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and emotional behavioral consequences between HS and HFHS diets.

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Oncology & Molecular Biology Paralell Oral Session
*Friday, September 15th, 14h00*

## PS081

### GE11 positive exosomes as a potential RNAi delivery system in clear cell Renal Cell Carcinoma

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**Aim:** Use GE11 positive (GE11+) exosomes as a targeted delivery system to EGFR overexpressing cells for the treatment of clear cell Renal Cell Carcinoma (ccRCC).

**Introduction:** ccRCC is the most prevalent subtype of renal cancer and the most lethal urologic tumor. Generally, it is radio-chemotherapy resistance, and frequently associated with relapse after 5–11 months upon targeted therapy treatment, which highlight the need to develop new therapeutic strategies. Exosomes, extracellular vesicles of 40–150 nm that mediate intercellular communication, have emerged as promising therapeutic tools due to their engineering potential and ability to evade the immune system.

**Methods:** EGFR is known to be overexpressed in ccRCC thus, the expression of GE11, a peptide that binds to EGFR, in exosomes membrane enable a targeted delivery of therapeutic molecules to EGFR overexpressing cells. Exosomes derived from HEK293T were engineered to express the GE11 peptide on their surface and incubated with normal or tumor renal cell lines.

**Results:** Our results revealed EGFR overexpression at the mRNA and protein levels in a ccRCC cell line, compared to a normal renal cell line. Furthermore, tumor cells presented increased protein levels of phosphorylated EGFR when compared to normal cells. These results support the hypothesis of using an EGFR-based exosomes delivery model, the GE11+ exosomes. A higher percentage of tumor cells internalized GE11+ exosomes compared to exosomes derived from HEK293T cells transfected with control condition. Additionally, tumor cells exhibited an increased mean of fluorescence intensity compared to the control, suggesting that each cell uptakes more GE11+ exosomes in an EGFR-dependent manner. Importantly, GE11+ exosomes were internalized in a greater proportion by tumor cells rather than normal renal cell lines.

**Conclusion:** Overall, the use of GE11+ exosomes as a new delivery system is a promising therapeutic strategy for ccRCC treatment. Ultimately, these exosomes can be loaded with RNAi-based drugs to target deregulated genes in ccRCC.

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## PS145

### Evaluation of combined cytoplasmic AR in tumour cells expression and tumour CD3 T-cells infiltrate as a prognostic score for patients with prostate cancer

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**Aim:** We aimed to assess the prognostic value of using a cumulative score evaluating the expression of Androgen Receptor (AR) and the presence tumour inflammatory infiltrate as a prognostic marker for prostate cancer (PCa).

**Introduction:** PCa is the most common male cancer, in Europe. Currently, at diagnosis, only tumour-based factors, including clinical stage, tumour grade and circulating concentrations of Prostate-Specific Antigen (PSA) are used to predict PCa outcome. However, this can vary within patients sharing the same clinical conditions, leading to patient's over/under treatment. It is now recognized that cancer progression is also dependent on tumour's interaction with its microenvironment, specifically with immune cells. Therefore, the development of predictive biomarkers, capable of combining these two factors should be considered.

**Methods:** Immunohistochemistry for AR expression and CD3 T-cells was performed on biopsies from a cohort of 361 patients diagnosed with PCa. Semi-quantitative weighted histoscore and quantitative assessments were used.

**Results:** High cytoplasmic AR expression in tumour cells and high CD3-T cells presence were associated with reduced overall survival ($p = 0.000055$, and $p = 0.004$, respectively), with strong association ($p = 0.001$) on X2 analysis. When patients were grouped as having: both markers low or one low and low/moderate and one high, and both high, this cumulative prognostic score was strongly associated with overall survival ($p = 0.000001$), being the mean overall survivals: 7.1 years (95% CI 6.5–7.6), 6.0 years (95% CI 5.4–6.6) and 3.8 years (95% CI 2.4–5.0), respectively. Moreover, on multivariate analysis, it was considered a significant independent predictor of overall survival (HR 1.982, 95% CI 1.018–3.859, $p = 0.044$).

**Conclusion:** These results confirm the clinical utility of assessing both tumour and microenvironment characteristics when predicting patients' outcome, and suggest that the presence