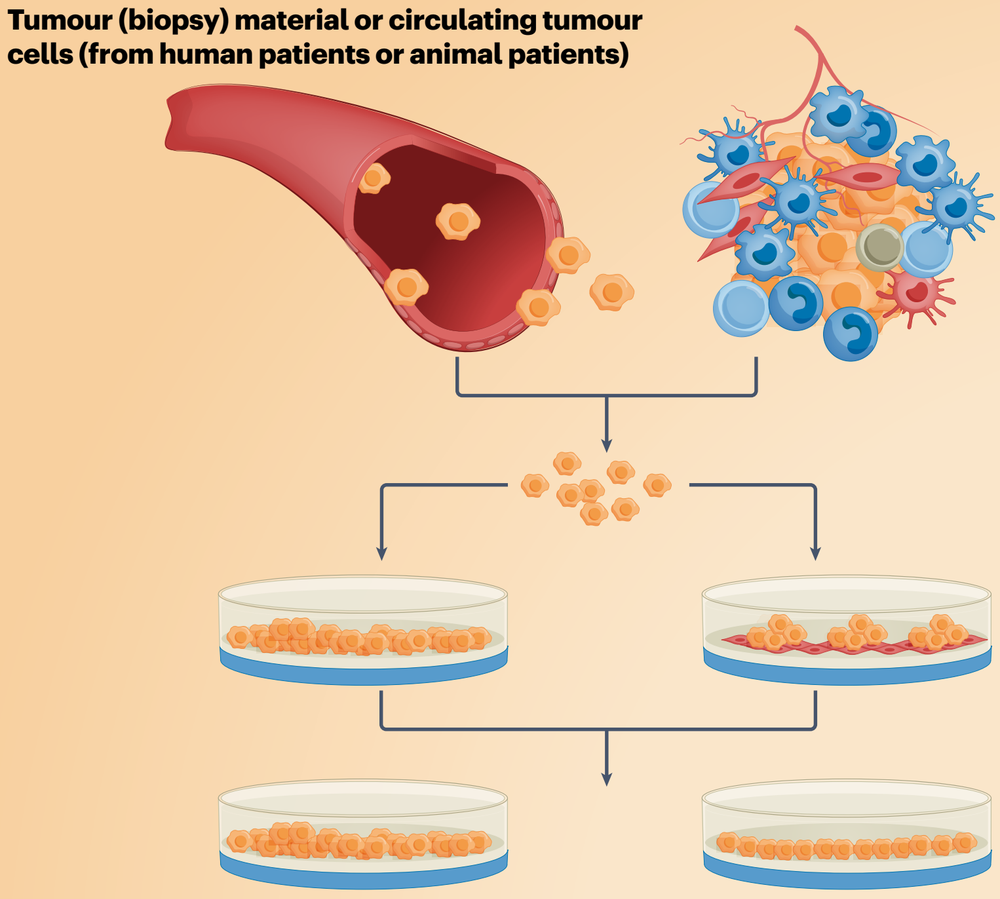
Drug-resistant cell lines in cancer

Jindrich Cinatl Jr, Mark N. Wass & Martin Michaelis

The occurrence of therapy resistance is the major reason for treatment failure in cancer. Resistance can be intrinsic or acquired. Conceptually, intrinsic resistance results from pre-existing resistance mechanisms, whereas acquired resistance results from directed evolution in response to the selection pressure imposed by anticancer therapies. To study acquired resistance, model systems are needed that reflect the evolutionary processes underlying resistance formation – most commonly, drug-adapted cancer cell lines. Three main methods are used to establish drug-resistant cell lines: continuous cell line exposure to stepwise increasing drug concentrations; pulsed treatment where exposure to the drug is alternated with recovery periods in drug-free medium; and one-step selection of pre-existing resistant subpopulations in a cancer cell line using a (comparatively) high drug concentration.

