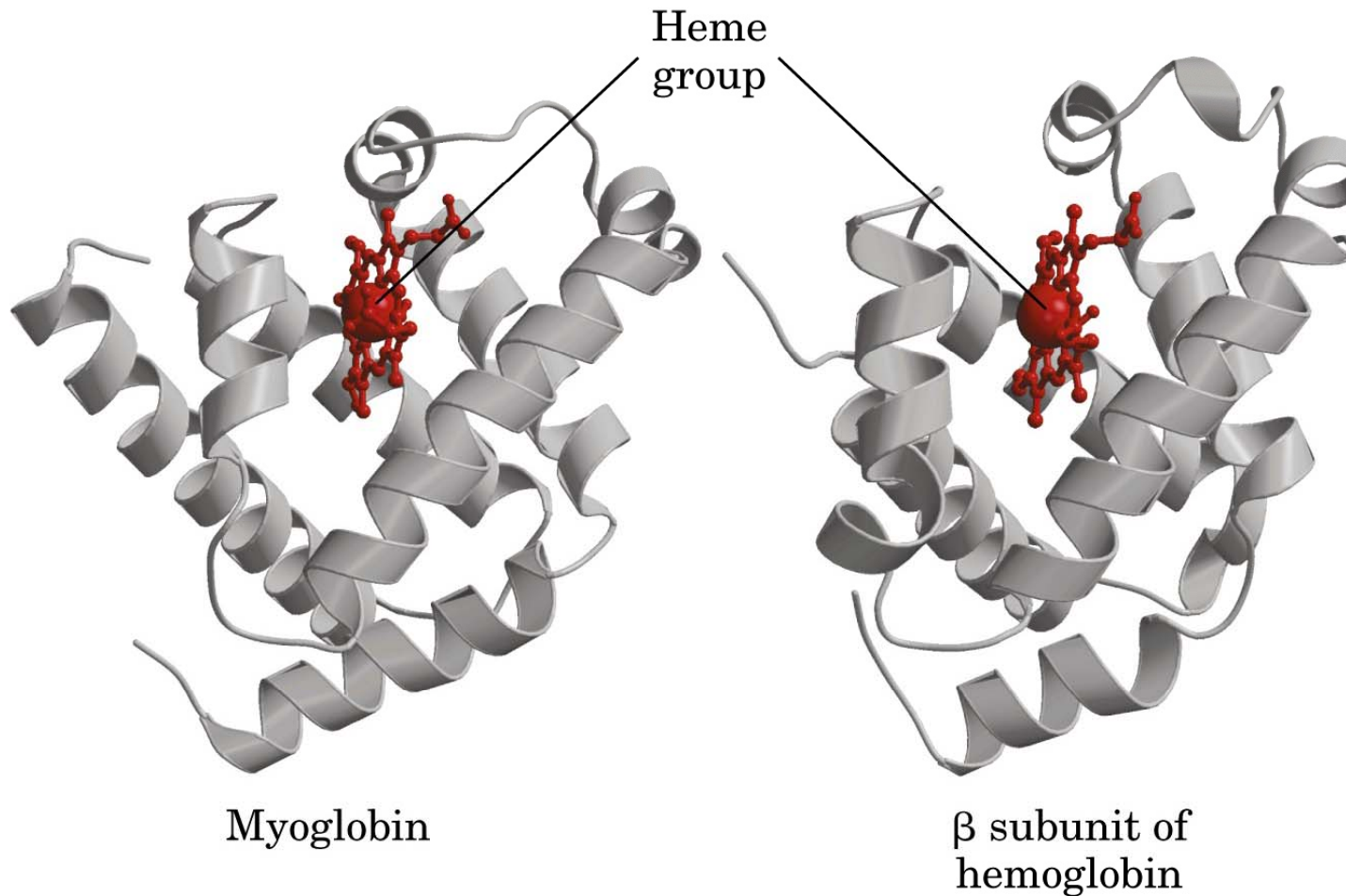


