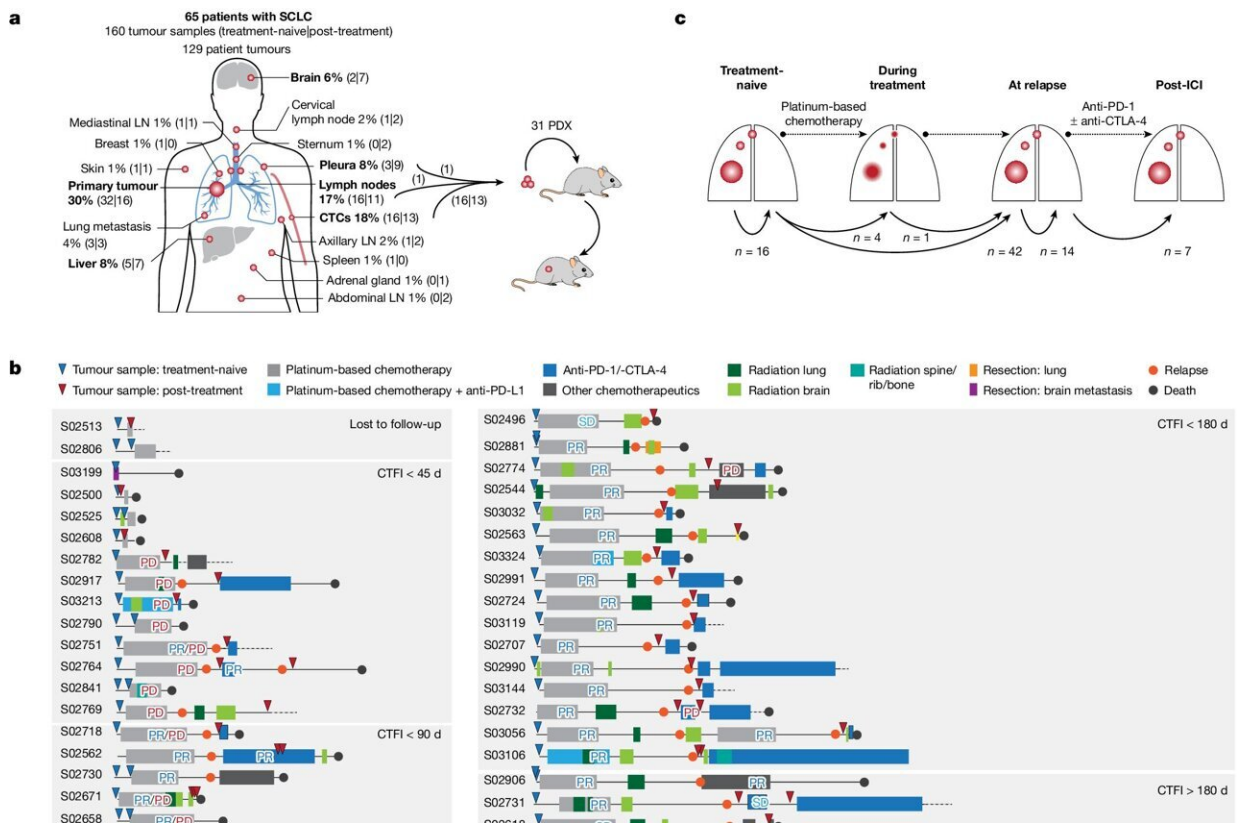


Scientists unravel mystery of drug response in small cell lung cancer

March 13 2024



Tumor samples and clinical history of 65 patients with SCLC. a, Tumor sites sampled from 65 patients with SCLC. Frequently sampled sites are highlighted in bold. Tumors were acquired either at the time of first diagnosis (treatment-naïve) or following initiation of treatment (post-treatment). Tumor samples analyzed as patient-derived xenotransplant (PDX) models are indicated. b, Schematic overview of the clinical course of 65 patients with SCLC. Patients were ordered according to their duration of response to first-line platinum-based chemotherapy, referring to a CTFI of 45, 90 and 180 days (National

