Book of Abstracts

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P12. THYMIDYLATE SYNTHASE GENE SILENCING BY POLYPURINE REVERSE HOOGSTEEN HAIRPINS IN PROSTATE CANCER CELLS AS CANCER THERAPY

E. Aubets, A.J. Félix, V. García, A. Aviñó, C. Plasencia, R. Eritja, V. Noé and **C.J. Ciudad**

Department of Biochemistry and Physiology, School of Pharmacy and Food Sciences, University of Barcelona, and IN²UB, Barcelona, Spain

AROMICS SL, Barcelona, Spain

IQAC-CSIC and CIBER-BBN, Barcelona, Spain

The Thymidylate synthase enzyme (TS) is widely studied as an anti-cancer target because of its role in the synthesis the novo of dTTP. Treatment with TS inhibitors (e.g. 5-FU) can lead to tumour resistance through overexpression of TS, either by chromosome aberrations or by alteration of molecular mechanisms that regulate gene expression of this gene. It has been proposed that G-quadruplex nucleic acid sequence motifs may regulate translation as well as transcription. Therefore, in the present work, we have explored the incidence of G-quadruplex motifs in the 5' untranslated regions (5'-UTR) of the mRNA of the thymidylate synthase gene as potential targets in cancer treatment. By using the QGRS mapper, a software for searching putative quadruplex forming G-rich sequences, we found a predicted G-quadruplex (G4). This prediction was confirmed by circular dichroism and UV melting measurements for the RNA sequence. In consequence, and to develop new therapeutic agents that could overcome resistance to TS inhibitors, we designed a Polypurine Reverse Hoogsteen hairpin (HpTYMS-G4-T-PPRH) against the complementary strand of this G4 sequence.

First, we demonstrated the ability of binding of the PPRH to its target sequence by gel-shift assays. HpTYMS-G4-T was able to bind to the template strand of the TS ds DNA target sequence in in vitro assays. Next, as TS is involved in dTTP synthesis, we compared the effect of this PPRH in PC3 cells incubated either in the presence or the absence of thymidine. The HpTYMS-G4-T PPRH was cytotoxic in both media, decreasing cell viability to less than 5% for at a concentration of 100 nM. These results raised the concept that TS could be involved in other proliferation pathways. The response of PC3 cells after treatment with HpTYMS-G4-T was dose dependent. This PPRH could be altering the transcription of TS gene at this site or the regulation of a G4 structure at this point. In conclusion, our results show the ability of the designed PPRH to bind to its target sequence of TS and to decrease PC3 cells viability. Therefore, PPRHs can be considered as a new type of molecules to modulate TS expression and overcome the resistance produced by traditional treatments.

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P13. FROM BIOMASS TO SUSTAINABLE NEW MATERIALS: NOVEL ASPECTS ON CELLULOSE UTILIZATION

S.V. Valenzuela[1,2], C. Buruaga[1,2], L.V. Cabañas[1,2], M. Larrosa[1], J. Martínez[1,2], P. Díaz[1,2], F.I.J. Pastor[1,2]

[1] Department of Genetics, Microbiology and Statistics, Universitat de Barcelona, Spain.

[2] Institute of Nanoscience and Nanotechnology (IN²UB), Universitat de Barcelona, Spain

Nowadays, enormous efforts are being done in the scientific community in order to develop sustainable alternatives to petrol derivatives like plastics for all kinds of applications, including packaging, building blocks, or biomedical devices, among others.

In this context, cellulose is an extraordinary renewable material for both its versatility and its abundance; it accounts for more than one third of the existing organic carbon sources on earth.

Considering this, as a group of Microbial Enzymes for Industrial and Environmental Applications, we are working on the biotransformation of natural polymers like vegetal cellulose, including the development of enzymes that catalyse its modification, hydrolysis, and/or synthesis. In addition, we are exploring the potential of bacterial cellulose, as an innovative source for new biomaterials, including its utilization as a platform for anchoring proteins, antimicrobial agents and other functionalization.

We have deep experience on the study of molecular biology of carbohydratases and esterases, and the identification and design of enzymes for biotechnological applications in pulp bleaching and paper recycling, production of biofuels, synthesis of new compounds from wastes, improvement of textile fibers, food industry, and development of new materials based on lignocellulose. With different approaches, we have expanded the toolbox of new enzymes, or their improvement by protein-engineering strategies, available for the community.

We aim at combining basic research with applied studies and innovation, and within this combination, we explore the development of new materials obtained through sustainable processes, and their modification in mild conditions by replacing chemical pollutants with enzymatic components. The developed materials display exceptional physicochemical properties, such as an ultrafine reticulated structure, high crystallinity, high tensile strength, high hydrophilicity and biocompatibility. These unique properties are allowing us to develop new biocomposites and to evaluate their applicability in several fields.

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