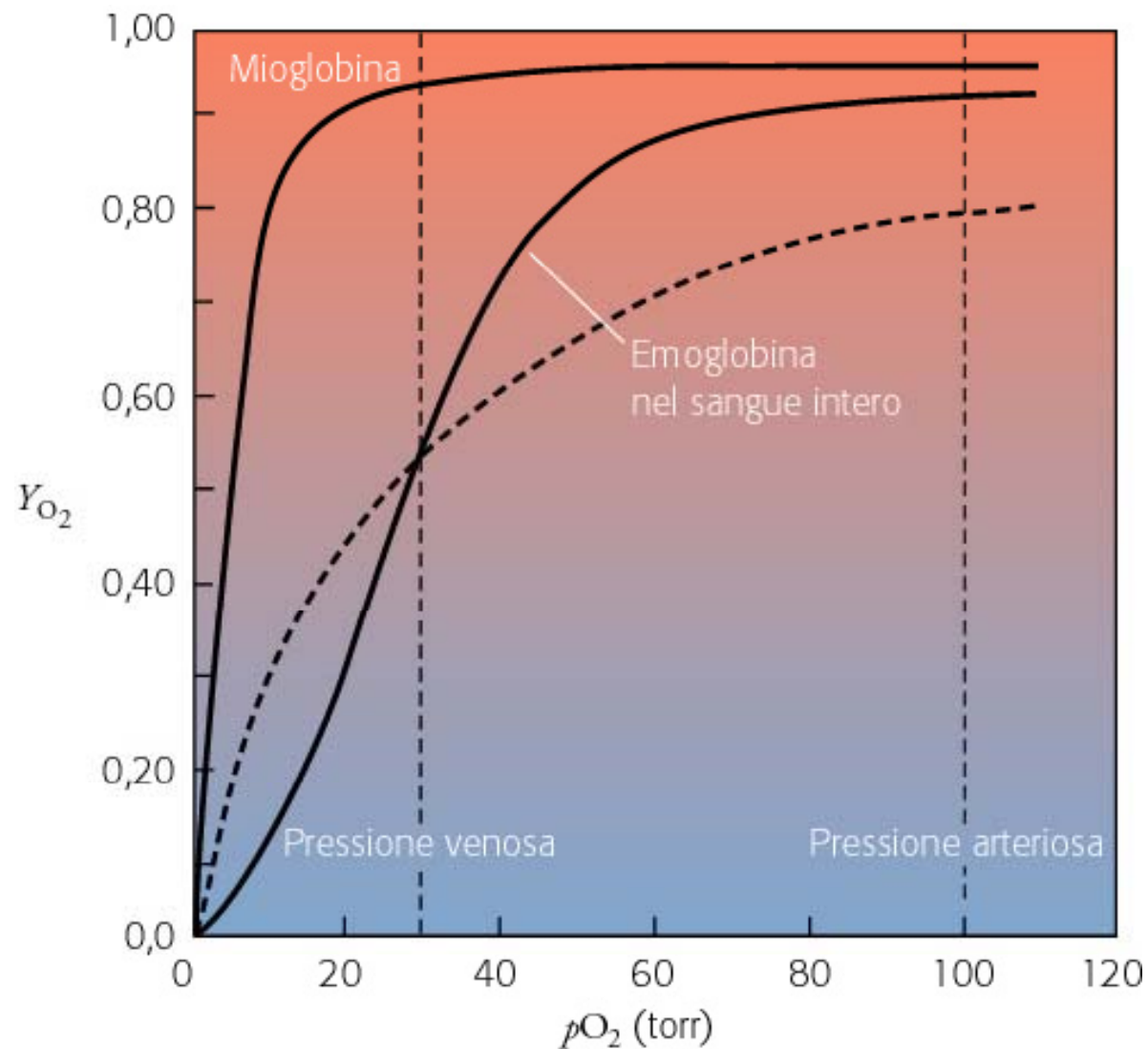
Le proteine che legano ossigeno:

