

VUS Olgu Örnek Çözümlmeleri

Dr.Pınar GENÇPINAR

27. ULUSAL
ÇOCUK
NÖROLOJİSİ
KONGRESİ
29 Nisan - 3 Mayıs 2026
Concorde Luxury Resort & Convention & Spa - KKTC

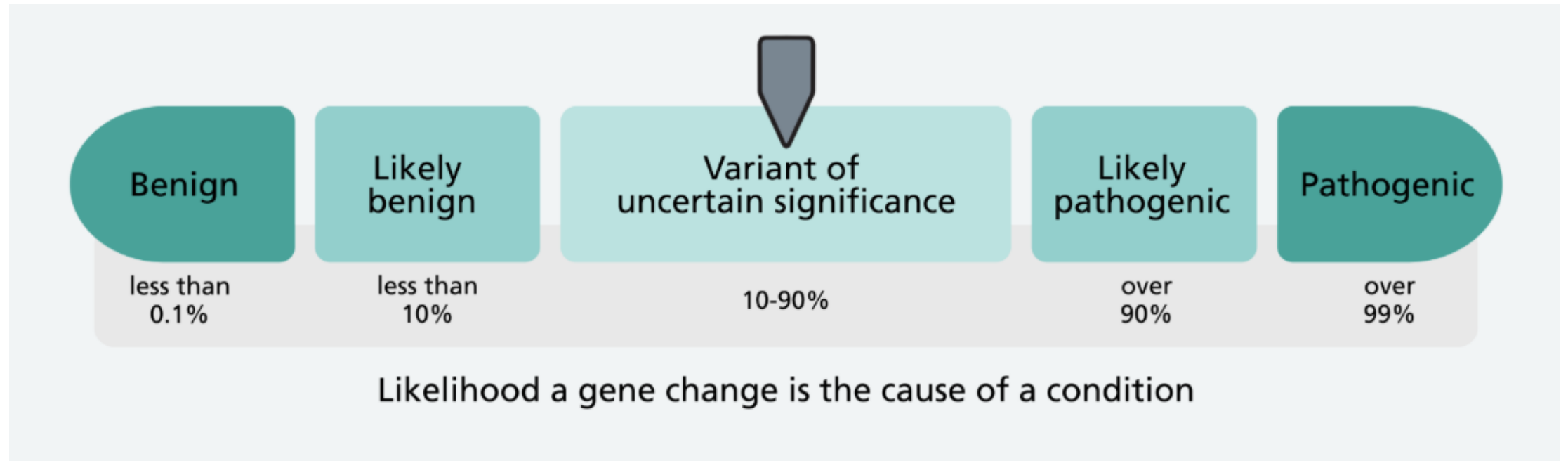


ÇOCUK NÖROLOJİDE GENETİK OKURYAZARLIK KURSU (İnteraktif Kurs)

