GLI transcription targets in melanoma cell lines

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Hedgehog-GLI signaling pathway is one of the key regulators of normal development. Its aberrant signaling activity has been implicated in the initiation, progression and relapse of various types of cancer, including melanoma. Previous studies in our laboratory demonstrated that BRAF and NRAS melanomas have different response to HH-GLI signaling pathway inhibition. Identifying GLI protein functions in melanoma cell lines with different mutational background represents a distinct potential for the development of combined therapy with HH-GLI signaling pathway and BRAF/NRAS inhibitors. For that purpose, chromatin immunoprecipitation sequencing (ChIP-seq) was performed. The mutational status of 14 collected melanoma cell lines was confirmed by Sanger sequencing and the cell lines were divided into three categories based on their mutational background: BRAF-mutated, NRAS-mutated, and wild-type for BRAF and NRAS. Three cell lines were selected for ChIP analysis based on protein expression of HH-GLI signaling pathway components: CHL-1 for the wild-type cell group, A375 for the cell group with BRAF gene mutation and MEL224 for the cell group with NRAS gene mutation. Purified chromatin samples were used for library preparation and proceeded for next-generation sequencing (NGS). Target genes were analyzed *in silico* and validated by quantitative polymerase chain reaction (qPCR). qPCR validation included selected 23 protein coding genes, 9 miRNAs and 3 lncRNAs involved in regulation of MAPK signaling pathway. Further analysis can bring new insights into HH-GLI and MAPK signaling interplay and development of combined therapy.