2) emoglobina



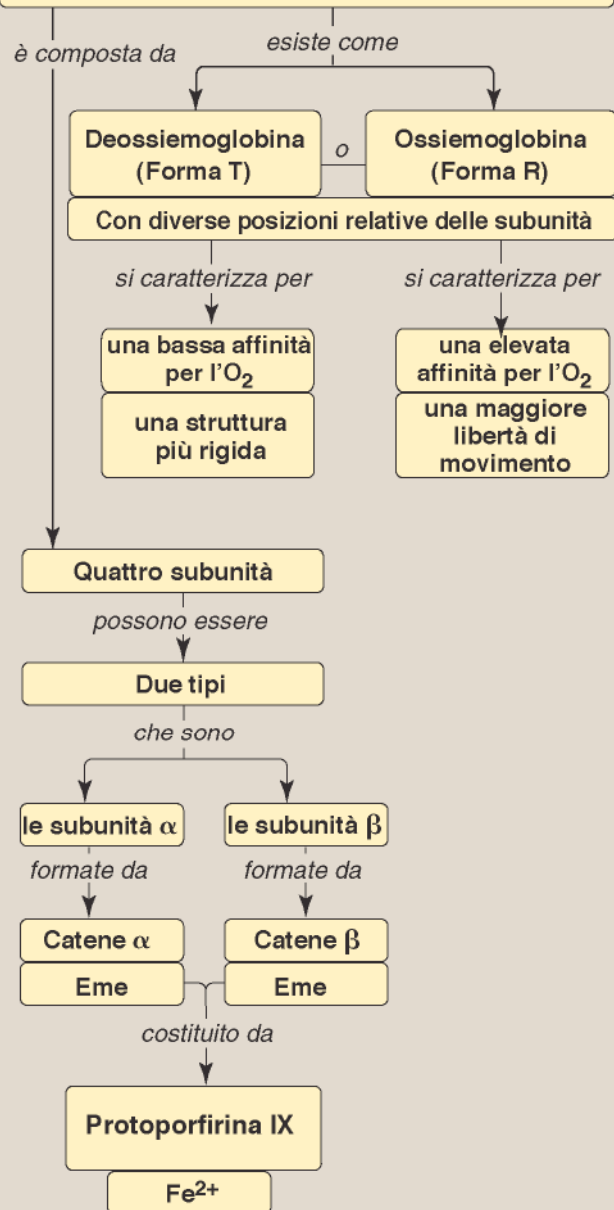
identità di sequenza: 18%

Il legame dell'ossigeno all'emoglobina

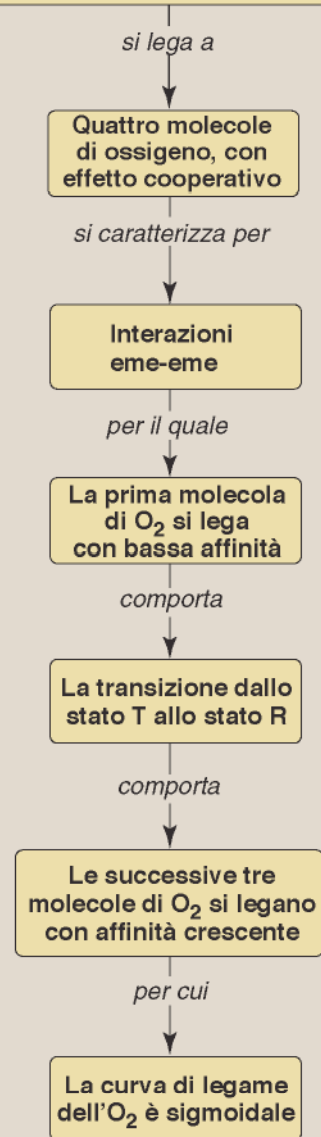


Emoglobina

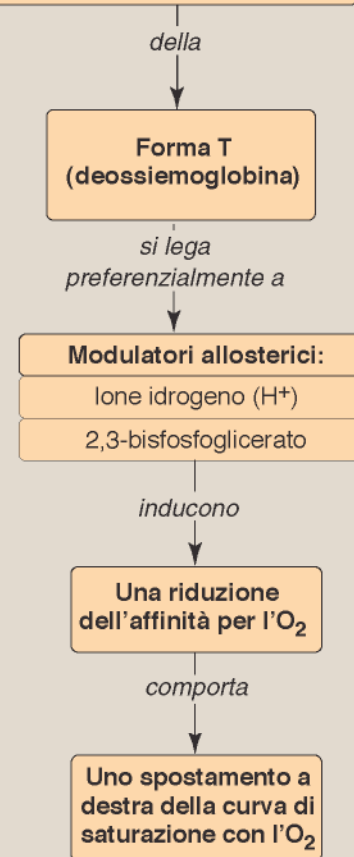
Struttura dell'emoglobina



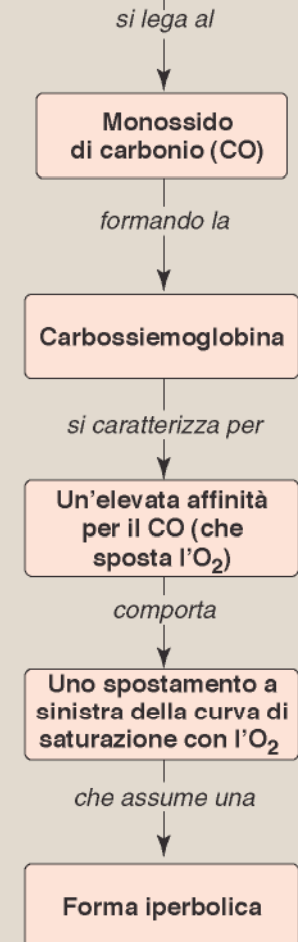
Legame con l'O₂



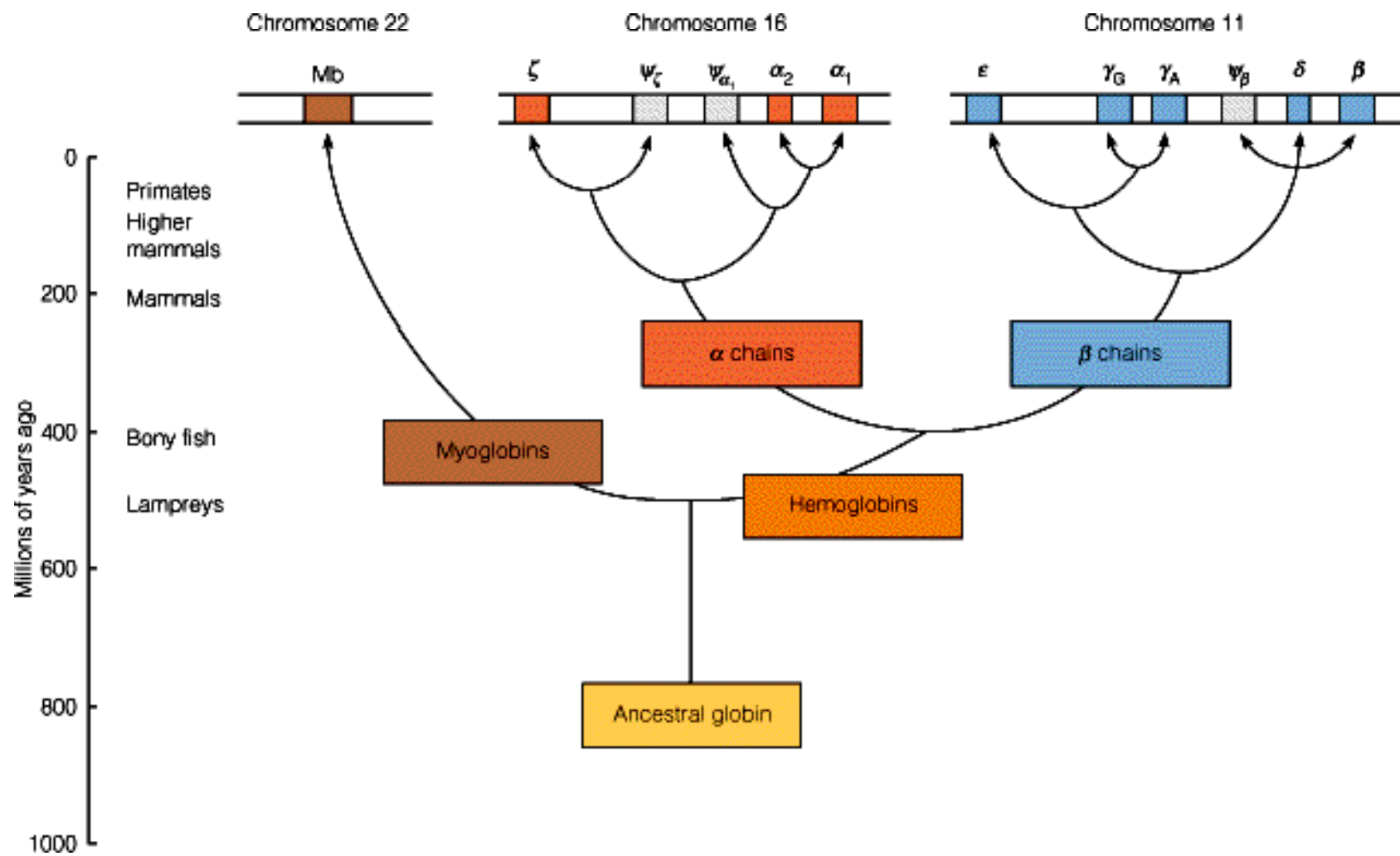
Effettori allosterici



Effetti del monossido di carbonio



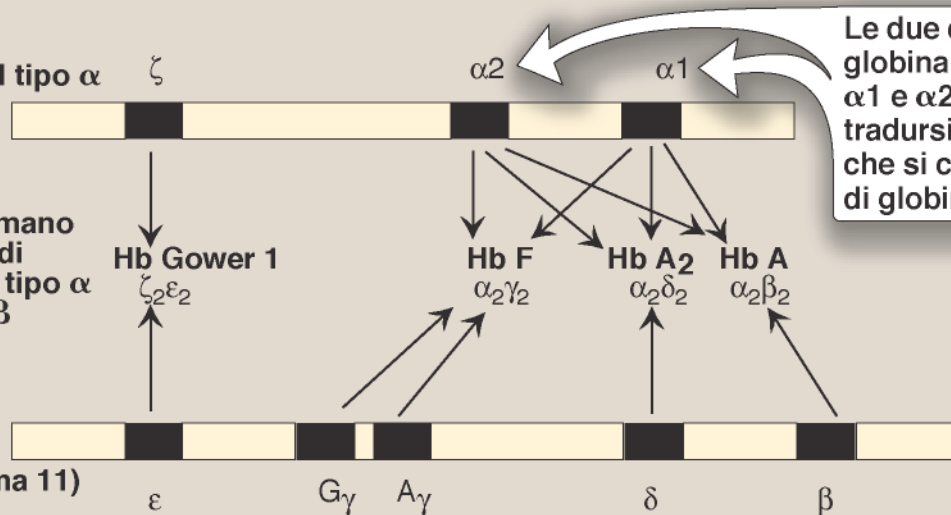
Differenti emoglobine