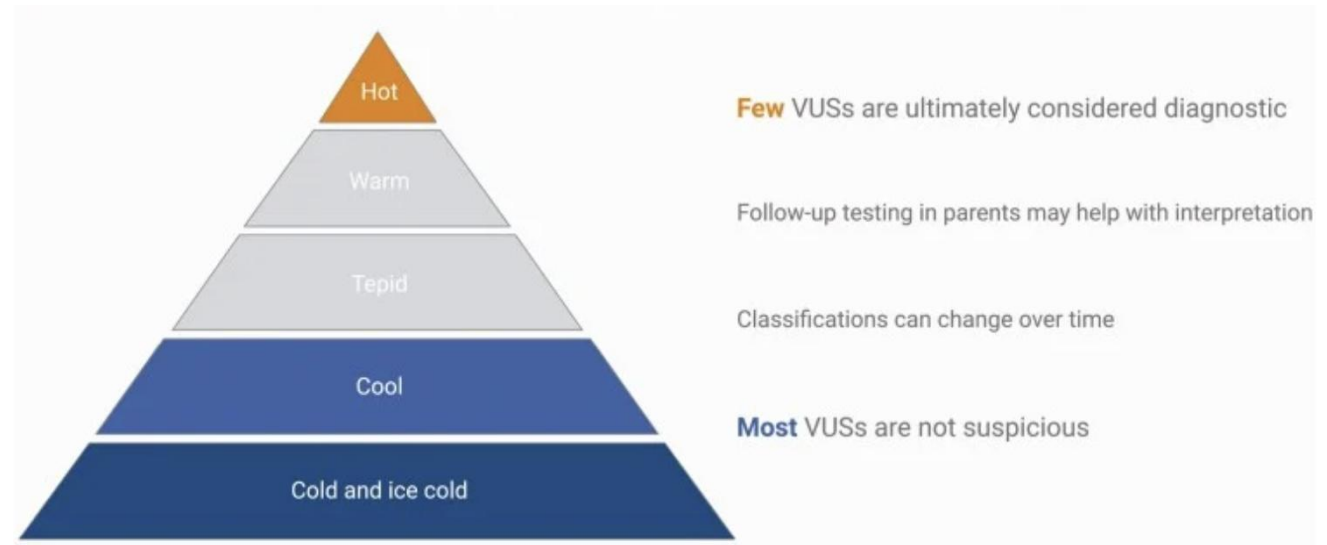
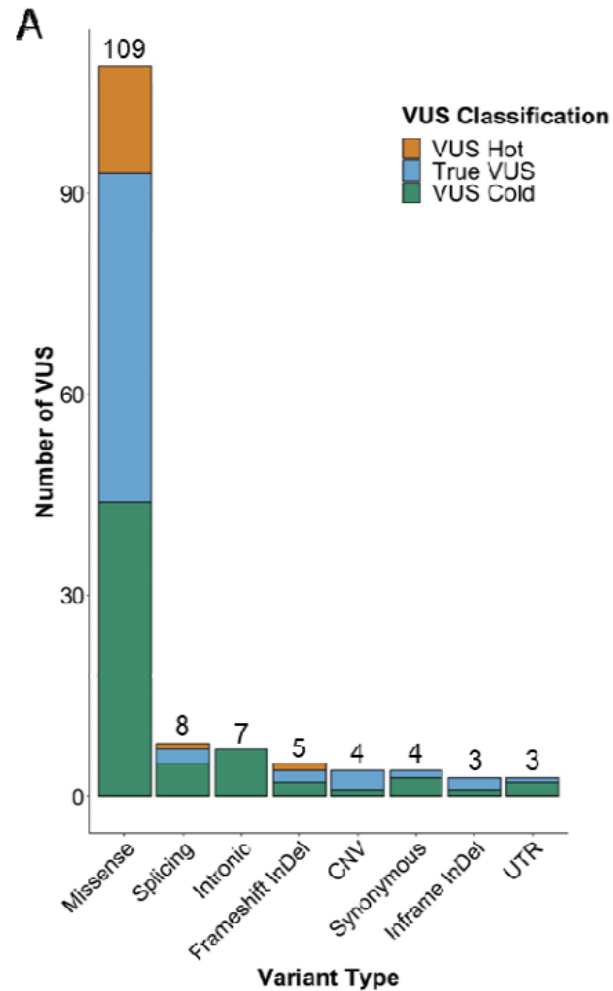
11:00-11:10 Açılış, Kursun Amaç ve Kapsamının Tanıtımı

Konuşmacı: Dr. Semra HIZ KURUL, Dr. İlknur EROL, Dr. Pınar GENÇPINAR

VUS



Nörogenetikte VUS Yorumlaması



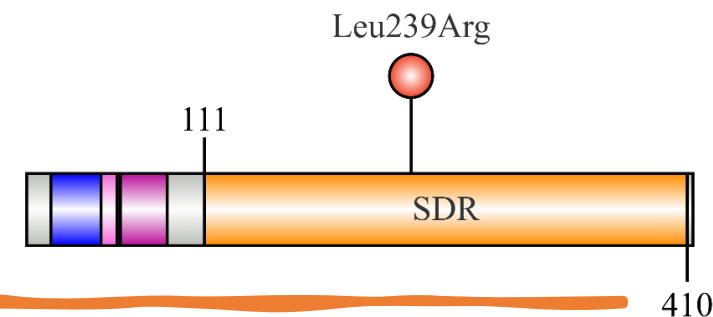
VUS (ACMG)

- Derin fenotipleme
 - HPO
- Segregasyon analizleri
 - Anne, Baba, Etkilenmiş diğer bireyler, Sağlıklı
- Hastalık/Gen özelinde veritabanları...
 - Clingen...
- Toplum özellikli veri tabanları
 - Turkish Variome
 - GenomAd
 - Iranome
 - India
- Fonksiyonel Analizler.....

