Scientists find natural mimetics of anti-cancer, anti-aging drugs metformin and rapamycin

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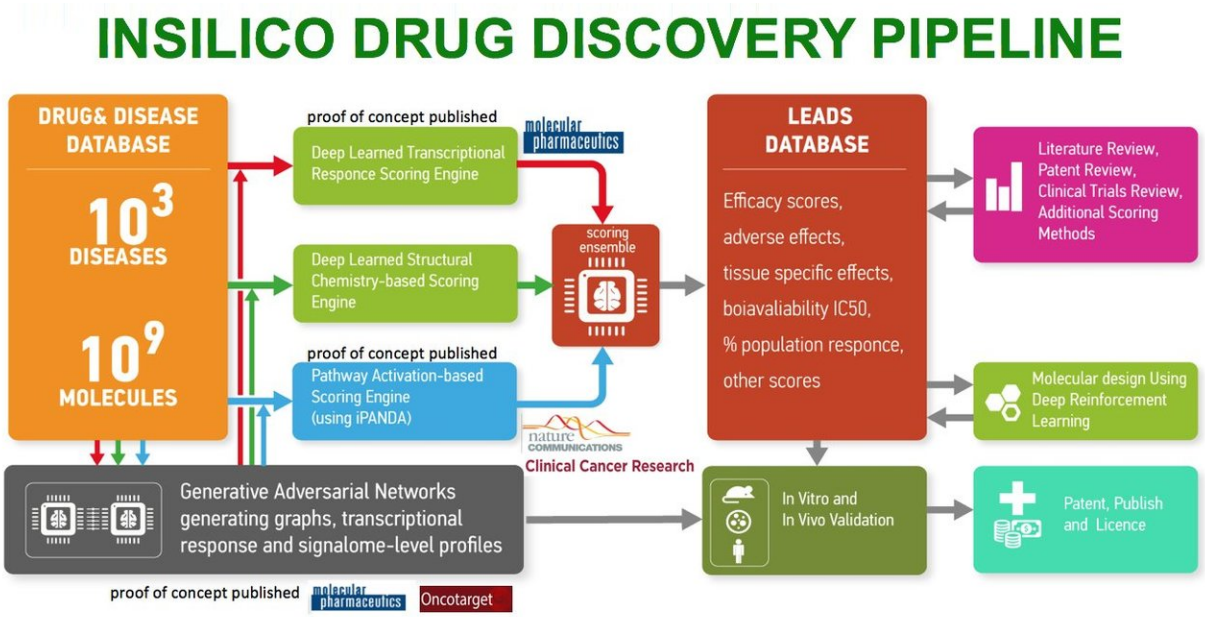

AI-driven drug discovery. Credit: Insilico Medicine

Researchers from the Biogerontology Research Foundation, Insilico Medicine, Life Extension and other institutions have published a study in the journal *Aging* on the identification of natural mimetics of metformin and rapamycin. Metformin, a common type 2 diabetes drug, and rapamycin, a common anti-rejection drug, have both been shown to have

substantial anti-aging and anti-cancer effects in a variety of model organisms. However, both compounds have known side effects and are regulated drugs for specific disease indications, factors that problematize their off-label use as healthspan-extending drugs.

In this study, the researchers applied deep-learning neural networks to profile the safety and gene- and pathway-level similarity of more than 800 natural compounds to metformin and rapamycin in an effort to identify natural compounds that can mimic the effects of these anti-cancer and anti-aging drugs while remaining free of the adverse effects associated with them.

"Earlier this year, we launched Young.AI, a comprehensive system utilizing the recent advances in deep learning for tracking a variety of aging biomarkers. One of the goals of our group is to identify the combinations of molecules that achieve the desired effects," said Alex Zhavoronkov, Ph.D., co-author of the study.

Their analysis identified many previously unreported metformin and rapamycin mimetics. In particular, they identified allantoin and ginsenoside as strong mimetics of metformin, epigallocatechin gallate and isoliquiritigenin as strong mimetics of rapamycin, and withaferin A as a strong mimetic of both. Additionally, their analysis also identified four previously unexplored natural compounds as fairly strong mimetics of rapamycin.

"Aging is not recognized as a disease, so we need strong potential geroprotectors of natural origin on the market—supplements that slow down aging, affecting the key mechanisms of aging at the molecular and cellular level," said Alexey Moskalev, Ph.D., a co-author of the study.

These findings are significant because, as naturally occurring compounds, such nutraceuticals are not subject to regulation by the FDA

and other regulatory bodies. Furthermore, because the researchers induced a deep-learning-based classification of the safety profiles associated with these compounds, the novel candidate mimetics the study identified are likely to have less adverse effects than metformin and rapamycin, though this needs to be further validated by clinical testing.

"This study is significant not only for the identification of novel candidate mimetics of metformin and rapamycin, which as natural compounds are not subject to regulatory bodies like the FDA and which have higher-scoring safety profiles as indicated by our deep-learned safety profile classification analysis, but also for demonstrating particularly powerful screening methods that can be applied to the identification of novel and safe mimetics of other known anti-cancer and healthspan-extending drugs and compounds," said Franco Cortese, co-author of the study and Deputy Director of the Biogerontology Research Foundation.

More information: Alexander Aliper et al, Towards natural mimetics of metformin and rapamycin, *Aging* (2017). DOI: 10.18632/aging.101319

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