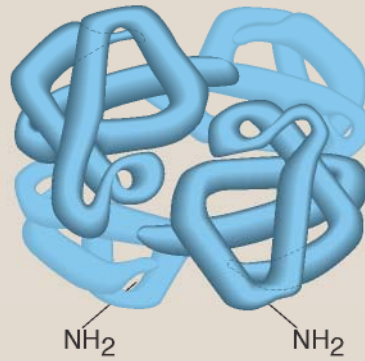
Geni delle globine del tipo α
(Cromosoma 16)

Le emoglobine si formano
per la combinazione di
catene di globine del tipo α
e di globine del tipo β

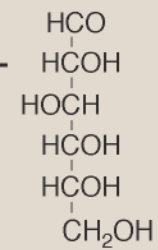
Geni delle globine
del tipo β (Cromosoma 11)



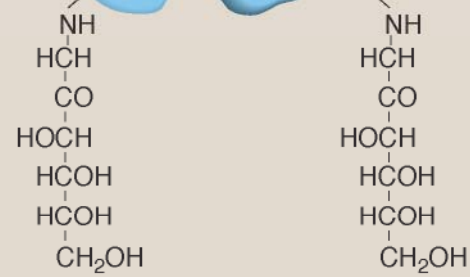
Tipo	Composizione (catene globiniche)	Frazione dell'emoglobina totale
HbA	$\alpha_2\beta_2$	90%
HbF	$\alpha_2\gamma_2$	<2%
HbA ₂	$\alpha_2\delta_2$	2-5%
HbA _{1c}	$\alpha_2\beta_2$ -glucosio	3-9%