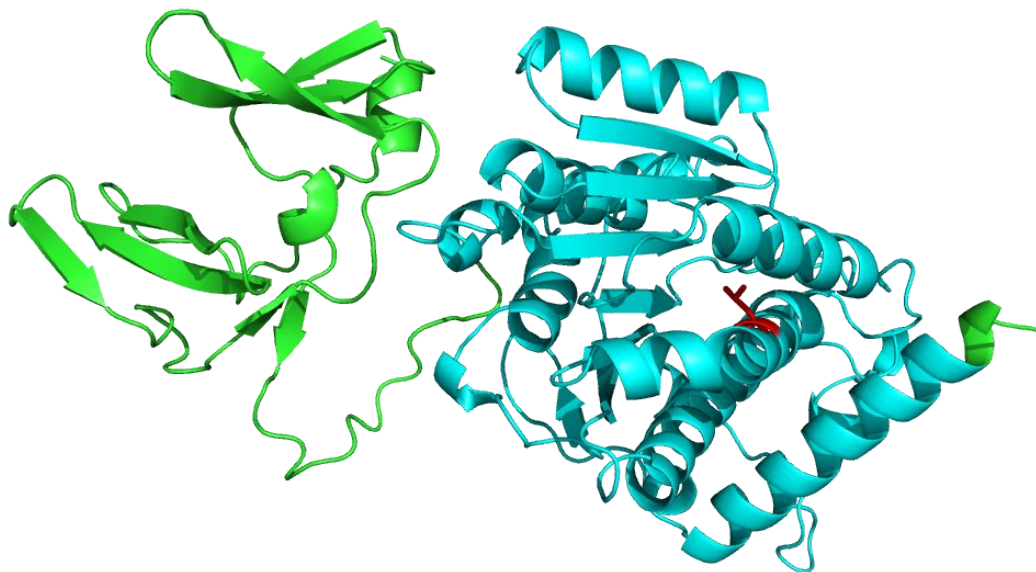
Fonksiyonel Analizler

- İn silico analizler
 - Hesaplamalı Dizi Analizi
 - Hesaplamalı Biyofizik
 - Hesaplamalı Yapısal Biyoloji
- Kök hc ve Organoid teknolojileri
- Gen Hedefleme ve Transgenik Modeller

WWOX gen Leu239Arg varyantı

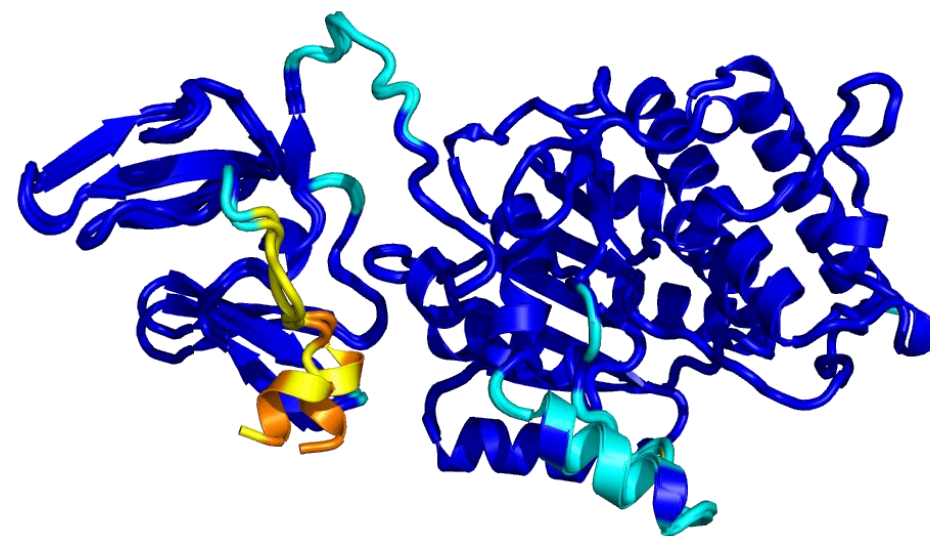


Structural location of the L239R mutation within the SDR domain of the WWOX protein.