Comprehensive Cancer Network (NCCN) guidelines). Patients who, following initiation of first-line treatment, were either lost to follow-up or underwent surgical resection of the primary tumor were sorted to separate panels. The treatment administered to each patient is annotated and the clinical response is described as either complete response (CR), partial response (PR), stable disease (SD), progressive disease (PD) or mixed response (PR/PD). A detailed description of all clinical characteristics is provided in Supplementary Table 1 and Methods. c, Schematic overview showing the analysis of paired, patient-matched tumor sites: paired studies of spatially distinct tumors at the time of first diagnosis (treatment-naive, $n = 16$); paired studies of tumor sites pretreatment and during treatment ($n = 5$) or at clinical relapse following completion of first-line platinum-based chemotherapy ($n = 42$); paired analyses of spatially distinct tumor sites at relapse ($n = 14$); and analyses of tumors acquired before and after subsequent lines of treatment with ICIs ($n = 7$). The scheme shows tumor sites in the lung, referring to primary and metastatic sites (larger and smaller red circles, respectively). LN, lymph node. Credit: *Nature* (2024). DOI: 10.1038/s41586-024-07177-7

Small cell lung cancer (SCLC) is a highly aggressive tumor of the lung that occurs especially in heavy smokers. Due to the rapid spread of this tumor type, most patients can only be treated with chemotherapy with remarkable initial anti-tumor efficacy. However, relapse often occurs over the course of time.

A research team at the University of Cologne led by Professor Dr. Roman Thomas, director of the Department of Translational Genomics and speaker of the Collaborative Research Center 1399 (CRC 1399, Mechanisms of Drug Sensitivity and Resistance in Small Cell Lung Cancer), has now identified the mechanisms governing this phenomenon for the first time: Due to predominant cell populations of [treatment](#)-sensitive cancer cells at the time of diagnosis, therapy is typically efficacious at the beginning.

Furthermore, the team shows that these large sensitive cell populations hide other numerous and very different cancer cells. These cells usually originate from early precursors of the original cells, are resistant to treatment and can multiply unchecked after successful treatment.

The study titled "Evolutionary Trajectories of Small Cell Lung Cancer under Therapy" is [published](#) in *Nature*.

Understanding development for targeted treatment

"It is a major challenge and an important goal to understand the exact development of tumors in individual patients during the course of treatment and relapse. Our analysis reveals mechanisms that are likely to be relevant for many advanced cancers," said Professor Dr. Julie George, lead author and co-speaker of the CRC 1399.

For example, the return of the tumor—which occurs in almost all patients—usually revealed a different dominant cell population. In further treatments during the course of therapy, for example with radiation, the cancer cells exhibited characteristics of the genetic damage caused by the first chemotherapy. In addition, the researchers were able to detect individual genetic characteristics in the [tumor cells](#), which are associated with a particular resistance to chemotherapy.

The findings of the study suggest that the potential success of further therapy developments could always be limited by the large number of therapy-resistant tumor cells. One [therapeutic approach](#) would therefore be to provide the most intensive initial treatment possible in order to minimize the number of cancer cells from which resistance can develop later.

"We have taken a decisive step forward in understanding this disease, and we very much hope that it will enable us developing new treatment

strategies that will lead to longer survival of the affected patients," said Professor Dr. Roman Thomas. "Although the results are somewhat sobering on the one hand, they offer the hope of new treatment options in the future on the other hand."

More information: Roman Thomas, Evolutionary trajectories of small cell lung cancer under therapy, *Nature* (2024). [DOI: 10.1038/s41586-024-07177-7](https://doi.org/10.1038/s41586-024-07177-7).
www.nature.com/articles/s41586-024-07177-7

Provided by University of Cologne

Citation: Scientists unravel mystery of drug response in small cell lung cancer (2024, March 13) retrieved 27 April 2024 from <https://medicalxpress.com/news/2024-03-scientists-unravel-mystery-drug-response.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.