CHARACTERIZATION OF THE FGFR3 REGULATORY NETWORK IN BLADDER TUMORS

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Bladder cancer is the fifth most frequently diagnosed cancer in Europe. Fibroblast growth factor receptor 3 (FGFR3) is a tyrosine kinase receptor found frequently altered through mutations or gene fusions in bladder cancer. Much is known about the oncogenic properties of an altered FGFR3 in bladder cancer, yet its regulatory network remains little studied. This project is part of a larger multidisciplinary collaboration group in which bladder cancer regulatory networks have been inferred using the LICORN ("Learning cooperative regulation network) algorithm, as well as web-based functional analysis tools such as IPA and Enrichr. Network reconstruction was carried out using transcriptomic data from human bladder tumors, as well as from *in vitro* and *in vivo* models of altered FGFR3 expression and/or activity. Following gene regulatory network reconstruction, our aim is to functionally validate such networks in different bladder cancer cell lines; and thus identify key regulatory elements that could be potential therapeutic targets in the future. The functional validation shall include a small screen using either CRISPR-Cas9 or siRNAs technologies followed by the evaluation of the impact on cell viability and expression of potential target genes. Once the key elements have been identified; their regulatory role in the FGFR3 network shall be confirmed by immunoprecipitation analysis; analysis of post-translational modifications, ChIP-seq etc…