OPINION

Design and development of robust and precision personalized medicine

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Frederike H. Petzschner recently published an article in Science titled 'Practical challenges for precision medicine' (Science, 2024, 383, 149–150; doi:10.1126/science.adm9218) expressing the view that machine learning tools are not suitable for advancing precision medicine. In this write-up, we present some evidences which show that mathematical genomics, mathematical proteomics, statistical genomics and statistical proteomics, along with machine learning tools can effectively guide the development of high-precision personalized medicine.

Here highlighted on a comprehensive approach, modelling both genetic and epigenetic components of diseases or behaviours using machine learning and computational biology (mathematical genomics, mathematical proteomics, statistical genomics and statistical proteomics)[1–3], followed by the design of 400 distinct 15 nm size particles for each target ailment. They focussed on particles such as 15 nm TiO_2 (rutile), 15 nm TiO_2 (anatase), 15 nm lignin-capped Ca_4Mn_5O and 15 nm lignin-coated ZnO and conducted extensive *in vitro* and *in vivo* screening. The outcomes are remarkably significant, including findings such as 15 nm TiO_2 (anatase) effectively controls acute cat experimental esophagitis with $70 \pm 8\%$ accuracy and 15 nm TiO_2 (rutile) enhances the growth of the gut beneficial bacteria (probiotics; *Bacillus coagulans*) by $80 \pm 11\%$ (ref. 4). Additionally, lignin-capped 15 nm Ca_4Mn_5O exhibited a $70 \pm 2\%$ control over diabetes *in vitro*, while lignin-capped ZnO displayed an $83 \pm 9\%$ efficacy in managing human skin infections caused by *Trichophyton* sp. Employing biochemistry and transcriptomics tools, we delved into the mechanisms behind these effects, uncovering insights such as 15 nm TiO_2 (rutile) acting on phosphoenolpyruvate sugar phosphotransferase systems. Similarly, TiO_2 (anatase) works on

the cat oesophageal epithelium and turns on phospholipase production and 15 nm size Ca_4Mn_5O can control diabetes by up-regulating TCA cycle. Finally, lignin-capped ZnO enters the fungal hyphae and dismantles the micro vehicular traffic. These results show that personal precision medicine can be developed using machine learning tools and aforesaid computational biology tools. This is an avenue for advancement in this field.

We tested the biosafety of the drugs derived from the aforesaid model. Fifteen mice per drug were kept following OECD protocols and kept single in a cage. Each mouse in a single treatment was challenged with 15 nm particles as drugs and physiological parameters were recorded at 15-day intervals (weight an blood parameters). In 85% of the mice, no detrimental effect was observed. Thus, the developed above-mentioned types of 15 nm particles are found to be biologically safe. Hence, we tentatively assert that the aforementioned combination strategy for precision personalized medicine, integrating machine learning and computational biology, is not only unique but also represents promising pathways for the future.

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