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Editorial

Cell culture models and nanobiotechnology—contemporary topics in advanced drug delivery research

Developing new medicines is a complex, time and money consuming process. Traditionally, a new medicine essentially involved the introduction of a new active pharmaceutical ingredient (API). Until recently, drug discovery was therefore considered as the major arena for pharmaceutical innovation, and this has been furnished by novel tools and trends, such as high-throughput screening, combinatorial and computational chemistry, bioinformatics, gen-, prote-, metabol- and 'whatsoever-'onomics. In contrast, the fact that new drug molecules need to reach their site of action appeared to be somewhat neglected. Without adequate formulation or delivery system, however, no new molecule would ever reach clinical trials or registration as a drug product. Unfortunately, preparing a drug formulation has often been regarded as a mere development task, somewhere downstream of the evolution of a newly discovered API, rather than as an area that would need some fundamental and systematic research. However, overcoming the biological barriers between the site of drug action and the site of drug administration has recently been recognised as an increasing challenge to the drug development process, which can only be met by adequate science.

The awareness of biological barriers has certainly been fostered by the emergence of the so-called 'biologicals', i.e. macromolecular drugs of biotechnological rather than chemical origin, such as peptides and proteins, or DNA/RNA-based drugs. Delivering these molecules to their site of action is by their nature—large size, poor lipophilicity and poor metabolic stability—at least difficult, if not impossible without advanced drug delivery technology. But the problem of biological barriers has also been encountered by those who are still occupied with the development of new small chemically defined API's. Aqueous solubility and membrane permeability have been identified as two key parameters of the biopharmaceutics classification system, and it turns out to be more and more difficult to find new drug candidates which show some favourable behaviour with respect to those parameters (sometimes termed 'drugability').

It has become essential to evaluate the pharmaceutical properties of new drug candidates as early as possible in order to avoid belated set-backs due to poor bioavailability in the first animal or even clinical trials. Clearly, for this purpose adequate methods are needed. Cell culture based screening systems, such as Caco-2 cell monolayers have become an industry standard and most likely will soon find entry in the official pharmacopoeias. Practically, all big pharmaceutical companies have set up and validated such systems, sometimes reaching an impressive degree of automation and throughput. Besides, smaller companies have been founded, specializing on such services for the small to medium sized pharmaceutical companies that do not have such facilities in house.

In contrast to small chemical molecules, development of the much larger biologicals usually does not require such permeability screening because their permeability is most likely poor anyway. Instead, novel drug delivery concepts and technologies are really necessary here because often even parenteral administration of the 'naked' drug will not be effective. Fortunately, a paradigm shift is taking place in the pharmaceutical industry, which has started to recognise the importance of drug delivery research, and is now much more inclined to look for delivery solutions, e.g. new polymers or routes of administration, in sight of the big regulatory hurdles and costs of clinical trials and product registration. Not too surprisingly, therefore, big companies are evolving departments, which are systematically occupied with drug delivery issues. Also, small new companies dedicated to drug delivery studies have started up, and some of these can already look back to some impressive success, both scientifically and economically.

Advanced drug delivery requires a thorough understanding of the biology of the barriers in order to identify the optimal delivery system design requirements. In this context, cell culture models of biological barriers can be extremely helpful because they allow the study of the mechanism of action and proof-of-concept safety and efficacy studies of novel drug delivery systems under well-defined conditions in vitro. At the same time, the translation of biologically determined design concepts into feasible technologies for novel drug delivery systems is necessary. Nanoparticles were proposed and developed as drug carriers by pharmaceutical scientists long before the term 'Nanotechnology' gained such tremendous popularity.

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The current public awareness and the enthusiasm of various scientists for nanotechnology nevertheless does offer a variety of new opportunities for advanced drug delivery research. On the other hand, potential risks associated with 'ultrafine' particles must not be ignored either and deserve a careful safety evaluation.

In this context, this *EJPB* Special Issue aims to shed some extra light on both cell culture models and nanobiotechnology. The reviews, research articles and technical notes compiled in this issue are based on presentations given by the speakers and participants of the 5th International Conference and Workshop on Cell Culture Models for Drug Delivery Research which was held on February 25—March 4, 2004 at Saarland University, Saarbrücken, Germany, and organised under the auspices of the GALENOS Network. The composition of selected contributions from this workshop is intended to give an overview of the current state of knowledge in the area of cell culture models and new strategies to overcome biological barriers.

As well as making interesting reading, we hope that this *EJPB* Special Issue provides a vivid picture of today's research on cell culture models. Readers that are not actively involved in cell culture models with their research may become inspired. Certainly, readers whose research is involved significantly in cell culture models will find food for thought and new concepts that may be introduced to their own work. Sincere thanks are given to the authors for their contributions.

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