Phenotyping in the Clinic

What is phenotyping, and how does it matter in your practice? Medical professionals are trained to evaluate the physiological and behavioral features of their patients. Phenotyping describes our ability to quantify and characterize these features and their correlation with the genetic code. A patient's clinical features, such as skeletal characteristics or hemoglobin A1c levels, are clinical descriptions of phenotypes.

GENETICS AND PHENOTYPE

Only a portion of the information stored within an individual's chromosomal DNA sequence is observable in their phenotype. These are often sequences that encode genes, control the regulation of gene usage (expression), or structural sequences that maintain the shape of chromosomes within the cell nucleus.

THE PATH FROM GENE TO FEATURE

As an example, Marfan syndrome is the phenotypic result of certain changes to the DNA encoding the fibrillin-1 gene *(FBN1)*. Genetic testing is used in the differential diagnosis of related disorders.

Inherited allelic variants can give rise to a non-functional form of the fibrillin-1 protein, a critical component of connective tissue.

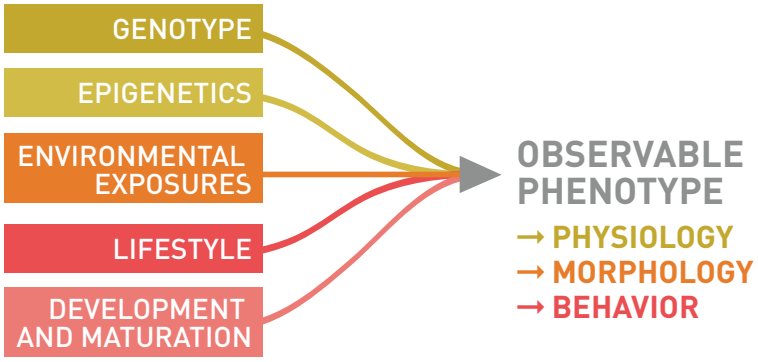
The resultant defects in connective tissue contribute to the clinical manifestations, or phenotype.

Phenotypic features of Marfan Syndrome vary depending on variation in other parts of a person's genome and range from mild (elongated bone structure, nearsightedness) to severe (aortic enlargement, mitral valve prolapse).

Even mildly affected individuals born with this condition could benefit from increased monitoring of their cardiac function and other health parameters.

CHARACTERIZING PHENOTYPE

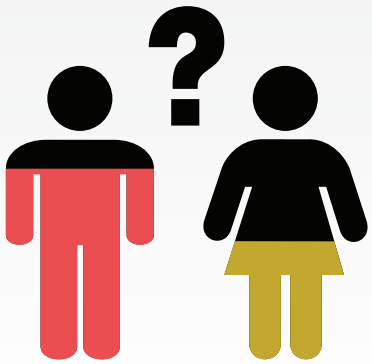
Researchers and clinicians use an evolving set of standardized *ontology terms*, or controlled vocabularies, to describe these observed traits. A typical examination relies on phenotyping to determine the current or ongoing state of health of the patient. Incorporating standardized language facilitates the comparison of case studies and identifying trends in phenotype-genotype connections using computational tools.



ENVIRONMENTAL INFLUENCE

Both the external and internal environments are important to consider when phenotyping a patient:

1. **Exposures:** The intensity and frequency of exposures to environmental factors like UV light, medications, and pollution
2. **Lifestyle:** As we each have some degree of control here, evaluating this area can be particularly crucial to finding a successful treatment strategy. Lifestyle includes such things as stress, diet, and activity level.
3. **Maturation:** The passage of time has important effects on our bodies; some phenotypic traits (i.e. traits related to pregnancy) usually only manifest after specific developmental milestones (i.e. puberty).



The exact proportion that genotype and environment contribute to phenotype varies widely among traits, and even among individuals.

Reference:
1. Cooper DN, Krawczak M, Polychronakos C, Tyler-Smith C, Kehrer-Sawatzki H. Where genotype is not predictive of phenotype: towards an understanding of the molecular basis of reduced penetrance in human inherited disease. Human Genetics. 2013;132(10):1077-1130. doi:10.1007/s00439-013-1331-2.

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