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CAMPUS TECNOLÓGICO E NUCLEAR

Data, hora, local/*Date, hour, local*: 30-11-2017, 11:00 - Auditório do CTN

Palestrante/*Speaker*: Helena Florindo — Intracellular Trafficking Modulation for Advanced Drug Delivery Research Group, Research Institute for Medicines (iMed.ULisboa), Faculty of Pharmacy, Universidade de Lisboa, Lisbon, Portugal

Título/*Title*: **Multicomponent Nanoscale Systems for Immune Modulation against Solid Tumors**

SHORT CV

Doctor Helena F. Florindo graduated in Pharmaceutical Sciences in 2003 at the Faculty of Pharmacy of Universidade de Lisboa, and received her PhD in Pharmaceutical Technology in 2008 (Universidade de Lisboa and The London School of Pharmacy, London, UK). She was Assistant lecturer between 2008 and 2013 and she is currently Assistant Professor at the Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmacy of Universidade de Lisboa. Since 2013 she is Group Leader of "Intracellular trafficking modulation for Advanced Delivery" research group of the Research Institute for Medicines (iMed.ULisboa). H. F. Florindo has been mainly focused on the development of targeted nanotechnology-based strategies to overcome physiologic barriers. Of particular interest is the elucidation of particle mechanism of action and understanding the fundamental issues related to the resultant efficacy by the interaction of these systems with targeted cells, in order to develop systems with a potential application in the treatment/prevention of a broad range of diseases, mainly infectious, inflammatory and cancer diseases.

ABSTRACT

Cancer tissues are heterogeneous, phenotypically and functionally diverse with several biological subtypes, which have limited the successful outcome of multiple therapeutic options, devised to destroy cancer cells. Immunotherapeutic approaches, in particular cancer vaccines, are between the most promising but also challenging alternative cancer treatments. One of the major advantages recognized to cancer vaccines in comparison to other immunotherapeutic approaches, is their ability to trigger a memory immune response toward cell presenting those antigens. Dendritic-cell (DC) targeting has been used as a promising strategy for the development of vaccines and immune modulation [1]. Several studies have shown that aliphatic polyester-based biodegradable nanoparticles (NPs) are potential vaccine delivery systems for cancer and infectious diseases and suitable platforms for immune modulation [2, 3]. By modulating the properties of those carriers, it will be possible to foster the accumulation of released antigen at specific sites within cytoplasm, potentiating a systemic and/or cellular based immune response. Therefore, nanocarrier properties can be fine tuned to potentiate a broad immune response, essential to meet the complexity underlying the immune-cancer cell interplay. Our research has been focused on the development of different formulations of biodegradable NPs with different combinations of tumor antigens, immune adjuvants, such as the Toll-like receptor ligands (TLRls), and/or gene regulators, such as small interfering RNA (siRNA) to target multiple and complementary tumor progression-related pathways. Mannose-grafted hybrid lipid/polymeric NPs and hyaluronic acid-coated NPs have been some of the systems prepared to specifically target antigenpresenting cells (APC), such as DCs, and tumor cells, respectively. It involves the optimisation of particle production parameters, such as size, surface charge, hydrophobicity, loading capacity, controlled release properties, biodistribution profiles and the evaluation of their *in vivo* efficacy. Of particular interest is the elucidation of the effect of particle composition, surface properties and targeting ligands on immune cell activation and functionality, both *in vitro* and *in vivo* using wild-type and solid cancer animal models (e.g. melanoma and breast carcinoma). Generally, NPs presented a mean diameter below 200 nm with low polydispersity index (PdI) values (≤0.2), and antigen and siRNA entrapment efficiency (EE) values of 75 % and 95 % respectively. NP formulations did not affect the viability of targeted cells, even at high NP concentrations. *In vitro* cellular uptake studies evidenced that both polymeric and hybrid NPs were efficiently taken up by DCs, in a time and concentration-dependent manner. This successful uptake profile was also confirmed in a wild type animal model, as well as the successful induction of antigen-specific T cell expansion. In melanoma and breast murine models, the produced NPs vaccine delivery systems demonstrated to significantly decrease tumor growth rate, especially when a single NP delivered a combination of tumor associated antigens and TLRls. Interestingly, the nature of immune response and overall efficacy were correlated to the type of antigen association to carriers. Our results confirm the successful development of biodegradable polymeric nanocarriers with great potential to be used for vaccine delivery and immunotherapy. Our data evidence the impact of NP surface properties and composition on the type of immune response and overall anti-tumor effect. This deeper understanding on the fundamental issues related to nanoparticle-immune cell cross-talk can guide the rational development of nano-immunotherapeutic systems with improved efficacy and safety, by avoiding off-target effects.

REFERENCES

[1] Conniot J et al, Front in Chemistry **2** (2014) 1-27; [2] Silva JM et al, J Control Release, **198** (2015) 91-103; [3] Silva JM et al Nanomedicine (Lond.) **9** (2014) 2639-2656.