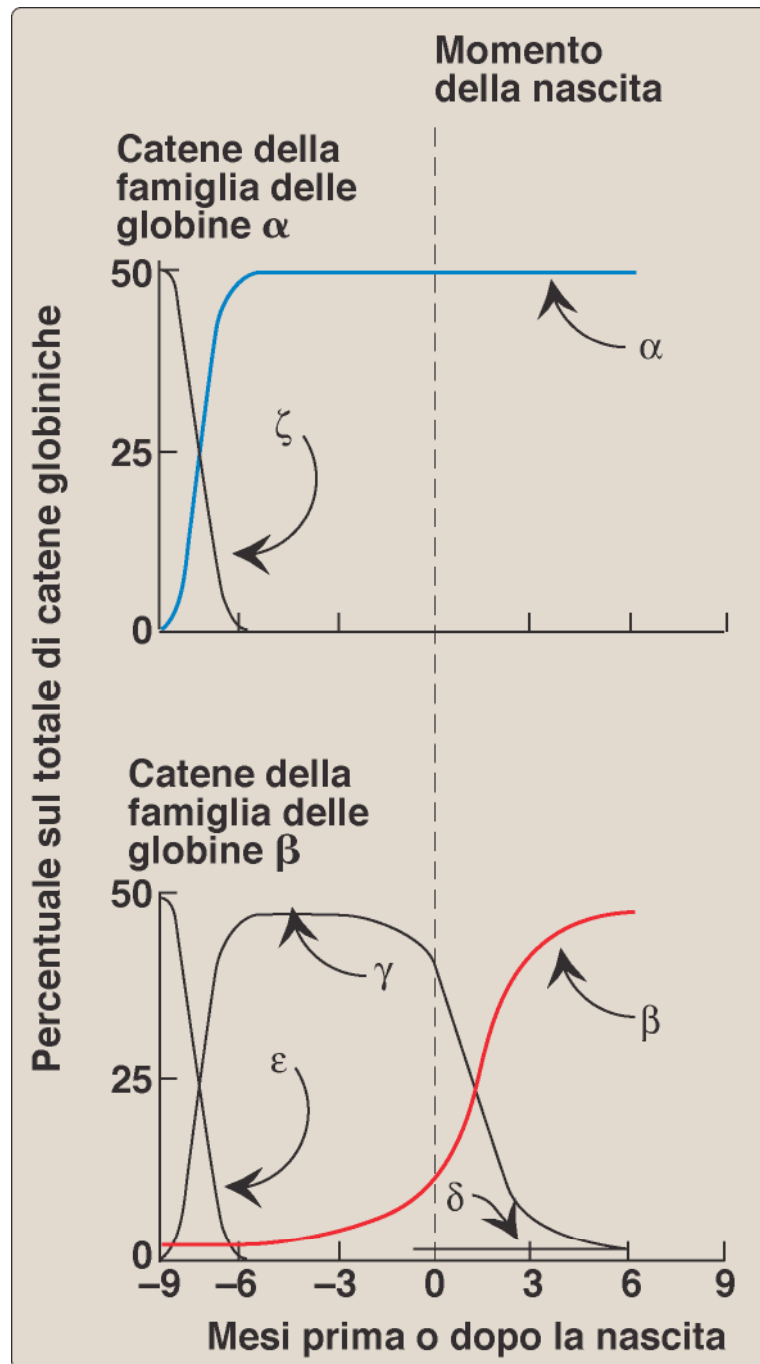
Emoglobina A



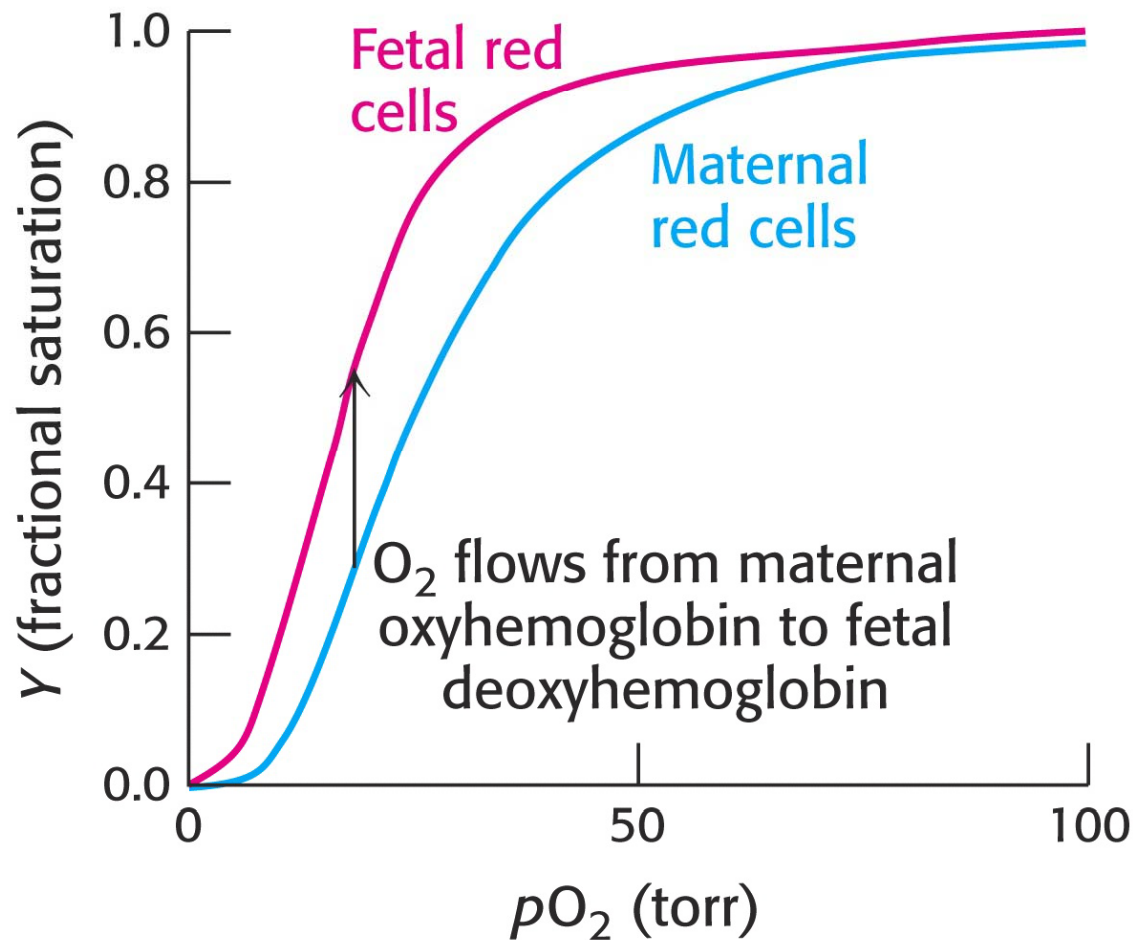
Glucosio



