Identification Of Pan-Cancer Small Cell Neuroendocrine Phenotypes And Vulnerabilities

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SUMMARY

UCLA researchers in the Department of Molecular and Medical Pharmacology have developed a classifier for the identification and treatment of small cell neuroendocrine cancers and small-round-blue cell tumors not previously identified.

BACKGROUND

Small cell neuroendocrine (SCN) cancers are an extremely aggressive cancer type that arise across many tissue types and are thought to be relatively rare. Transdifferentiation from other cancer subtypes to a small cell neuroendocrine subtype has been observed to be an escape route from targeted therapy, and may be a resistance mechanism to more traditional chemotherapies. Furthermore, the treatment course for cancers with SCN features will likely be different than those of other subtypes, highlighting the need for correct classification of tumors with these features, and for the development of therapeutic approaches targeted at the specific vulnerabilities of these tumor types. Traditionally, determination of SCN cancers is done either on the basis of pathological diagnosis, often with immunohistochemistry of a small handful of markers such as Synaptophysin (SYP), Chromogranin (CHGA), Transcription termination factor 1 (TTF1) or Neural Cell Adhesion Molecule 1 (NCAM1). However, we have documented that many tumors with SCN features are heterogeneous for these markers, and hence can be missed using this classification modality. Hence the development of tests to identify SCN cancers is necessary for both reliable SCN diagnosis and treatment.

INNOVATION

UCLA researchers have created a pan-cancer small cell neuroendocrine classifier from omics data and functional screens that identifies tumors with small cell neuroendocrine phenotype, despite not being initially annotated as such by pathology calls. The molecular profiling-based classifier identifies tumors with either pure SCN histology or mixed ‘SCN and non-SCN’ histology. The benefit of this method is that it uses information across all genes in the genome and hence does not suffer from the heterogeneity problem of small subsets of markers. Additionally, the method harvests pan-cancer small cell neuroendocrine similarities at the level of both molecular profiles and functional dependencies to evaluate drug sensitivities in tumors of multiple tissue types. Finally, the technology could be used to help identify unannotated cases of small cell neuroendocrine cancer as well as predict their responses to a wide array of drugs. The researchers have generated a list of candidate drugs and gene disruptions to which SCN cancers are particularly vulnerable.

APPLICATIONS

- Small cell neuroendocrine cancer (SCN) diagnosis
- Small-round-blue cell tumor (SRBC) diagnosis
- Identification of SCN and SRBC drugs
- SCN and SRBC therapy

ADVANTAGES

- User-friendly method (based on PCA)
- Increased accuracy of tumor classification
- Drug efficacy assessment
- Drug sensitivity determination

STATE OF DEVELOPMENT

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OTHER INFORMATION

KEYWORDS

small cell neuroendocrine cancer, cancer therapy, tumor classification, omics data, genome, drug candidates, drug sensitivity, cancer diagnosis

CATEGORIZED AS

- **Biotechnology**
  - Bioinformatics
  - Genomics
- **Medical**
  - Diagnostics
  - Disease: Cancer
  - Screening
- **Research Tools**
  - Bioinformatics

RELATED CASES

2019-479-0

This technology has been used to identify similarities between blood SCN cancers as well as lung and SCN malignancies in tumor samples.

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Published Application	2022244263	08/04/2022	2019-479
European Patent Office	Published Application	3976195	04/06/2022	2019-479

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Treatment Of Melanoma With Ferroptosis Inducing Agents
- Statistical Comparison of Rank Lists and Molecular Profiles
- Microfluidic and Solid-State Beta Camera In-Vitro Kinase Radioassay

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