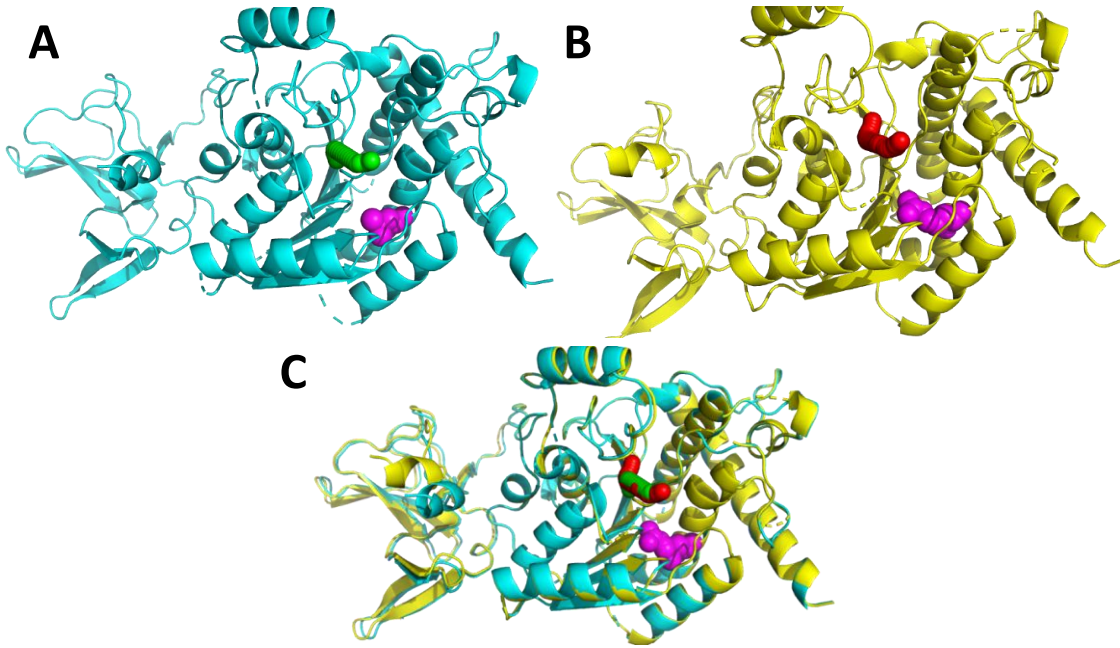
AlphaFold2-Multimer v3 (ColabFold v1.5.5),
AlphaFold 3

Structural superposition of Wild-Type (WT) and Mutant (MT) WWOX models.



(FoldX 5.1, PremPS, Maestro WEB, DynaMut v1/v2, DUET, I-Mutant 2.0, mCSM, SDM) +
Missense3D (Structural damage)

WWOX gen Leu239Arg varyantı



- Prank score: 26.53 $\rightarrow$ 26.76
- Tunnel radius: 3.239 $\rightarrow$ 3.222 Å
- Oxidoreductase activity score: 0.667 $\rightarrow$ 0.650