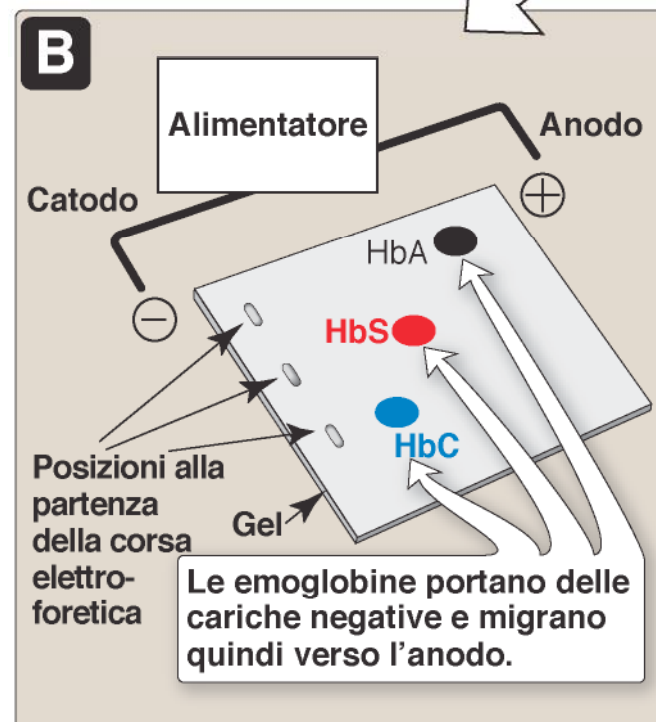
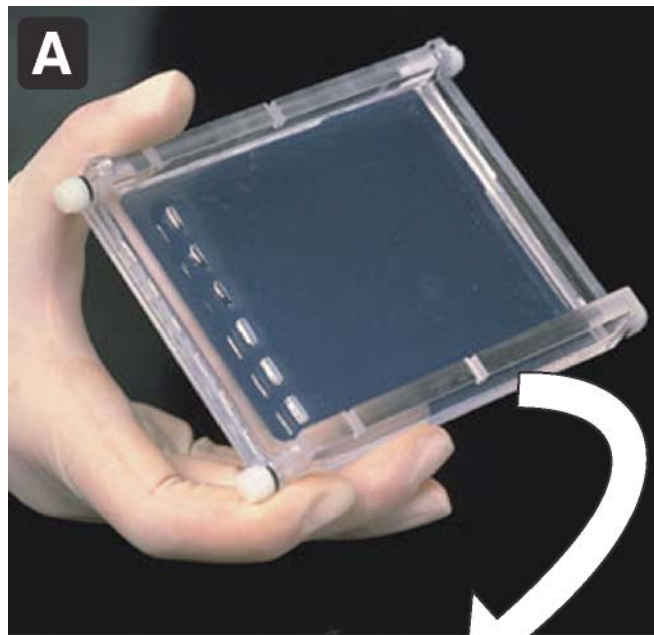
Emoglobina A_{1c}

