

the BET bromodomain and extra-terminal protein family of histone acetylation readers suppresses the expression of Perilipin-2, a crucial component of lipid droplets, disrupting the lactate-dependent lipid metabolic rewiring. *In vivo*, the inhibition of the metabolic-epigenetic regulatory loop, induced by cancer-associated fibroblasts, reduces growth and metastatic dissemination of prostate cancer cells, thus confirming its translational relevance as a therapeutic target in prostate cancer progression. Clinically, expression of Perilipin-2 is elevated in tumors with a higher Gleason grade and in castration-resistant prostate cancers, compared to primary cancer lesions. As a take-home message, I underline that lactate delivered in the tumor microenvironment due to Warburg metabolism plays both a metabolic and an epigenetic role in promoting prostate cancer malignancy.

ShT-04.3-1

Determining the structure of the enterococcal polysaccharide antigen

J. Davis¹, R. Smith¹, E. Maes², Y. Guerardel², S. Mesnage¹

¹The University of Sheffield, Sheffield, United Kingdom,

²University of Lille, Lille, France

Enterococcus faecalis is an opportunistic pathogen, commonly found in the healthy human gut, which can also cause life-threatening diseases such as meningitis and septicaemia. The enterococcal polysaccharide antigen (EPA) is a surface exposed polymer produced by all *E. faecalis* strains, and is a major virulence factor, being essential for host immune evasion during infection. It is comprised of a repeating rhamnose backbone which is decorated with strain specific teichoic acid decoration subunits. Work by our group (Smith R et al. (2019) PLoS Pathog 15, e1007730) has shown that these strain-specific decoration subunits are responsible for the biological activity of EPA, rather than the highly conserved polyrhamnose backbone. Structural characterisation of EPA decoration subunits could therefore provide key insights into strain-strain phenotype variation and pathogenicity. Recently, the structure of EPA produced by a clinical isolate (V583; Guérardel Y et al. (2020) mBio 11, e00277-20) has been solved, which has paved the way for more detailed analysis of EPA structural diversity and molecular activity. Here, for the first time, we have solved the structure of the EPA decoration subunits in the model clinical isolate, OG1RF. EPA was purified enzymatically from the cell wall of OG1RF, then broken into three uniform fragments, corresponding to the polyrhamnose backbone and two decoration subunits, using HF acid treatment. A specialised pipeline of 2D NMR experiments (HSQC, COSY, TOCSY, ROESY and HMBC) was then employed to allow the assignment of each sugar residue, and subsequently solve the structures of the purified decoration subunits. OG1RF decoration subunits were found to differ in size, composition, and level of branching, when compared to V583. This variant structure may help to explain the increased pathogenicity of OG1RF, as compared to V583, and is hopefully one of the first steps towards understanding how EPA impacts *E. faecalis* pathogenesis.

ShT-04.3-2

β-glucans derived from mushroom *Coriolus versicolor* for applications on skin wound healing

A.S. Fernandes, P.M. Rodrigues, M. Pintado, F.K. Tavaría
Centro de Biotecnologia e Química Fina - Escola Superior de Biotecnologia da Universidade Católica Portuguesa, 4050-313 Porto, Portugal

The beneficial effects of natural compounds in cosmeceutical and biopharmaceutical fields have been extensively studied over the years, and gained popularity because of their distinct advantages, including fewer side effects, better tolerance, and relatively low expenses. Currently, with the growing demand for the use of nature-derived molecules, the research aiming for new biomolecules has increased. Beta-glucans have proved their pluripotent bioactivity (antioxidant, anti-inflammatory, antimicrobial, anti-cancer, regenerative effects, immunomodulation, healing properties) in skin cells. These properties are dependent on several aspects, such as the source, molecular weight, solubility, degree of branching, charge of polymers, and structure in aqueous media. The versatility of these molecules makes them a challenge for the studies of structure-activity relationships, once each different compound (with a unique structure) will show different biological activity. Regarding the high levels of environmental and endogenous stresses that the skin is exposed leading to premature aging and chronic inflammation, this ongoing work aims to explore the ability of β-glucans extracted from *C. versicolor* to act as antioxidant and anti-inflammatory molecules in the skin and to eventually promote wound healing and tissue cicatrization. Therefore, assays exploring cytotoxic, antioxidant, and anti-inflammatory activities of different β-glucans in keratinocytes (HaCaT) and human fibroblast (HFF) cell lines were performed. The effects of β-glucans on angiogenesis were assessed by the migration (wound healing activity) and the tube formation assay (differentiation and vascular formation) using cell models of human umbilical vein endothelial cells (HUVEC) and mouse macrophage cells (RAW 264.7). Lastly, two well-known ECM components, hyaluronic acid, and collagen were evaluated to understand the effects of β-glucans in the production of these components in a human fibroblast cell line (HFF).

ShT-04.3-3

Unravelling the molecular recognition of the cancer and pathogenic immune-related lectins LactiNAc by human immune-related lectins

C. Lima¹, H. Coelho¹, A. Gimeno², F. Trovão¹, A. Diniz¹, J. Dias¹, J. Jiménez-Barbero³, F. Corzana⁴, A. Carvalho¹, E. Cabrita¹, F. Marcelo¹

¹UCIBIO, FCT-NOVA, Lisbon, Portugal, ²1315 - CIC BioGUNE, Derio, Spain, ³CIC BioGUNE, Derio, Spain, ⁴Department of Chemistry, Universidad de la Rioja, Logroño, Spain

Cancer and infection diseases have a negative impact on society and it is well established that lectin/glycan interactions modulate how the human immune system faces these major diseases. In this perspective, discovering exactly how lectins enrolled in immune response interact with the glycan epitopes is crucial for the discovery of new and alternative therapies towards these diseases (E. Rodríguez, et al. (2018) Nat. Rev. Immunol. 18, 204-211; D. A. Wesener, et al. (2017) Curr. Opin. Struct. Biol. 44,