Analysis of prominent molecular biomarkers in tissue biopsies for TGCT diagnostics

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Testicular germ cell tumours (TGCT) make up 95% of testicular tumours and are divided into seminoma (SE) and non-seminoma (NSE), considered to originate from germ cell neoplasia in situ (GCNIS). GCNIS is driven by an interplay of genetic, epigenetic and micro-environmental factors leading up to an arrest of gonocyte differentiation. Currently used biomarkers for testicular cancer lack specificity and sensitivity; and are used as accessories in diagnostics. Due to the difference in treatment and outcome depending on diagnosis better biomarkers are needed, which molecular methods from tissue biopsies promise. We have analysed prominent TGCT biomarkers (POU5F1, NANOG, KIT, SALL4, HOXA9 and MGMT) in silico mRNA gene expression, DNA methylation and patient's gene expression on the protein level to see the diagnostic potential or limitations of certain methods. TGCT patient data from TCGA dataset and healthy adult testis data from GTEx dataset was analysed using XENA, UALCAN and cBioPortal platforms. For immunohistochemical detection, 108 FFPE non-seminoma TGCT's from KBC SM and 48 tumour-free testes were used. Slides were analysed semi-quantitatively by pathologists and analysed in GraphPad Prism using Mann-Whitey and Kruskal-Wallis tests. The results have confirmed the efficiency of molecular methods, discriminating TGCT from healthy tissue (mRNA levels of all investigated genes) and discriminating SE from NSE (mRNA level of KIT and DNA methylation of MGMT and HOXA9), however discriminating individual NSE components and GCNIS proves to be a challenge and is only possible using gene expression on the protein level. Relying purely on molecular methods could mask the presence of individual NSE components found in TGCT, making the pathologist's expertise irreplaceable in diagnostics. More detailed investigation of the molecular profile of individual NSE components is the last hurdle for novel molecular methods to find widespread clinical use in TGCT diagnostics.