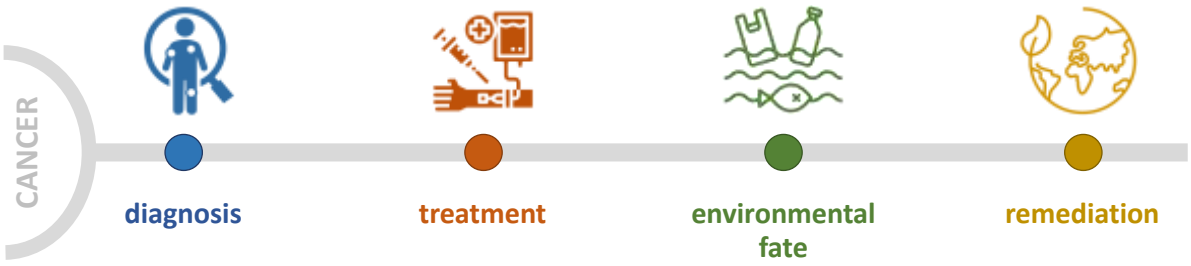
PATh/IonCytDevice Workshop

September 21st 2020

A Technological Perspective on Cancer: from Diagnosis and Treatment to Environmental Fate and Remediation



BOOK OF ABSTRACTS

Organizing Committee:

Mara G. Freire
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Francisca Silva
Rita Teles

Program

9:15 – Opening session (*Ana C. Sousa and Mara G. Freire*)

Diagnosis *(Chair João Rocha)*

9:30 – Lab-on-chip platforms for biological analysis (*João Conde*, INESC MN, IST)

10:00 – Discussion

10:10 – ZnO-based transducer platforms for biosensing applications (*Joana Rodrigues*, I3N-UA)

10:30 – Improvement of cancer biomarkers detection using ionic-liquid-based aqueous biphasic systems for human fluids pre-treatment (*Matheus Pereira*, CICECO-UA)

10:50 – Discussion

11:00 – 11:20 – Break

Environmental Monitoring and Toxicity Assessment *(Chair Isabel Lopes)*

11:20 – Anticancer drugs in the Environment: Occurrence, Risk Assessment and Degradation (*Teresa Gouveia, LEPABE-FEUP*)

11:50 – IonCytDevice: Removal of cytostatics from cancer patients' urine using supported ionic liquids (*Francisca e Silva*, CICECO-UA)

12:10 – Ecotoxicological tools to assess the adverse effects of cytostatic in freshwater environments (*Cátia Venâncio*, CESAM-UA)

12:30 – Occupational exposure to antineoplastic drugs – Portuguese reality and way forward (*Susana Viegas, ENSP-NOVA*)

12:50 – Discussion

13.00 – 14:30 – Lunch Break

New perspectives with ILs *(Chair Pedro Carvalho)*

14:30 – Task-Specific Ionic Liquids for Pharmaceutical Applications (*Luís Branco*, LAQV-REQUIMTE, UNL)

15:00 – Discussion

15:10 – Enhancing the applicability of ionic liquids by manipulating their structure (*José Esperança*, LAQV-REQUIMTE, UNL)

15:40 – Discussion

15:50 – 16:10 – Break

New strategies for cancer treatment *(Chair Ramiro Pastorinho)*

16:10 – Metabolic profiling and modulation in cancer treatment (*Iola Duarte*, CICECO-UA)

16:40 – Discussion

16:50 – Acute lymphoblastic leukemia: From basic science to new therapies? (*João T. Barata*, IMM-UL)

17:20 – Discussion

17:30 – Final Remarks/Closing Session

SPONSORS

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PATh/IonCytDevice Workshop Participants

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Lab-on-chip platforms for biological analysis

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Microfluidic lab-on-chip sensing platforms are currently being intensively studied for detection of bioanalytes (such as DNA, proteins, cells, metabolic products) in applications such as food safety, environmental control and health monitoring. These systems have compelling potential advantages, such as portability, speed, sensitivity, multiplexing, no need for highly skilled operators or laboratory infrastructure, and low cost.

To take full advantage of the miniaturization of the biosensor, it is crucial to also address issues which I will discuss in some detail: (i) fluidic handling directly from sample; (ii) consideration of the interfering effects of the often chemically and physically complex biological sample matrix; (iii) on-chip transducer integration – in our case typically thin-film silicon photosensors; and (iv) strategies for simultaneous (multiplex) detection of various target molecules.

I will present applications we are working on as case studies of integrated lab-on-a-chip analytical systems: (1) detection of microbiological entities such as antibiotic-resistant bacteria; (2) monitoring of therapeutic antibodies such as Infliximab; and (3) detection of disease biomarkers such as NCL and PSA.