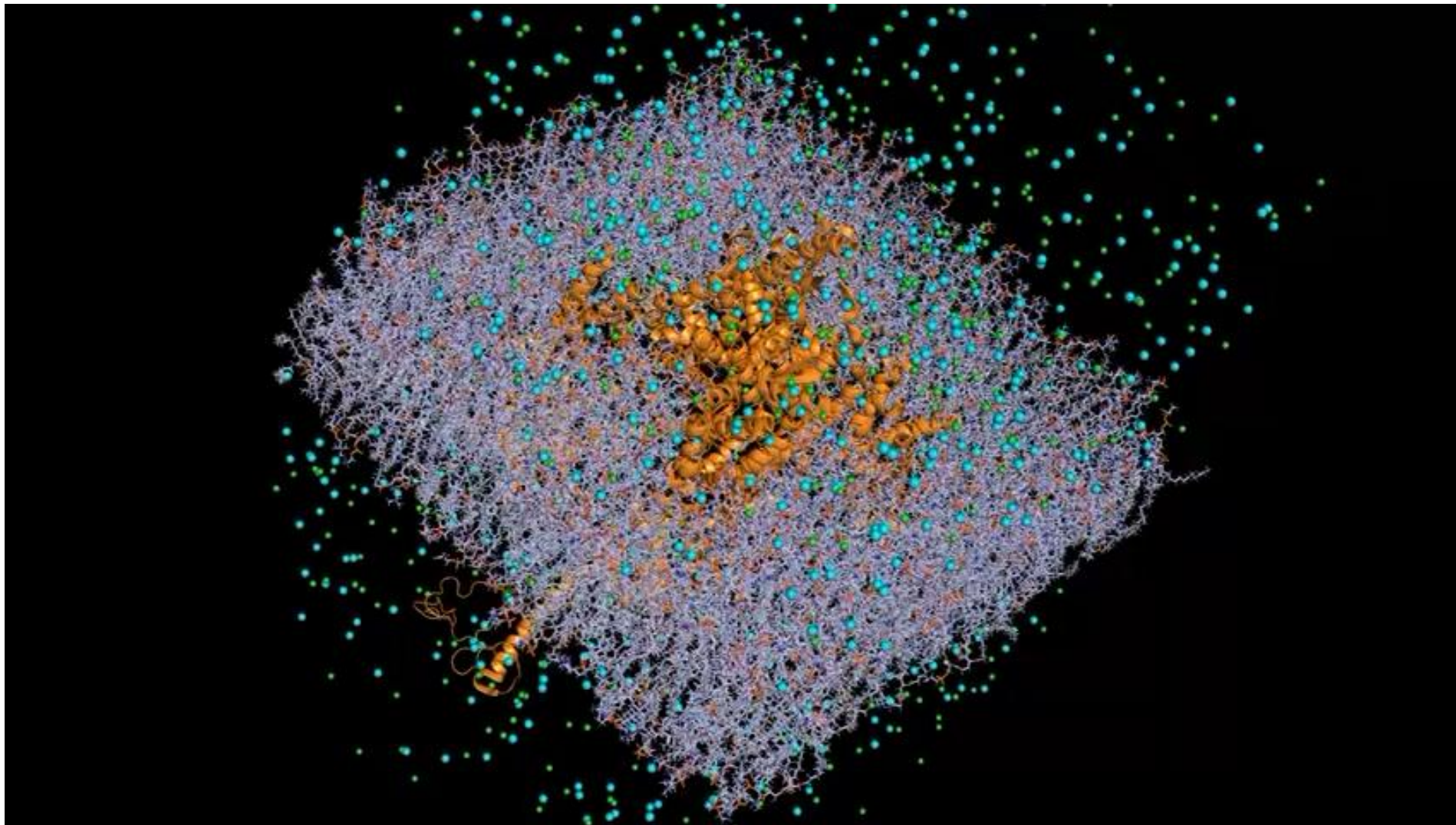
Active site largely preserved

- $\Delta\Delta G = +12.136$ kcal/mol (FoldX)
- Consensus from multiple predictors indicates destabilization (FoldX, DynaMut, mCSM, DUET, I-Mutant2.0, SDM, PremPS, Maestro)

Strongly destabilizing mutation

Hesaplamaalı Biyofizik

- Moleküler modelleme
- Atom düzeyinde simülasyonlar
- Gelişmiş örnekleme araçları



Will variants of uncertain significance still exist in 2030?

