



## How one cell gives rise to an entire body

By Elizabeth Pennisi | Apr. 26, 2018, 2:00 PM

Mendelian ideal: dominant/recessive - unlinked

Genetic realities:

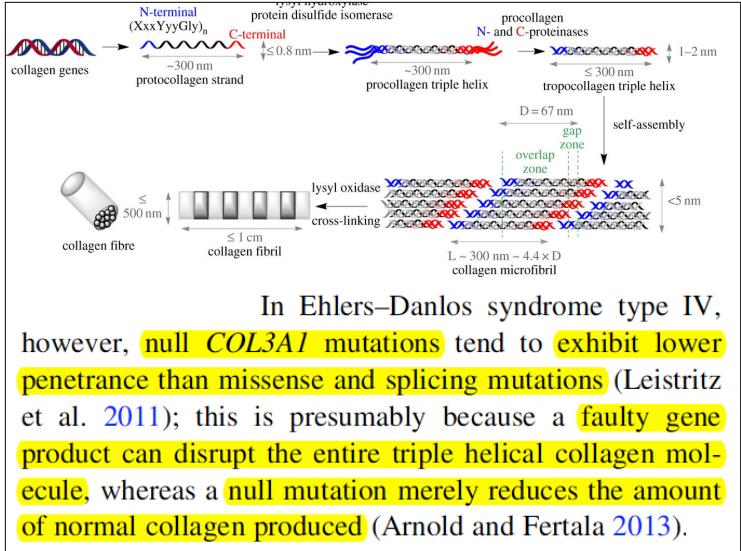
- linked alleles
- imprinted alleles (paternal or maternal allele expressed)
- changing alleles (anticipation / shortening)
- synthetic interactions
- interactions (penetrance/expressivity)

Hum Genet (2013) 132:1077–1130  
DOI 10.1007/s00439-013-1331-2

REVIEW PAPER

## Where genotype is not predictive of phenotype: towards an understanding of the molecular basis of reduced penetrance in human inherited disease

David N. Cooper · Michael Krawczak ·  
Constantin Polychronakos · Chris Tyler-Smith ·  
Hildegard Kehrer-Sawatzki



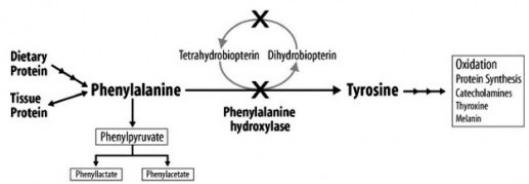
In Ehlers–Danlos syndrome type IV, however, **null COL3A1 mutations** tend to **exhibit lower penetrance than missense and splicing mutations** (Leistritz et al. 2011); this is presumably because a **faulty gene product can disrupt the entire triple helical collagen molecule**, whereas a **null mutation merely reduces the amount of normal collagen produced** (Arnold and Fertala 2013).

One rather well-understood example of incomplete penetrance of a dominantly inherited mutation is factor V Leiden (*F5*, Arg534Gln; Arg506Gln in legacy nomenclature; rs6025) which occurs at polymorphic frequencies (2–5 %) in European populations, but is associated with a sixfold increased risk of venous thrombosis and a two- to threefold increased risk of pregnancy loss (Kujovich 2011).

vast majority of factor V Leiden carriers appear to be clinically unaffected.

## Treating genetic diseases

## Phenylketonuria (PKU)



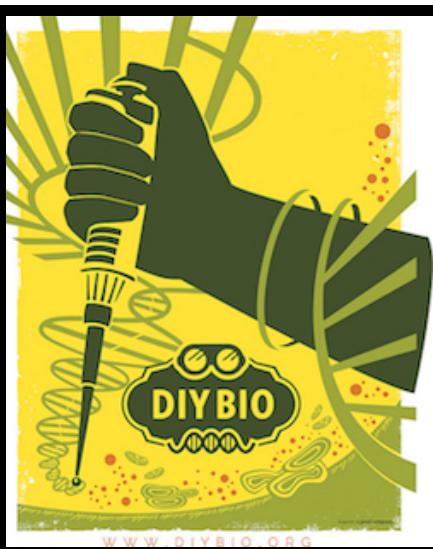
A classic example is phenylketonuria, where inactivating mutations in the *PAH* gene encoding the enzyme phenylalanine hydroxylase lead to severe intellectual disability in the context of a normal diet, whereas a life-long phenylalanine-restricted diet makes possible a relatively healthy life (Blau et al. 2010).

## Doctors Successfully Treat Rare Genetic Disorder in Utero

The disorder, called X-linked hypohidrotic ectodermal dysplasia, leaves patients unable to produce sweat, which can be life-threatening.



ISTOCK, WAVEBREAKMEDIA



# 'I want to help humans genetically modify themselves'

Former Nasa biochemist Josiah Zayner became an online sensation by conducting DIY gene therapy on himself. He explains why he did it



▲ Josiah Zayner with his Crispr gene-editing kit. Photograph: Courtesy Josiah Zayner / The ODIN

## What rules should apply to DIY bioengineering?

Final will be cumulative... review midterms 1 and 2

What treats you like for the Friday film screening?