Establishment of cancer cell lines from tumour material

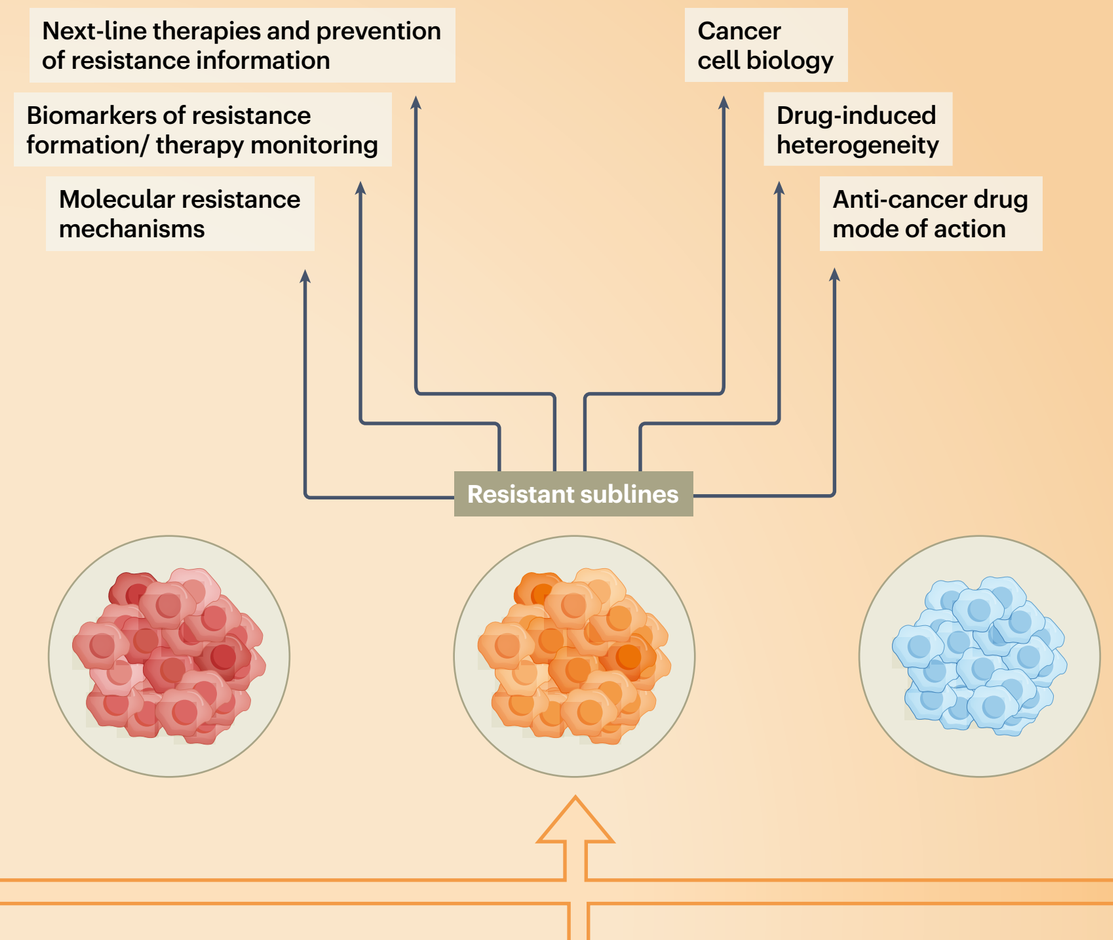
Tumour material is dispersed and cultured in the absence (left) or the presence (right) of a feeder layer (typically inactivated fibroblasts) until it develops into a permanent cell line, which may grow as a monolayer, in agglomerates and/or as non-adherent culture.

