Biochemistry 4

- iClicker 16A
- Protein Pathology
- Hemoglobin
  - Christchurch
  - Woolwich
- iClicker 16B

- Due in Lab next week
  - Pre-Lab 7
  -
- Register your iClicker
-

#3 → 4 & 3 carriers
is correct, submit
for re-grade

Mutations

① mutations → lead to changes in genes
→ create new allele

② genes encode proteins ∴ mutations cause changes in amino acid sequence → 1° structure
∴ proteins made wrong → not modified later

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ex. 1 $Hb_{christchurch}$ disease (Hb_C)

Hb = 2 β-globin, 2 α-globin

β-globin = 146 amino acids

type of β-globin	β-globin a.a. #71	side chain of #71	phenotype

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normal	phenylalanine	$-CH_2-$  hydrophobic	normal
Hb_C	serine (all remaining 145 a.a. unchanged)	$-CH_2-OH$ hydrophilic	hemolytic anemia (blood cells break)

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where is a.a. #71 in the Hb protein?
in the hydrophobic core of protein

changes in gene → changes in 1° structure →
changes in 2°, 3°, 4° structure →
disease

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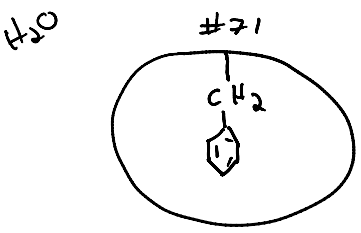
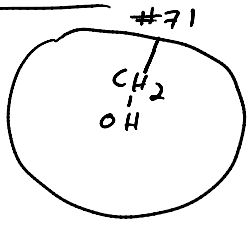
normal β-globin

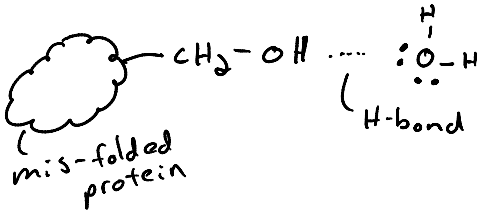


"happy" in the phobic core

Hb_C



① philic serine would prefer to be in water ∴ will be outside the protein

② 

③ clumps of mis-folded protein = "Heintz body"

④ Heintz bodies weaken red blood cells

⑤ weak blood cells break hemolysis → anemia

Genetics – different alleles produce different β-globin proteins

Rules

① at protein level, it is always co-dominance
→ both alleles make protein

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② alleles act independently to give a phenotype

③ "doing something is dominant to not"

allele	β-globin produced	contribution to phenotype
H	normal (#71 = phen.)	normal (rec.)
H^c	christchurch (#71 = serine)	hemolytic anemia (dominant)

which is dominant?

genotype	β-globin produced	phenotype
$H\ H$	normal (100%)	normal
H^cH^c	christchurch (100%)	hemolytic anemia
$H\ H^c$	normal (50%) + christchurch (50%)	hemolytic anemia

christchurch Hb still form Heintz bodies even though normal Hb is still present

∴ hemolytic anemia

∴ disease phenotype of H^c is dominant

"doing something (making Heintz bodies) is dominant"

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ex. 2 Hb woolwich → affects amino acid #132, on surface of protein

allele	β-globin produced	contribution to phenotype
H	normal #132 = lysine (ionic bonds / H-bonds)	normal (dom)
H^w	woolwich #132 = glutamine (− H-bonds)	Hb is present and no Heintz bodies, but doesn't bind O_2 (rec)

genotype	β-globin produced	phenotype
$H\ H$	normal (100%)	normal
$H^w\ H^w$	woolwich (100%)	Hb does not carry O_2
$H\ H^w$	normal (50%) + woolwich (50%)	normal has enough functional Hb to carry O_2

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