## Evolutionary studies as guidelines

• The median score for other nonpolar amino acid substitutions was M=0.903 (IQR 0.167-0.99), and for the rQTY substitutions, it was just M=0.435 (IQR 0.018-0.974). Moreover, the rQTY substitutions also showed a lower impact compared to all 19 amino acids M=0.8955 (IQR 0.15-0.99). (Figure S3 and Figure S4). The narrower Interquartile Ranges (IQR) for other polar amino acid changes could be indicative of a more definitive damaging impact on protein function, potentially due to structural limitations that have led to a less tolerated substitutions.

• Conserved = Less selection pressures

After removing the nonlinear effect of evolutionary conservation, partial Spearman's correlation coefficient between amino acid pairs became more negative: -0.214, +0.0923, +0.165, +0.347, respectively. Apparently, residual evolutionary pressures acted as a confounding variable to reduce the negative correlations between aminoacids. Hence, suggesting that evolutionary pressures such as the need for specific structural motifs and functions may have played a more significant role in shaping the diversity of alpha helices.

- Sequance based approaches can possibly incline toward conformations mirroring the consensus that does not necessarily represent the global energy minimum.
- Alongside the MSA utilization, gene deterministic approaches aims to predict a single, most likely protein structure based on the given input data and does not produce a probability distribution with the Boltzmann form, contrary to the probabilistic occurrence in nature.

## Distortions and misuse of genetic and evolutionary science

- Genetic screening
- Publication biases and reduce in scientific accountability
- This can be prevented by population genetics, mRNA research, and evolutionary studies. Better statistics is crucial.
- Cultural issues:

 Genetic determinism is the belief that human behaviour is directly controlled by an individual's genes or some component of their physiology, generally at the expense of the role of the environment, whether in embryonic development or in learning. Biological determinism has been associated with movements in science and society including eugenics, scientific racism, and the debates around the heritability of IQ, the basis of sexual orientation, and sociobiology

- Scientific racism misapplies, misconstrues, or distorts anthropology craniometry, evolutionary biology, and other disciplines or pseudodisciplines through proposing anthropological typologies to classify human populations into physically discrete human races, some of which might be asserted to be superior or inferior to others.
- Scientific racism was common during the period to the end of World War II, Since the second half of the 20th century, scientific racism has been discredited and criticized as obsolete, yet has persistently been used to support or validate racist world-views.

 Racial hygiene was historically tied to traditional notions of public health, but with emphasis on heredity. In 1869, Francis Galton (1822– 1911) proposed the first social measures meant to preserve or enhance biological characteristics, and later coined the term "eugenics".

 Galton introduced correlation and regression analysis and discovered regression toward the mean.

Clinicians should consult geneticist and structural biologist rather
than blind fully screening mutations and sequencing DNA

- Politicians should not allow funding to more and more genome wide association studies (GWAS)
- Scientist should use the vast unnecessary genome data for alternative projects.

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