Douglas M. Fowler^{1,2,3,*} and Heidi L. Rehm^{4,5,*}

NAR Genomics and Bioinformatics, 2024, **6**, lqae154
<https://doi.org/10.1093/nargab/lqae154>
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Standard Article

OXFORD

There will always be variants of uncertain significance. Analysis of VUSs

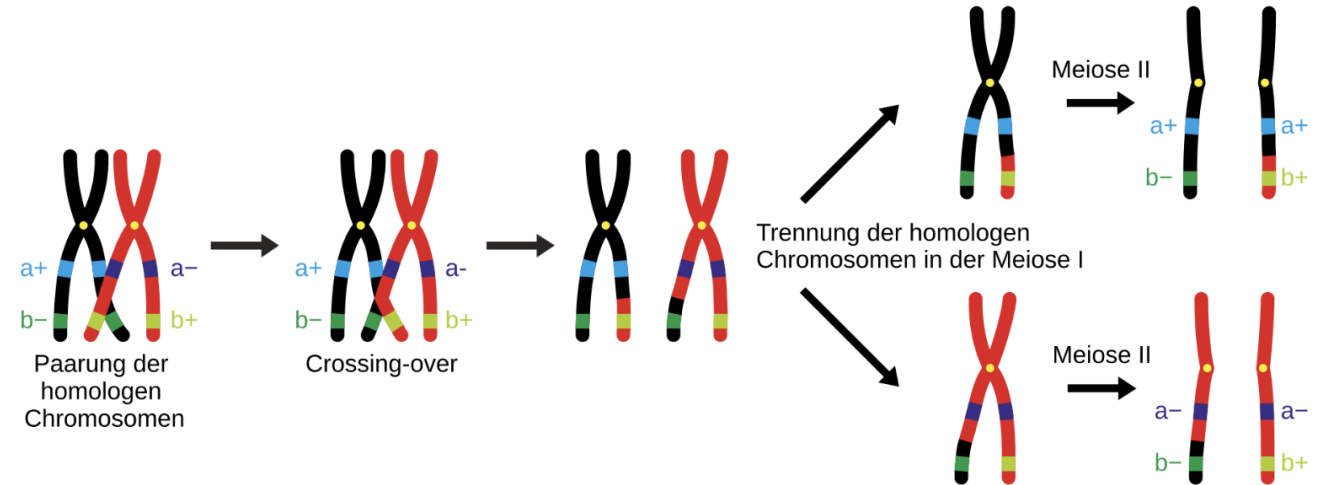
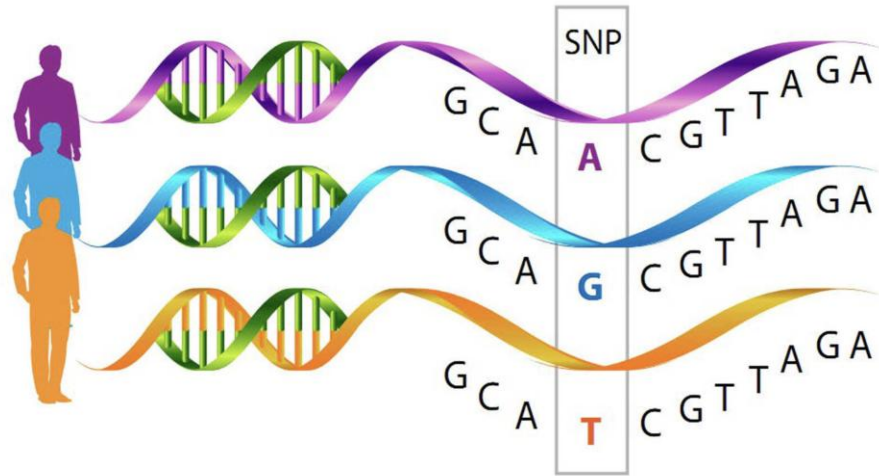
Haoyang Zhang¹, Muhammad Kabir², Saeed Ahmed³ and Mauno Vihinen^{4,*}

Department of Experimental Medical Science, BMC B13, Lund University, SE-22184 Lund, Sweden

*To whom correspondence should be addressed. Tel: +46 72 5260022; Email: mauno.vihinen@med.lu.se

Present address: Saeed Ahmed, Department of Computer Science, University of Swabi, Swabi, Khyber Pakhtunkhwa 94640, Pakistan.

VUS? SNP?



Çeşitlilik&Evrım



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29
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2026

Until
29
APR
2026

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Teşekkürler

NEURO-GENOMICS
LAB



Nadir ve Tanısız Hastalıklar
Araştırma ve İletişim Kulübü

