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

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 The outdated disease classifications hinder precision medicine and effective drug development, emphasising the need for a shift towards defining diseases based on molecular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.