ZnO-based transducer platforms for biosensing applications

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One of the most imperative challenges of the scientific community nowadays is to find solutions to aid in the maintenance and improvement of human health. Hence, considerable efforts are being devoted to the development of low cost, simple and user-friendly devices capable to detect, monitor and prevent diseases. In this sense, our research addresses these challenges by developing zinc oxide (ZnO)-based nanostructured materials to be used as the transducer component for the fabrication of biosensing devices.

ZnO is one of the most widely studied semiconductors, exhibiting a set of properties with interest for a wide range of applications, especially in the sensing field. The unique photoluminescence (PL) properties of its nanostructures offer a potential transduction platform for sensing, which can be coupled to the standard electrochemical response. Therefore, both optical and electrochemical transduction signals can be combined in a single sample/device. Enhanced data acquisition and counter-proof measurements are thus expected, minimizing false-positives and detection errors. Moreover, the formation of ZnO composites with carbon allotropes (*e.g.* graphene) can alter the properties of both components, resulting in advantageous properties and enhanced sensing performance. In our project, ZnO nanostructures and ZnO/nanocarbon composites are being produced by innovative and up-scalable laser processing techniques and tested as transducer platforms for the detection of analytes with clinical interest, *e.g.* hCG or glucose. In this presentation, some of the relevant results already obtained in the framework of this project will be discussed. For instance, it was observed that the intensity of the PL outcome of ZnO structures functionalised with anti-hCG antibodies is sensitive to the concentration of hCG in the tested solutions and that the behaviour was reproducible for the different sensors tested. Moreover, control samples were also produced and no significant variations of the signal were identified, suggesting that the changes were indeed related to biorecognition events.

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Improvement of cancer biomarkers detection using ionic-liquid-based aqueous biphasic systems for human fluids pre-treatment

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Human samples (e.g. serum and urine) are usually used in diagnostic assays for several diseases, including cancer. Nevertheless, the identification and quantification of target cancer biomarkers in these samples, which most of the times are proteins, suffer interferences by other metabolites, such as high-abundant proteins (human serum albumin (HSA) and immunoglobulin G (IgG))[1]. Accordingly, the depletion of high-abundant proteins is required as well as the concentration of the target biomarkers for a more reliable identification and quantification of cancer biomarkers. Traditional sample pre-treatment methods are based on multi-step approaches, are of low reproducibility, time-consuming and typically require the use of toxic volatile organic solvents. In this work we propose the use of ionic-liquid-based aqueous biphasic systems (IL-based ABS) as a simultaneous depletion and concentration pre-treatment platform of human samples (serum and urine). The reproducible depletion of high-abundant proteins, combined with the concentration of target cancer biomarkers, was achieved by an accurate choice of the ILs chemical structures and compositions of the phase-forming components of ABS. Examples will be presented with prostate specific antigen (PSA) and Lactate dehydrogenase (LDH) from urine and serum samples, respectively.

References

[1] Zolotarjova et al., Proteomics. 2005, 5(13), 3304-3313.

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Anticancer drugs in the Environment: Occurrence, Risk Assessment and Degradation

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Cancer is the second leading cause of death worldwide and its prevalence is increasing in first world countries. The forecasts point out that 23.6 million of new cancer cases will be diagnosed in 2030, which corresponds to an increase of almost 70% compared to 2012. Although there isn't yet a cure for cancer, most of these pathologies are treated by chemotherapy, using pharmaceuticals designated as cytostatics or anticancer drugs. However, anticancer drugs are not specific for damaged cells, being able to inhibit healthy tissues, which represent a risk for any living being. Upon administration to patients, part of these drugs is excreted and launched to the urban sewage system. Many studies have demonstrated that the conventional treatments currently implemented at wastewater treatment plants (WWTPs) are not being effective in the degradation of anticancer drugs. Therefore, these hazardous drugs are getting surface waters, posing the aquatic biota, the environment and potentially the humans at serious risks.

The identification of the anticancer drugs of most concern in wastewaters and surface waters and their removal/degradation in WWTPs are research topics of utmost importance. This lecture will be focused in the presentation of the results obtained so far at LEPABE under these topics of concern.