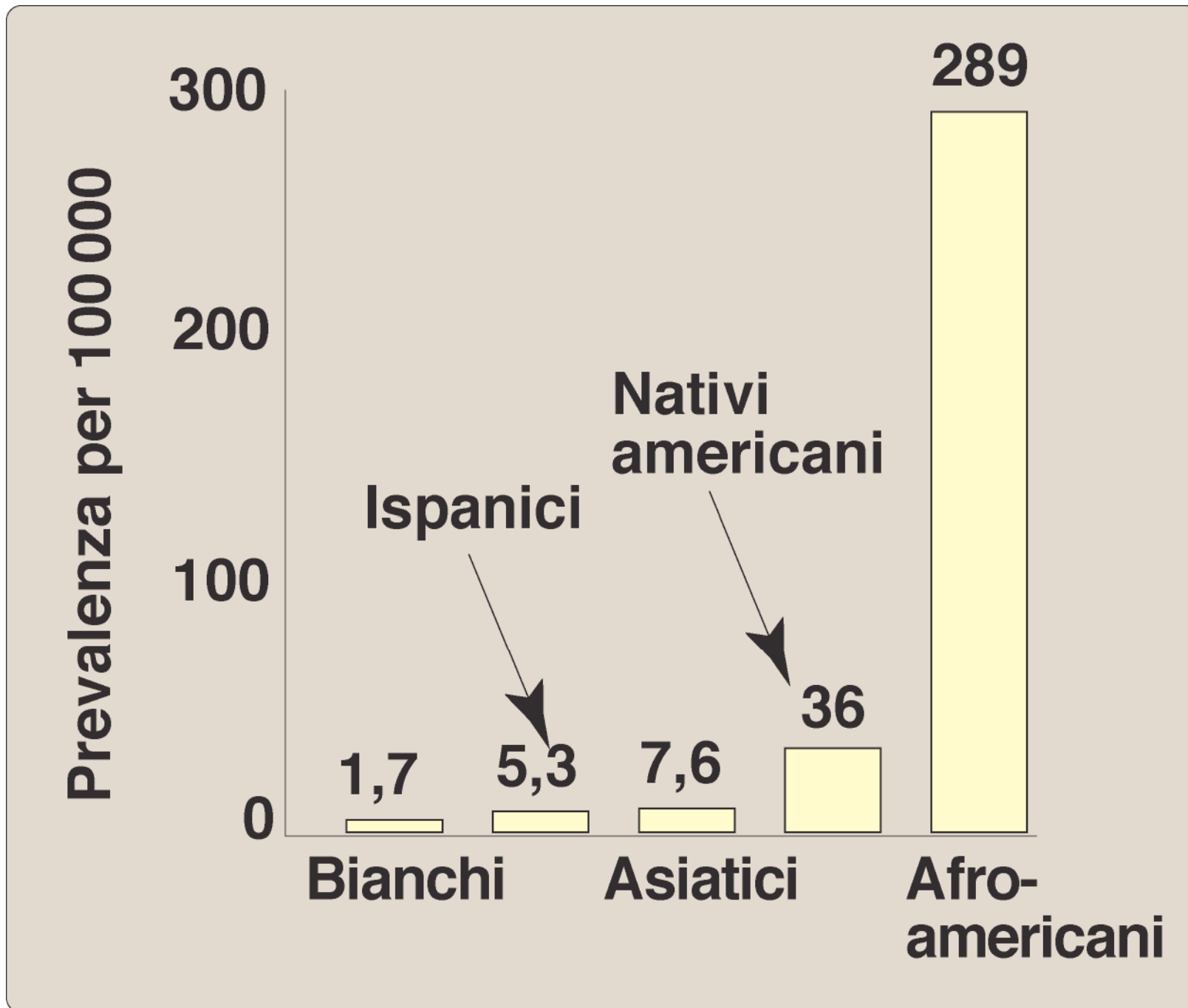


L'emoglobina fetale ha una bassa
affinità per il BPG

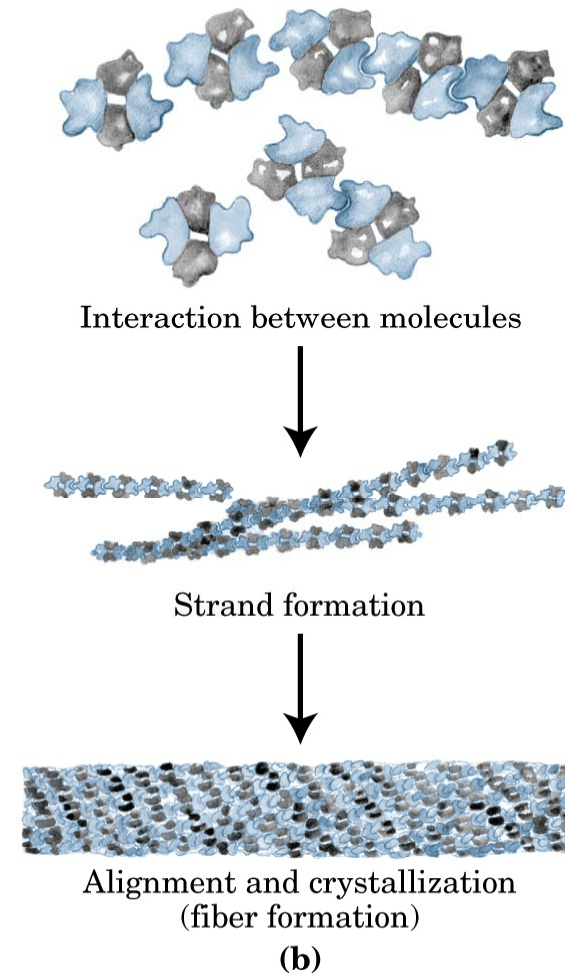
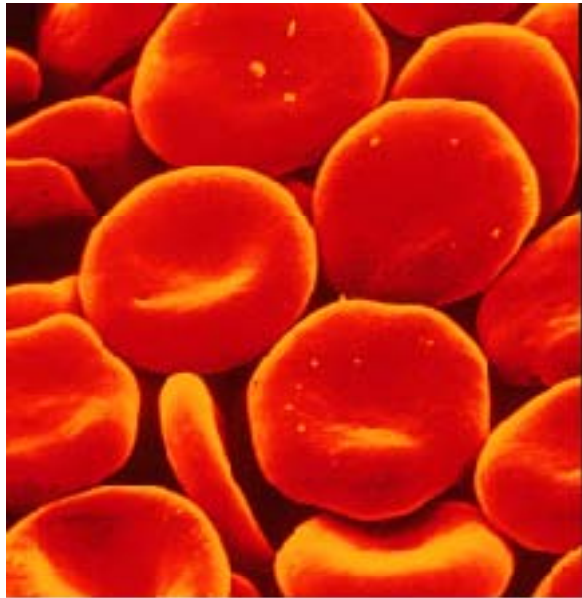


