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Improved genetic risk model for predicting and subtyping disease

Researchers at Stanford have developed the first polygenic risk model of its kind for estimating personalized genetic risk profiles. No other genetic model is able to identify biological drivers of disease risk and generate disease subtypes.

While many versions of polygenic risk scores (PRS) have been developed and used with some success to identify individuals at high risk for diseases like cancer and obesity, current methods are inadequate. This is because simple linear models can effectively predict outcomes but do not generally account for disease subtypes or pathways.

In contrast, the new model is based on latent trait-related genetic components. Each component has genetic determinants which can be expressed as a component PRS. This innovative "palette" approach breaks down genetic risk into its constituent pathways, and may better describe the clinical manifestations of complex disease.

Stage of Development
Based on a test set of more than 67,000 individuals from UK Biobank, the researchers found that the most at-risk individuals (2% percentile) have 2.5-kg/m2 higher Body Mass Index, 3.5-fold risk of myocardial infarction, and 4.8-fold risk for gout compared to the general population. They further characterized individual and population-wide genetic risk profiles for each trait, and replicated these trends in an independent set of nearly 25,500 other participants of the Biobank.

Applications

- Identifying biological drivers and disease subtypes with genetic data
- Clinical trial design
- Disease risk prediction and public health screening

- Drug development
- Diagnostics

Advantages

- No methods currently subtype disease based on genetics.
- No methods currently provide biological interpretation of disease risk prediciton.

Publications

- M. Aguirre, Y. Tanigawa, G. Venkataraman, R. Tibshirani, T. Hastie, M.A. Rivas Polygenic risk modeling with latent trait-related genetic components bioRxiv Preprint posted Oct. 17, 2019.

Patents

- Published Application: 20210065846
- Issued: 12,100,480 (USA)

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