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Ecotoxicological tools to assess the adverse effects of cytostatics in freshwater environments

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Cytostatic drugs are a class of pharmaceuticals widely used for cancer treatment. Thus, their discharge to environmental matrices is inevitable and they have become a great environmental problem. There is an urgent need to study and develop technologies aimed at the treatment and remediation of wastewaters receiving these chemicals to reduce their potential environmental effects. Accordingly, this work used ecotoxicological studies to: i) predict the environmental impacts of three cytostatics in freshwater biota; ii) evaluate the efficiency of a new methodology to remove cytostatic from the urine of oncologic patients. This was accomplished using standard species, belonging to three key functional groups.

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Occupational exposure to antineoplastic drugs – Portuguese reality and way forward

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According to epidemiological reports, animal carcinogenicity data, and the outcomes of in vitro genotoxicity studies, several antineoplastic drugs have been classified by the International Agency for Research on Cancer (IARC) as belonging to the group of human carcinogens (Group 1), probable human carcinogens (Group 2A), or possible human carcinogens (Group 2B).[1] Along with the increasing number of cancer patients, a higher number of workers are potentially needed to handle production and administration tasks relative to antineoplastic drugs. Workers may be exposed to a drug at different stages of its life cycle – from manufacture to transport and distribution, during its use in health care or home care settings, or at its final waste disposal. Health care workers who prepare or administer hazardous drugs or who work in areas where they are used may be exposed to these agents in the air, on work surfaces, contaminated clothing, medical equipment, patient excreta, and other surfaces. These workers include shipping and receiving personnel, pharmacists and pharmacy technicians, nursing personnel, and environmental services personnel. Workers employed in the synthesis and production of these products and staff involved in cleaning, transport, and disposal of hazardous drugs or contaminated material may all be exposed.[2,3] In Portugal, since 2010, several papers and technical reports have been publishing demonstrating that workplace surfaces are contaminated with these drugs. Although with the implementation of several risk management measures there is still a scenario of probable exposure by skin absorption of the workers working in Portuguese health care facilities. Recently, the European Commission has initialized a study concerning a possible EU initiative to protect workers from exposure to hazardous medicinal products. This might result in new developments concerning workers protection.

References

[1]IARC, 2012 Available at http://monographs.iarc.fr/ENG/Monographs/vol100F/index.php;
[2]Viegas S et al. Arh Hig Rada Toksikol 2017;68:287-297;
[3]Viegas S, et al. Arh Hig Rada Toksikol 2018;69:238-249

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Task-Specific Ionic Liquids for Pharmaceutical Applications

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The development of Ionic Systems based on Biocompatible Ionic Liquids in combination with different pharmaceutical drugs seems a very attractive research topic to study [1]. Nowadays, the possibility to discovery sustainable and efficient solutions related to costly problems from pharmaceutical industry such as polymorphism, drug diversification and as modulators of Biopharmaceutical Drug Classification System (BCS) is essential. In last years, our research team already reported examples of API-ILs based on anti-inflammatory (e.g. ibuprofen); antibiotics (beta-lactams and fluoroquinolones); anti-tumoral (bisphosphonates) and anti-viral drugs and anti-tuberculostatic with significant advantages comparing with original APIs [2-6]. It is important to note that some beta-lactam antibiotics as API-ILs reveals a very high anti-bacterial activity especially against resistant bacteria (RDIC values >100 and 1000) which agrees with theoretical prediction of drug improvement [3]. Although these recent developments, API-ILs seem to be an ideal drug delivery system for APIs by improving bioavailability (solubility, permeability) and eliminate polymorphism.

Herein, we will present our latest developments in the field of API-ILs including β-lactam antibiotics, Mefloquine, isoniazid and bisphosphonate derivatives. Some of API-ILs are very promising for further application as ionic formulations for pharmaceutic industry.

References

[1]Marrucho & Branco et al. Annual Rev. Chem. Biom. Eng. 2014, 5, 527.
[2]Ferraz & Branco et al. RSC Adv. 2014, 4, 4301.
[3]Santos & Branco ChemMedChem 2019, 907.
[4]Teixeira & Branco et al. ChemMedChem 2019, 14, 1767.
[5]Ferraz & Branco et al. Pharmaceutics 2020, 12, 221.
[6]Teixeira & Branco et al. Pharmaceutics 2020, 12, 293.

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Enhancing the applicability of ionic liquids by manipulating their structure

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Ionic liquids containing the bis(trifluoromethyl)sulfonylimide anion, $[NTf_2]^-$, present high chemical and thermal stability, low viscosity and melting point temperatures. We present the manipulation of the cation in order to break the hydrophobicity of BILs.

