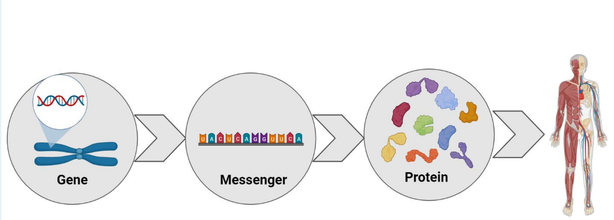
Connecting the dots: Unravelling human diseases through genetics and blood protein levels

Mine Koprulu, Julia Carrasco-Zanini

Introduction

Our genes and proteins

- Every cell in our body has a DNA that is unique to us.
- This code contains our genes, which are like instruction manuals for creating proteins.
- Proteins are important for many things in our body ranging from their role in fighting infections to carrying out various functions that keep us healthy.
- Proteins are the majority (>95%) of drug targets.

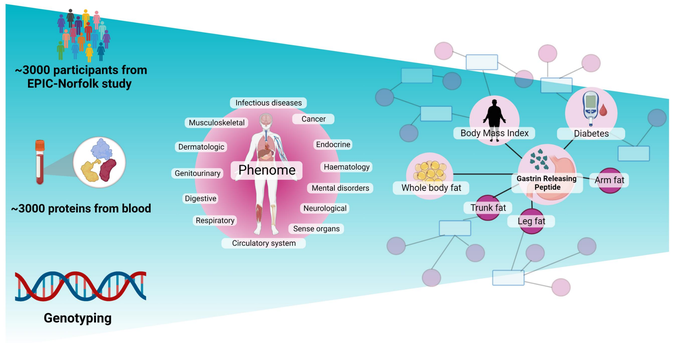


Why should we study genes or proteins?

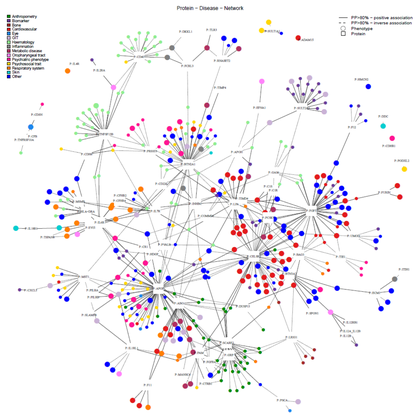
- Changes in our genetic code or blood protein levels can impact our risk for disease such as diabetes.
- Studying genetic changes, blood protein levels and other biological data help us:
  - Better understand disease mechanisms, in other words, how diseases act in our body.
  - Identify disease-causing proteins, which can be targeted for more effective therapies.
  - Identify markers that might indicate you are at high risk of a specific disease.

Identifying disease-causing proteins

- Genetic sequencing and measurement of blood protein levels of ~3.000 proteins was performed in ~3,000 EPIC-Norfolk participants.



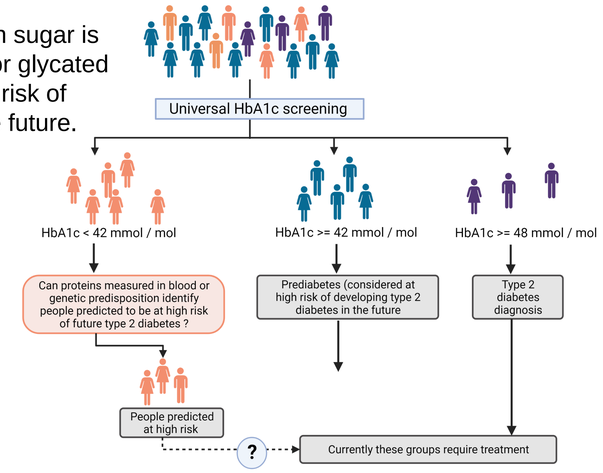
- Combining these different layers of biological data allowed us to identify disease-causing proteins, such as gastrin releasing peptide (GRP) for diabetes.



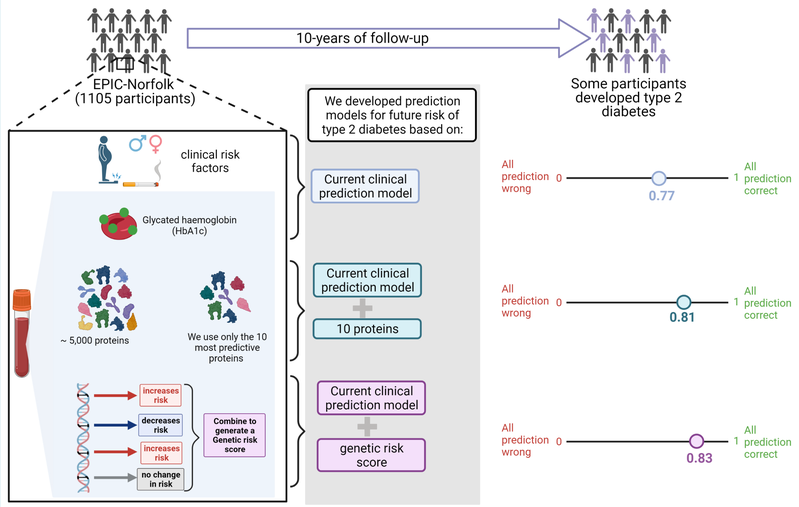
- Applying the same methods, we identified **hundreds of disease-causing proteins for many diseases**.
- In theory, changing levels of disease-causing proteins back to what they are in “healthy” people can prevent of treat some diseases.
- Identifying disease-causing proteins can facilitate the development of more effective drugs and therapies for many diseases.

Improving identification of people at high risk of future diabetes

- Currently we use a marker of how much sugar is stuck to red blood cells (called HbA1c or glycated haemoglobin) to identify people at high risk of developing type 2 diabetes (T2D) in the future.
- Can blood protein levels or genetics improve identification of people at high risk of diabetes?



- Assessing genetic predisposition (by the genetic risk score) can improve the way we identify people at high risk of future diabetes, beyond what is currently done by the NHS.
- Currently, healthcare systems consider people with prediabetes are at a sufficiently high risk (**~1 in 5 will develop diabetes in the next 20 years**) to warrant treatment to prevent development of diabetes.



- People with high genetic predisposition are only at about half the risk (**~1 in 10 will develop diabetes in the next 20 years**) compared to people with prediabetes.
- Whether intervention is warranted in people with a high genetic predisposition is a political and economic decision.