however, the catalytic activity is not eliminated as was shown when the carbonanotubes were loaded with doxorubicin (antitumor agent). With this investigation, they have shown that LcL activity can be maintained when these are properly chemically conjugated to the carbon nanotubes (CNTs), when the carbonanotubes are loaded with the antitumor agent doxorubin and that this system is applicable for the imaging of the uptake of CNTs by different organs in mice.

Developments in nanotoxicology

The toxicity of many nanomaterials remains unclear. An example of this is the limited information available of the interactions with the cell membrane or the toxicity of singe wall carbon nanotubes (SWNT) complexed with polyamidoamine (PAMAM). The identification of the main physicochemical characteristics of these nanocomplexes is required to determine their toxic potential. To the knowledge of Cancino and coworkers (4), the interaction between SWNT and the cell membrane component dipalmitoylphosphatidylcholine (DPPC) has not been studied previously. They presented a new strategy to investigate the toxicity of nanomaterials using Langmuir monolayers as membrane models. They showed that the nanocomplexes of the SWNTs and the PAMAM dendrimers adsorp onto the Langmuir films and form stable interacting sites. The packing of the lipids was affected as was shown by an expansion of the monolayer. From the surface pressure measurements, it could be concluded that the nanocomplexes are adsorped/incorporated onto the interface of the monolayer. From the dilatational surface elasticity measurements it is indicated that the charged groups of the nanocomplexes affect the interactions with the membrane, which results in a decrease in surface pressure and elasiticity and thus a great loss of film structure. Taking all the data together including Brewster angle microscopy results, they suggest that the nanomaterials are incorporated across the monolayers, causing perturbations or pore formation in the membrane. As can be concluded from the above results, this strategy might be very useful for the investigation of the interactions at the molecular level of many different types of nanomaterials on different types of Langmuir monolayers, but it may also be helpful for building pore like nano-structures as is desirable for systems were cell permeation is required.

Related to this topic, it is exciting to announce that Prof Bengt Fadeel edited the *Handbook of Safety Assessment of Nanomaterials; From toxicological testing to personalized medicine*, which will be published on January 31, 2014 (5). Examples of topics included in this 500 page handbook are: neurotoxicity and dermatotoxicity of nanomaterials, pulmonary and cardiovascular toxicity of nanomaterials, and also predictive nanotoxicology, personalized medicine and ethical considerations. Shortly before its publication, I will highlight this handbook more extensively.

ISA-TAB-Nano

Thomas and coworkers (6) note that the nanomedicine community has not yet adopted standardized spreadsheet-based formats to capture and share data within labs and among public repositories. Moreover, most of the data

are shared via publications and due to the lack of standardization, difficult to re-use. Within their paper they presented an extended overview of the ISA-TAB-Nano, which is a spreadsheet-based exchange format for information associated to the characterization and description of nanomaterials. The "ISA-TAB" was initially developed for the "omics" communities to share data and metadata associated with different technologies and assay types in their experiments. (Note, "omics" stands for proteomics, genomics, metabolomics and transcriptomics.)

As nanomedicine is a complex multidisciplinary field, such an open access data system might contribute to the efficient sharing of data and preventing the repeated discovery of the "nanowheel". Even if data are sensitive due to e.g., the commercialization or ongoing patenting of a product, parts might still be sharable and helpful for others. The *Nanotechnology Working Group of the US National Institutes of Health National Cancer Informatics Program*, which includes representatives from over 20 organizations, has developed the investigation/study/assay ISA-TAB-Nano. The first three spreadsheets are adapted from the original ISA-TAB (Investigation, Study and Assay) and the Materials file is new and can be used to describe the complexity of nanomaterials and associated small molecules. The main features of each file format and how to use them are extensively discussed in Thomas et al.'s paper. For further reading and to download the ISA-TAB-Nano files: https://wiki.nci.nih.gov/display/ICR/ISA-TAB-Nano.

It would be helpful to know what *you* think of the use of such a system to share your data with other researchers in the field. Are you really willing to? Let me know by using the mail address below.

Upcoming events

Simultaneously to the publication of this issue, the *CLINAM and ETPN Summit* takes place *from June 23 to 26th in Basel, Switzerland*. The focus topic of this year is "Nanomedicine and Targeted Medicine – the paradigm of precise, highly effective and safe medicine with subtle influence for the benefits of patients and mankind". For more details, see also de "News from the CLINAM-Foundation" written by Beat Löffler, CEO of CLINAM.

Another event is the *NANOTEXNOLOGY 2013 from 6 to 13 July,* which will be held in Thessaloniki, Greece. This event also includes, the 10th International Conference of Nanosciences and Nanotechnologies (9–12 July) and one can participate in a series lectures on the emerging field of nanosciences and nanotechnologies during the *7th International Summer Schools on Nanosciences and Nanotechnologies (ISSON13)*. Three complementary schools will be organized: (1) nanosciences and nanotechnology, (2) organic electronics and (3) nanomedicine respectively. The ISSON13 program will comprise plenary and parallel sessions and enable students to fix and attend the lectures according to their preferences. For further reading, see also: http://www.etp-nanomedicine.eu/public/news-events/events/isson-2013/.

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Please use "What's up" as the subject.

References

1. Banerjee A, Onyuksel H. Nanomedicine: nanotechnology, Biology and Medicine. 2013. http://dx.doi.org/10.1016/j.nano.2012.12.005.
2. Garay RP, El-Gewely R, Armstrong JK, Garraty G, Richette P. Antibodies against polyethylene glycol in healthy subjects and in patients treated with PEG-conjugated agents. Expert Opin Drug Deliv 2012;9:1319–23.
3. El-Sayed R, Eita M, Barrefeld A, Ye F, Jain H, Fares M, et al. Thermostable luciferase from luciola cruciate for imaging of carbon nanotubes and carbon nanotubes carrying doxorubicin using in vivo imaging system. Nano Lett 2013;13:1393–8.
4. Cancino J, Nobre TM, Oliveira ON Jr., Machado SA, Zucolotto V. A new strategy to investigate the toxicity of nanomaterials using Langmuir monolayers as membrane models. Nanotoxicology 2013;7:61–70.
5. Fadeel B. Pan Stanford Series on Biomedical Nanotechnology; Handbook of Safety Assessment of Nanomaterials; From toxicological testing to personalized medicine. 2014. ISBN 9789814463362.
6. Thomas DG, Gaheen S, Harper SL, Fritts M, Klaessig F, Hahn-Dantona E, et al. ISA-TAB-nano: a specification for sharing nanomaterial research data in spreadsheet-based format. BMC Biotechnology 2013;13:2.