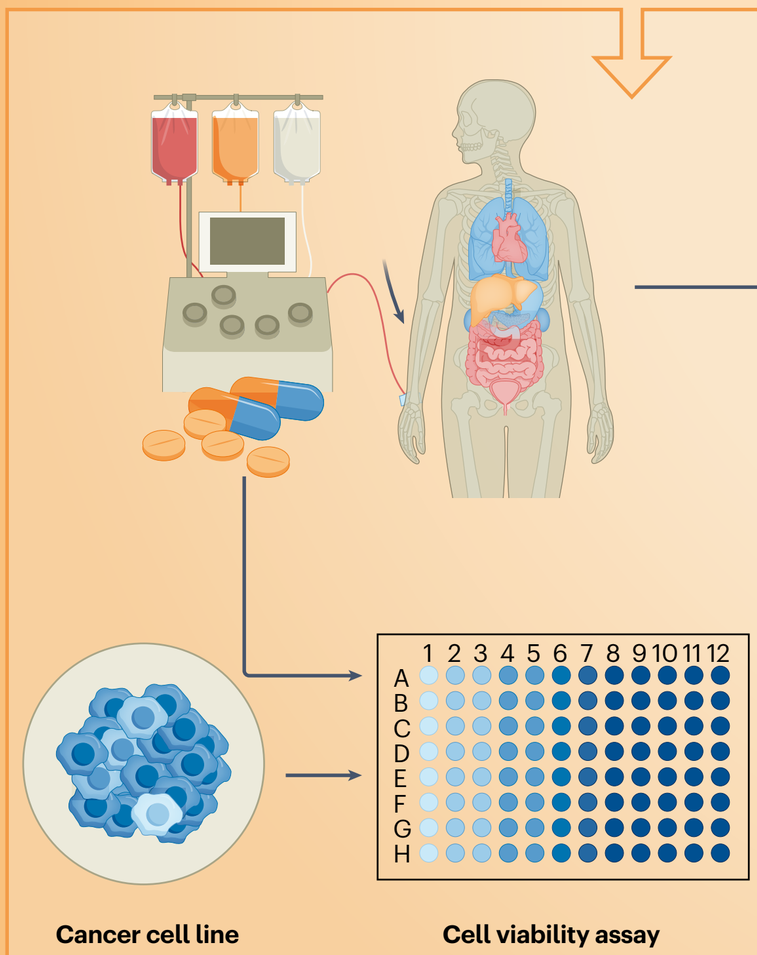


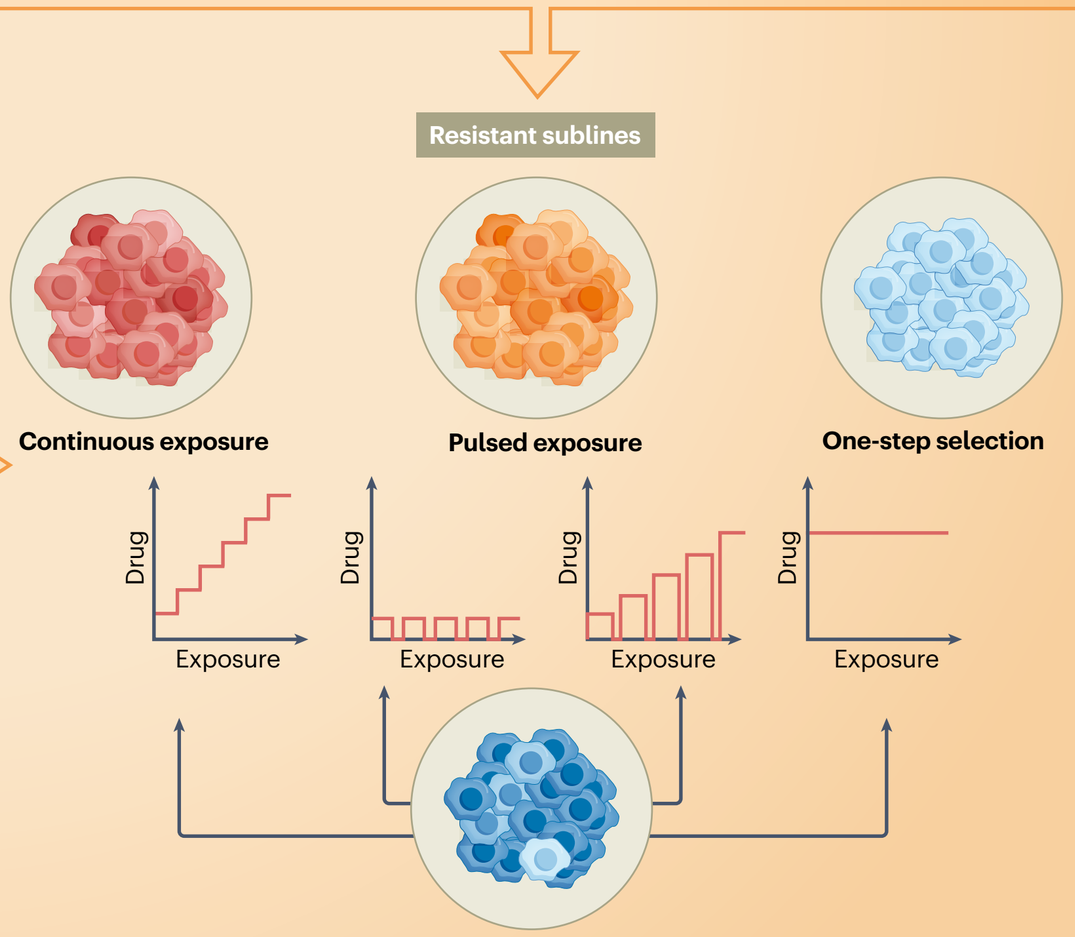
Applications of drug-adapted cancer cell line

