

Mechanism-based diagnosis of cyclic GMPopathies and pharmacological interventions

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Propositions belonging to the thesis

Mechanism-based diagnosis of cyclic GMPopathies and
pharmacological interventions

Alexandra Petraina, 1st of June 2023

1. Most non-communicable diseases are defined by describing a symptom in an organ, not by a causal molecular mechanism.
2. Consequently, most therapeutic drugs have high numbers needed to treat and to most patients provide no benefit.
3. To achieve precision medicine, we need a mechanism-based redefinition of diseases and the diagnostics to detect and monitor them.
4. Disease mechanisms are best described by protein-protein interaction modules and targeted by multiple drugs through synergistic network pharmacology.
5. The failure of some of the previous cGMP-based drug trials may be due to lack of mechanism-based patient inclusion diluting any treatment effect by non-responder patients.
6. One important disease module involves dysfunctional cGMP signalling as detected in peripheral blood to stratify patients with cardiovascular phenotypes for mechanism-based intervention.
7. sGC stimulators can be repurposed in a mechanism-based and precise manner for diseases where the apo-sGC/sGC ratio is increased.
8. I have not failed. I've just found 10,000 ways that won't work. (Thomas Edison)
9. There is no perfect time for anything. There is only now. (Jack Canfield)
10. First say to yourself what you would be; and then do what you have to do. (Epictetus)