Liquid-liquid equilibria data of binary mixtures composed of either n-alkyl alcohols or water and a series of $[NTf_2]^-$-based ionic liquids with specially-designed quaternary ammonium cations, $[N_{i\,j\,k\,l}]$ is presented. Grafting different functional groups to the ammonium cation has allowed us to tune the miscibility behaviour of BILs and, furthermore, to increase the hydrophilicity of the cation in order to achieve a $[NTf_2]^-$-based ionic liquid completely miscible with water at or below room temperature. The main conclusions are: (i) adding hydroxyethyl groups to the ammonium cation is an effective way to increase the hydrophilicity of these $[NTf_2]^-$-based ionic liquids and (ii) MD simulations have shown that in the case of mixtures of $[NTf_2]^-$-based ionic liquids and water at equimass composition, the OH groups of the cation are fully integrated in the continuous H-bonded network of water.[1]

We also studied the effect of the manipulation of the ammonium cation on distinct properties of ionic liquids. The most relevant result is the strong evidence that the replacement of a methyl group by a hydroxymethyl group in the cation has an almost-null contribution to the overall molar volume of the ionic liquid. Most of the effect comes from the fact that the intrinsic van der Waals volumes of $-CH_3$ and $-CH_2OH$ are not that different (14.7 and 17.8 $cm^3 \cdot mol^{-1}$); the remainder of the effect comes from the fact that hydrogen bonding between hydroxyl groups or between them and the charged moieties of the ionic liquid can lead to further contractions of the free volume that annuls the modest intrinsic volume contribution of the OH group.[2]

Aqueous biphasic systems (ABS) composed of cholinium-derived bistriflimide ionic liquids (ILs) and carbohydrates were investigated as an alternative process to simultaneously separate and recover antioxidants and carbohydrates from food waste.

Cytotoxicity assays toward human intestinal epithelial cells (Caco-2 cell line), demonstrated a significantly lower toxicity than other well-known and commonly used fluorinated ILs. With the studied systems, the separation of the two products occurs in one-step, where carbohydrates are enriched in the carbohydrate-rich phase and antioxidants are mainly present in the IL-rich phase. The results show that these ILs could be used in other industrial food waste valorization processes.

References

[1]A. Mão de Ferro, *et. al.* PCCP, 20, 19307-19313, 2018.
[2]A. Mão de Ferro, *et. al.* J. Chem. Eng. Data, 64, 4932-4945, 2019.
[3]C.M.S.S. Neves, et. al. Frontiers in Chemistry, 7, article number 459, 2019.

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Metabolic profiling and modulation in cancer treatment

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Cancer cells undergo profound metabolic reprogramming to sustain survival and proliferation, with compelling evidences showing strong interconnections between cancer-related signaling pathways and several metabolic alterations.[1] The altered metabolic program of cancer cells further impacts other cells residing in the tumor microenvironment and contributes to regulate processes deeply involved in cancer development, such as angiogenesis, inflammation and cancer immunity.[2] Hence, targeting tumor cell metabolism to achieve therapeutic benefit in cancer treatment has been continuously harnessing increased interest. As will be shown in this communication, metabolomic profiling of cancer cells, and of their modulation by therapeutic agents, is a powerful strategy to reveal cellular metabolic adaptations, identify response biomarkers and improve understanding of cellular processes at the molecular level. Examples to be discussed comprise: i) assessment of anticancer compounds using *in vitro* and *in vivo* tumor models ii) modulation of the metabolism-phenotype axis in tumor-associated macrophages.

References

[1]Guerra et al., J Agric Food Chem. 2018, 66, 10663-10685.
[2]Dias et al., Eur J Cancer 2019, 121, 154-171.

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Acute lymphoblastic leukemia: From basic science to new therapies?

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Acute lymphoblastic leukemia (ALL) is the most common childhood malignancy. Despite remarkable improvements in treatment outcome, some 10 to 20% of pediatric ALL cases relapse. In adults the scenario is dimmer, with more than 40% of the cases relapsing. Relapsed patients have extremely poor prognosis. In addition, current chemotherapeutic regimens are aggressive and can lead to substantial long-term side-effects. As such, a better understanding of the biology of ALL is necessary, in order to try and develop novel therapeutic strategies that can improve treatment outcome while decreasing treatment-driven toxicities. In our lab, we have been investigating the role of cell-intrinsic alterations and microenvironmental cues in leukemia development and progression. The characterization of these processes has led to the identification of potential molecular targets for therapeutic intervention (e.g. Chk1, PI3K, or CK2), which we have explored in pre-clinical studies using available clinical-grade small molecule inhibitors. These efforts have sparked our interest in developing novel therapeutic tools (e.g. antibody-based) and strategies (which I will briefly mention) aiming at providing clinical benefit to patients in the future.

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