USING MICRO-RNA EXPRESSION TO PREDICT RESPONSE TO NEO-ADJUVANT CHEMOTHERAPY IN UROTHELIAL CARCINOMA OF THE BLADDER - PRELIMINARY RESULTS AND FUTURE PLANS

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Urothelial carcinoma of the bladder is a frequent oncological disease. Although several clinical trials attempted to determine the best approach to muscle-invasive disease, currently there is still no agreement as to the optimal treatment modalities and to their sequence. The decision whether to administer neo-adjuvant chemotherapy is currently based solely on clinical parameters, with no validated biomarkers available.

Micro-RNAs (miRNAs) are short RNA molecules within the cell that have a role in post-transcriptional gene expression regulation by binding to mRNAs. Their cardinal role in many types of cancer has only been realized in the past few years, and their potential to serve as prognostic or predictive biomarkers is currently extensively studied.

Our goal was to study whether miRNAs can serve as predictive biomarkers for response to chemotherapy. To this end, we extracted miRNAs from paraffin-embedded pre-operative muscle-invasive tumor biopsies of patients diagnosed with urothelial carcinoma, who have either been found to respond or not to respond to neo-adjuvant chemotherapy in the surgical specimen ('responders' vs 'non-responders', respectively). The expression pattern of ~ 900 miRNAs was compared using a commercial miRNA array. Whereas the vast majority of miRNAs expressed on the array exhibited a similar expression pattern in responders and non-responders, two miRNAs were significantly lower in the 'responders' in comparison to the 'non-responders' (p value<0.001 and $q<0.1$ using the false detection rate (FDR) method). Interestingly, both miRNAs can potentially down-regulate the mRNA of PTCH1, a tumor suppressor gene along the sonic-hedgehog pathway, already known to be implicated in urothelial carcinoma. We now plan to assess the levels of both these miRNAs in a larger cohort of responders and non-responders using quantitative reverse-transcription PCR. A putative model, future research directions and potential implications will be discussed.