GCT-P08 Analysing large scale TGCT data from The Cancer Genome Atlas (TCGA): Challenges and considerations

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Background: Understanding molecular events resulting in testicular germ-cell-tumour (TGCT) pathogenesis and progression will facilitate development of new biomarkers and identification of genes/pathways for targeting with novel therapeutic agents. To this end, development of The-Cancer-Genome-Atlas (TCGA), which includes TGCTs from adult patients, has allowed progress [1]. However, TCGA has no normal gonadal control tissue for direct comparison with TGCT data. We sought to integrate two largescale datasets to further extend molecular observations in TGCTs.
Methods: RNA-Seq count data downloaded from TCGA website for all tumours including TGCTs (n = 137) and from Genotype-Tissue Expression (GTEx) portal (https://gtexportal.org/) including normal testis samples (n = 225). Attempts to normalise the two datasets were undertaken using approaches including comBat, surrogate-variable-analysis (SVA), linear models (EdgeR & Voom) and count-depletion approaches.
Results: The two (TGCT and testis) RNASeq datasets demonstrated major batch effects that were far greater than the gene expression variation within them. This was also true for other cancer datasets (e.g. liver), where internal normal controls were available to validate batch correction. Results were explored using differential gene-expression-analysis, principal-components-analysis and tSNE to determine if batch effects from sample origin could be successfully modelled into the expression analysis. We conclude that analysis of TCGA data without embedded control samples is challenging and suggest potential bioinformatic approaches to overcome such issues. We believe these batch effects cannot be removed, but can be substantially mitigated. This will be important to maximise the outputs/understanding from such publicly-available resources, as further analyses are being published without proper handling of such effects.

Reference

[1] Shen *et al.*, Integrated Molecular Characterization of Testicular Germ Cell Tumors. *Cell Rep*. 2018;23:3392–3406.

GCT-P09 Promising outcomes of extracranial germ cell tumours (eGCTs) in children & adolescents: Perspective from a developing country

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Background: The purpose of this single-centre study was to analyse the outcomes of extracranial GCTs in children treated on a multi-modality regimen.
Methods: Retrospective audit of children (<16 years) with a confirmed diagnosis of extracranial GCT over a period of 7 years (January 2009 to December 2015). All completely excised teratomas and stage I gonadal tumours (Low-Risk: LR) were observed. While stage IV ovarian & stage III–IV extragonadal GCTs (High-Risk: HR) received 6 chemotherapy cycles, the remaining (Intermediate-Risk: IR) received 4 cycles of chemotherapy.
Results: 198 children (out of 224 enrolled) were analysed; male: female ratio 1.57:1; median-age 3.1 years. Gonadal GCTs (n = 107) were more common than extragonadal (n = 98) with ovary as primary site in 75 children (37.9%) and sacrococcygeal site being the most common extragonadal location (19%). Stage-wise distribution revealed: Stage I&II = 29 each (14.6%); Stage III = 83 (41.9%); Stage IV = 57 (28.8%) patients. LR, IR and HR disease were noted in 29 (14.6%) patients, 88 (44.4%) and 81 (41%), respectively. Thirty patients relapsed (median time to relapse: 8.5 months) and 21 children died (disease related = 12 [4 progressive disease; 8 relapses]; toxic deaths = 7; unknown = 2). The 5-year EFS/OS was 76.5%/87.6% respectively with gonadal site, LR and non-metastatic disease associated with statistically better EFS (median follow-up: 47.2 ± 31.1 months). LR and IR GCTs had excellent outcome, warranting a shift to reduced therapy and decreased late-effects. In HR GCTs however, intensifying therapies to improve outcomes must be balanced against the risk of cumulative toxicity.

GCT-P10 Management of Stage 1 Ovarian Tumours: Is Surveillance Enough? Pan Anglian Experience 2005–2018

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Background: Surveillance is standard-of-care for all post-surgical stage 1 paediatric and testicular germ cell tumours (GCT). New European Society for Medical Oncology (ESMO) guidelines for adult gynaecology GCT patients still recommend adjuvant BEP chemotherapy for specific patients with stage 1 disease.
Methods: Review impact of change to post-surgical observation only, for all stage 1 ovarian tumours within regional Pan-Anglian GCT Multidisciplinary Meeting (PAGCT-MDT). Retrospective review of PAGCT-MDT recommendations and patient outcomes (2005–2018).
Results: 28 patients with a stage 1 ovarian tumour were discussed, aged between 11 and 69 years. All patients underwent primary oophorectomy before referral to PAGCT-MDT. 3 patients underwent surgery with bilateral salpingo-oopherectomy (BSO) with total abdominal hysterectomy (TAH): a 36-, 37- and 51-year-old with dysgerminoma, mixed GCT and carcinoid ovary, respectively. From 2005 to 2013: 4 dysgerminoma, 3 immature teratomas (IT) and 1 yolk-sac tumour (YST) stage 1 patients were offered 3 cycles of adjuvant BEP. One IT, post-BEP, relapsed then progressed through 4 lines of therapy and died. 1 YST patient was observed but relapsed within 4 months and was subsequently cured with BEP. After 2014, when surveillance only was recommended: 5 dysgerminoma, 4 IT, 2 non-specified GCT were observed. 1 YST received adjuvant BEP. Surveillance-only patients are disease-free at median follow-up of 2 years. Overall, 27/28 stage 1 patients are alive and disease-free. Avoidance of adjuvant chemotherapy for stage 1 ovarian tumours has not been shown to disadvantage survival for our patients. Fertility-sparing surgery for patients in child-bearing years should always be considered.