Aim: SCEC is a rare, aggressive tumor treated with regimens derived from pivotal studies of small cell lung cancer (SCLC), without robust data demonstrating the similarities between these two neuroendocrine cancers. This study was designed to investigate the gene expression profile and CNVs of SCEC, and compare it with the known data of SCLC and adeno/squamous cancer of the esophagus (EAC/ESCC) by bioinformatics approach.

Methods: De novo expression profile and array-based Comparative Genomic Hybridization (aCGH) was performed on 3 pairs of primary SCEC and corresponding normal samples. The expression data were complemented with public domain data sets from the GEO repository using the same working platforms. After normalization, primary tumors were submitted to statistical analysis for identifying differentially expressed genes (DEGs). Copy number associated aberration in gene expression (CNV-FC), Pearson correlation coefficients (r) between copy number and expression for the recurrent genes were computed. The genes with CNV-FC ≥ 2 and r ≥0.6 were selected as possibly cancer-associated genes.

Results: SCEC shared more DEGs in common with SCLC than EC (829 vs. 450), leading to greater correlation between SCEC and SCLC (r = 0.60 for SCEC vs. SCLC, 0.51 or 0.45 for SCEC vs. ESCC or EAC, 0.73 for ESCC vs. EAC). Functional annotation showed that a higher proportion of biological processes and pathways were in common between SCEC and SCLC, associating with mitosis, DNA repair, P53 and RB pathway etc (Benjamini p < 0.05). Comparing with EC, SCEC shared more co-up regulated DEGs coding for these pathways with SCLC (584 vs. 155). Overlapped gene interactive network between SCEC and SCLC was centered by NUF2. There were 39 individual genes selected as cancer-associated (median CNV-FC 5.4). The gene representing the highest correlation to separate SCEC from adjacent noncancerous tissue was PTP4A3 (CNV-FC: 21362, r = 0.998).

Conclusions: This bioinformatics analyses revealed that SCEC and SCLC displayed notably similar patterns of gene expression and CNVs on multiple biological processes. NUF2 and PTP4A3 might play a key role in carcinogenesis and metastasis of SCEC.

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