Drug adapted cell lines are used to:

- Investigate resistance mechanisms
- Identify biomarkers
- Identify next-line therapies and/or therapies that delay resistance formation
- Investigate the impact of resistance formation on cancer cell biology
- Study drug-induced clonal selection
- Investigate the mode of action of anti-cancer drugs







Cell line selection for the generation of drug-resistant sublines

If clinical plasma levels are available, it is recommended to select (commercially available) cell lines that are sensitive to clinical drug concentrations for the establishment of acquired resistance models. Three-dimensional model systems (e.g. cancer cell spheroids, cancer cell organoids) are also under investigation.

Cancer cell line adaptation to anti-cancer drugs

Adaptation to drugs can be induced by continuous cell line exposure to stepwise increasing drug concentrations, pulsed treatments with a fixed dose or increasing doses, or one-step selection of pre-existing resistant subpopulations in a cancer cell line.

CancerTools.org
CancerTools.org is the first-of-its-kind global, non-profit, cancer-focused, research tools biorepository. As part of Cancer Research UK, we are determined to accelerate cancer discoveries. For 40+ years, scientists from over 180 leading academic universities and cancer centres across the globe have deposited their novel research tools with us, allowing us to build a unique collection of cancer-relevant reagents. The collection features a wide range of cell lines, antibodies, organoids, mouse models, PDX models, cell culture media and more, all applicable to a wide array of cancer research areas.

With in-bound shipping, storage, production, maintenance, and worldwide distribution, we are dedicated to making these valuable research tools accessible to the wider scientific community- to ensure you are always equipped with the materials you need to continue making discoveries.

Affiliations
Jindrich Cinatl Jr[1], Mark N. Wass[2] & Martin Michaelis[1,2]
[1]Dr Petra Joh Research Institute, Frankfurt am Main, Germany. [2]School of Biosciences, University of Kent, Canterbury, UK.

Competing interests
The authors declare no competing interests.

Peer review information
Nature Communications thanks the anonymous reviewer for their contribution to the peer review of this work.

Acknowledgements
The authors thank Marcel Tisch and Servier for providing images via bioicons.com.

Edited by Joanne Clancy; copyedited by Cecilia Derrick; designed by Karen Moore.

© 2024 Springer Nature Limited. All rights reserved.

https://www.nature.com/articles/s41467-024-52441-z

Open Access. This article is licensed under a Creative Commons. Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this license, visit http://creativecommons.org/.

nature communications

CancerTools.org
Global Research Tools Collaborative