

De-novo construction of organ-agnostic cancer modules and therapeutic application

Citation for published version (APA):

Mohamed Mamdouh Abdelkareem Gomaa, Z. (2023). *De-novo construction of organ-agnostic cancer modules and therapeutic application*. [Doctoral Thesis, Maastricht University]. Maastricht University. <https://doi.org/10.26481/dis.20231127zm>

Document status and date:

Published: 01/01/2023

DOI:

[10.26481/dis.20231127zm](https://doi.org/10.26481/dis.20231127zm)

Document Version:

Publisher's PDF, also known as Version of record

Please check the document version of this publication:

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

[Link to publication](#)

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license above, please follow below link for the End User Agreement:

www.umlib.nl/taverne-license

Take down policy

If you believe that this document breaches copyright please contact us at:

repository@maastrichtuniversity.nl

providing details and we will investigate your claim.

Most diseases are currently treated symptomatically due to a lack of understanding of their underlying causal mechanisms. The outdated disease classifications hinder precision medicine and effective drug development, emphasising the need for a shift towards defining diseases based on molecular mechanisms. To fill this gap, the current disease classifications are critically reviewed, emphasising their drawbacks in supporting mechanistic disease definitions. To address these challenges, a data-driven strategy is outlined, advocating for disease classifications based on both molecular and clinical data and offering examples of successful partial implementations as evidence of its potential effectiveness.

It follows naturally that should we be able to understand the underlying mechanisms that govern a specific disease, we could then target different members of the perturbed mechanism. Ideally, this can be achieved by repurposing drug candidates already approved for other diseases that share common genetic elements with the disease under investigation. Disease mechanisms typically involve small networks or disease modules rather than individual proteins. Consequently, we propose targeting disease networks via modulation at various sites i.e., synergistic network pharmacology. It is essential to differentiate this approach from current combination therapy, which involves mechanistically unrelated drugs and does not specifically target causal genes.

In the field of oncology, a significant shift is underway towards the development of biomarker-targeted agents. This shift has been prompted by a profound realisation that cancers are not homogeneous entities based solely on organ location. Instead, they exhibit increasing heterogeneity at the genetic levels. This understanding has highlighted the paramount role of precision medicine in the field, where therapies can be tailored to target specific disease mechanisms in individual cancer patients. Therefore, we evaluate the efficacy of utilising existing oncology databases to predict perturbed networks and identify potential drug candidates that can be repurposed for cancer therapy.