

Cancer is a leading cause of morbidity and mortality worldwide and it is estimated that deaths from this disease will rise to over 13 million in 2030 (1). Cancer treatment frequently comprises a combination of surgery, radiotherapy and chemotherapy but even when complete resection of the tumor is possible, chemotherapy is generally required. Chemotherapy has been used for more than 70 years, since nitrogen mustard was used for the first time in the treatment of lymphomas (2). Since then many new cytotoxic drugs have emerged, but none have made sufficient impact in extending patient survival.

The clinical use and efficacy of conventional chemotherapeutics is hampered by several limitations, among them the lack of selectivity, narrow therapeutic index and the development of drug resistance mechanisms. Moreover, it is now established that cancer represents a heterogeneous population of diverse diseases, its molecular diversity combined with the selection of resistant phenotypes of cancer cells, where both early diagnosis and treatment are posing significant challenges in developing an effective treatment regimen for this disease. It is widely believed early diagnosis of cancer will enable better management/treatment strategies.

In the past decade a considerable amount of work has been done to address the daunting problems in cancer by developing multidisciplinary nanotechnology platforms to diagnose and treat cancer (3, 4). This research has led to the emergence of a new platform "nanomedicine" which opened up entirely new therapies that a conventional treatment modality cannot offer, such as the delivery of drugs to specific targets through systemic administration. However, the efficiency of the most successful nanomedicine [Doxil<sup>®</sup>] (5) relies on passive targeting to tumour sites that is governed by the Enhanced Permeability Retention (EPR) effect (6). The current trends in nanomedicine involve the concepts of seek and destroy where in a targeting molecule highly specific for receptor over-expressed in tumours (active targeting) is coupled to the carrier that also contains imaging agents and drugs together providing a multimodal approach in the battle against cancer (7). The majority of this research is presently being done at an academic level and the success at large requires this research to go beyond the proof of concept level which may take several years yet and most importantly must strike a balance between innovation and translational potential incorporating defined "go, no-go" decision points just as we deal with risk vs benefit in medicines (8).

The articles presented in this issue cover a broad spectrum of the emerging nanotherapeutics field, from those researchers devising novel delivery carriers for existing and proven standard of care therapeutics (Shahin et al., Prasad et al., Ma et al., Maksimenko et al., Blanco et al., Yang et al., Koshkaryev et al., Vijayaraghavalu and Labhasetwar; Pegoraro et al.), to explorations of synergistic interactions between excipients and the encapsulated drugs in overcoming drug resistance (Thakur et al., Lasa-Saracibar et al.), development of novel biomarker assays (Fan et al.) and optical guided surgery (Wenk et al.). This issue also features reviews on effective delivery of taxanes exploring lipid-based nanosystems (Feng and Mumper) and photodynamic therapy using nano-sensitizers (Lim et al.), highlighting the current status and future course of action in these areas.

In the sphere of early detection and imaging, Liu et al., have described the application of gold nanoparticle/quantum dot sensor arrays to enable differentiation of cancer cell types, and cancer cells and metastatic cancer cells from non-cancer cells by means of cell surface properties. The results of controlled *in vitro* studies are promising. Gold in imaging is further exploited in nanocrystalline form by Chanda et al., as an x-ray contrast agent while a nanopore-based assay early detection strategy is presented by Fan et al. in which

a panel of unique biomarkers for metastatic melanoma has been identified. It will be exciting to follow the development of these and other similar technologies and the benefits afforded them by use of nanotechnology.

Alkyl-lysophospholipids such as edelfosine have anti-neoplastic effects and Lasa-Saracibar et al., demonstrated that its encapsulation in lipid nanosystem helps overcome drug resistance in leukemic cell lines. Similarly Thakur et al., have used miltefosine (also a class of alkyl-lysophospholipids) nanovesicles containing paclitaxel for therapy of glioblastoma multiforme. While each of these agents is approved therapeutic molecule for certain cancers, it will be interesting to note how the technology will develop as a carrier system with other active agents. Landesman-Milo et al., have described hyaluronan grafted lipid nanoparticles that are able to delivery siRNA specifically to cancer cells.

Prasad et al., have demonstrated the promise of doxorubicin and mitomycin C co-encapsulated into polymer-lipid nanoparticles in an *in vivo* setting that is more efficacious than liposomal doxorubicin, a commonly utilized therapeutic strategy in the clinic for treatment of breast cancer. The optical guided surgical process using RGD-based nanoprobe in cat model of highly infiltrative fibrosarcomas offers a new hope for the tumours that are less accessible for surgical intervention (Wenk et al.).

In the past the delivery of peptides and proteins as therapeutics has been hindered due to rapid degradation and elimination *in vivo*. In addition, there are obstacles to intracellular delivery at the desired site. The application of nanotechnology has shown great promise in overcoming these obstacles. Kim et al., have presented work with a targeted nanoparticle carrier which delivers the intracellularly acting EV peptide specifically to lung cancer cells by use of anisamide, a ligand for the sigma receptor. Peptides are also employed to target liposomal chemotherapeutics to tumor sites as in work in this issue by Shahin et al., where the p18-4 peptide enabled the specific binding of liposomal doxorubicin to MDA-MB-435 breast cancer cells *in vitro*. Though in its infancy, this proof of concept work will pave the way to potentially less toxic therapeutic strategies *in vivo*. Targeting to tumor sites may also be achieved by means of antibody conjugation—a methodology employed by both the Sharifzadeh et al., and Yokoi et al., in this issue. Yokoi et al., have exploited the specific expression of CD59 on pancreatic tumors to design in a murine system, nanocarriers targeted to pancreatic tumors by conjugation of a Ly6C Ab (murine CD59 homolog), resulting in increase of pancreatic tumor associated drug of 100-fold as compared to non-conjugated carrier while Sharifzadeh et al. exploit tumor associated glycoproteins with novel chimeric nanoconstructed antigen receptors. Therapy for pancreatic tumors is also addressed in the work by Singh et al., in which the authors identify miRNA implicated in chemosensitivity with downstream potential of nanotherapeutics targeting these sequences.

Overall, this is an exciting time in the field of nanotherapeutics, with advances being made in several arenas, including diagnostics, therapeutics and theranostics and we look forward to the continued work of the authors in this issue as well as others, in the coming years.

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