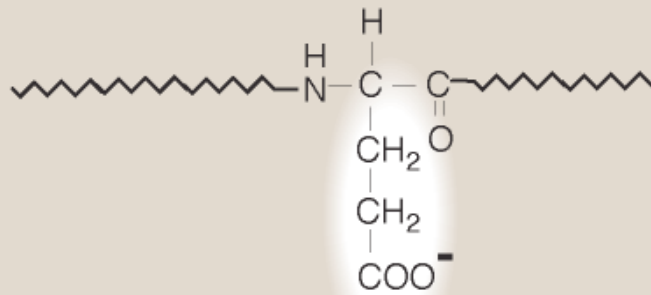
Emoglobinopatie





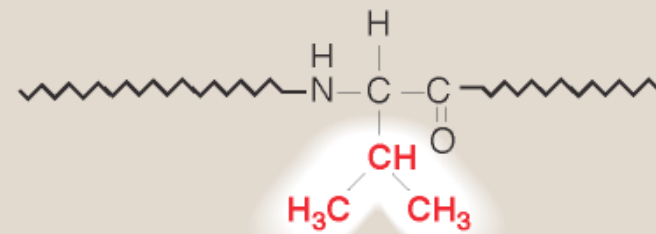
Emoglobina S e anemia falciforme





Val · His · Leu · Thr · Pro · **Glu** · Glu · Lys ~~~~~
 1 2 3 4 5 6 7 8

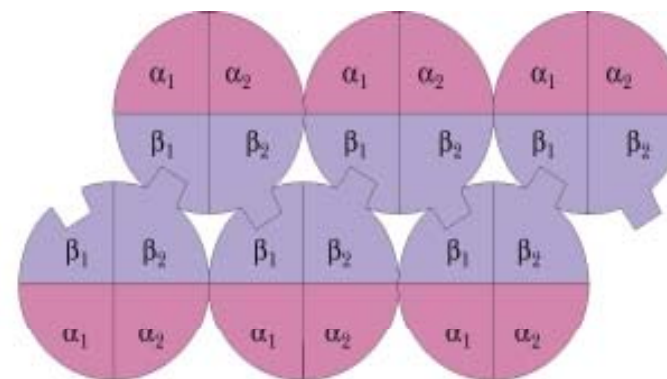
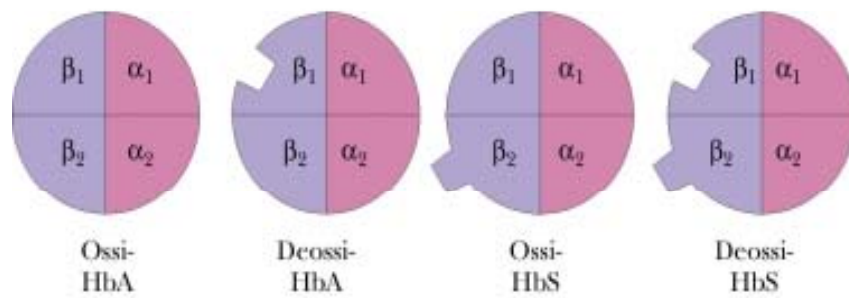
HbA



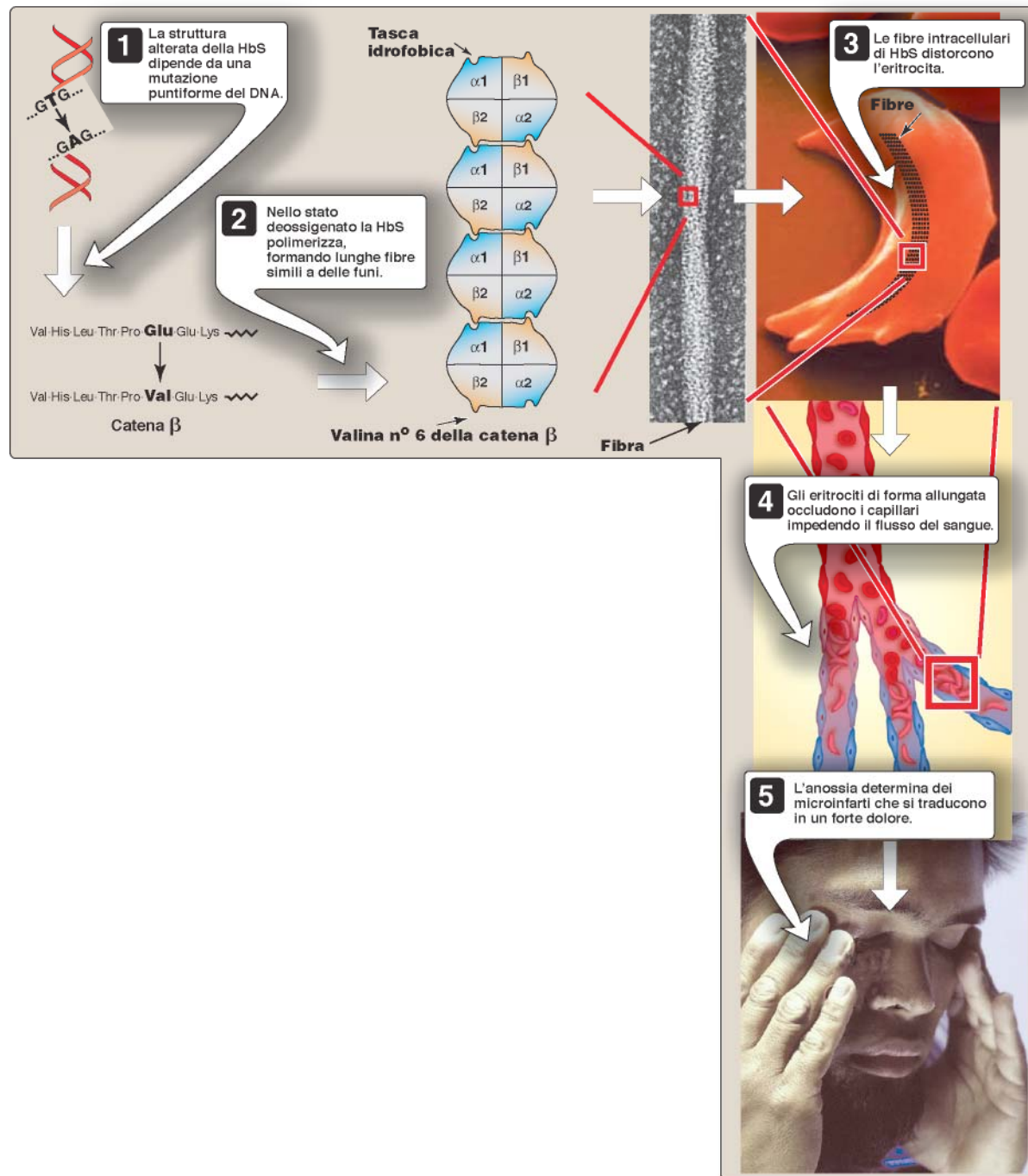
Val · His · Leu · Thr · Pro · **Val** · Glu · Lys ~~~~~
 1 2 3 4 5 6 7 8

Val
1

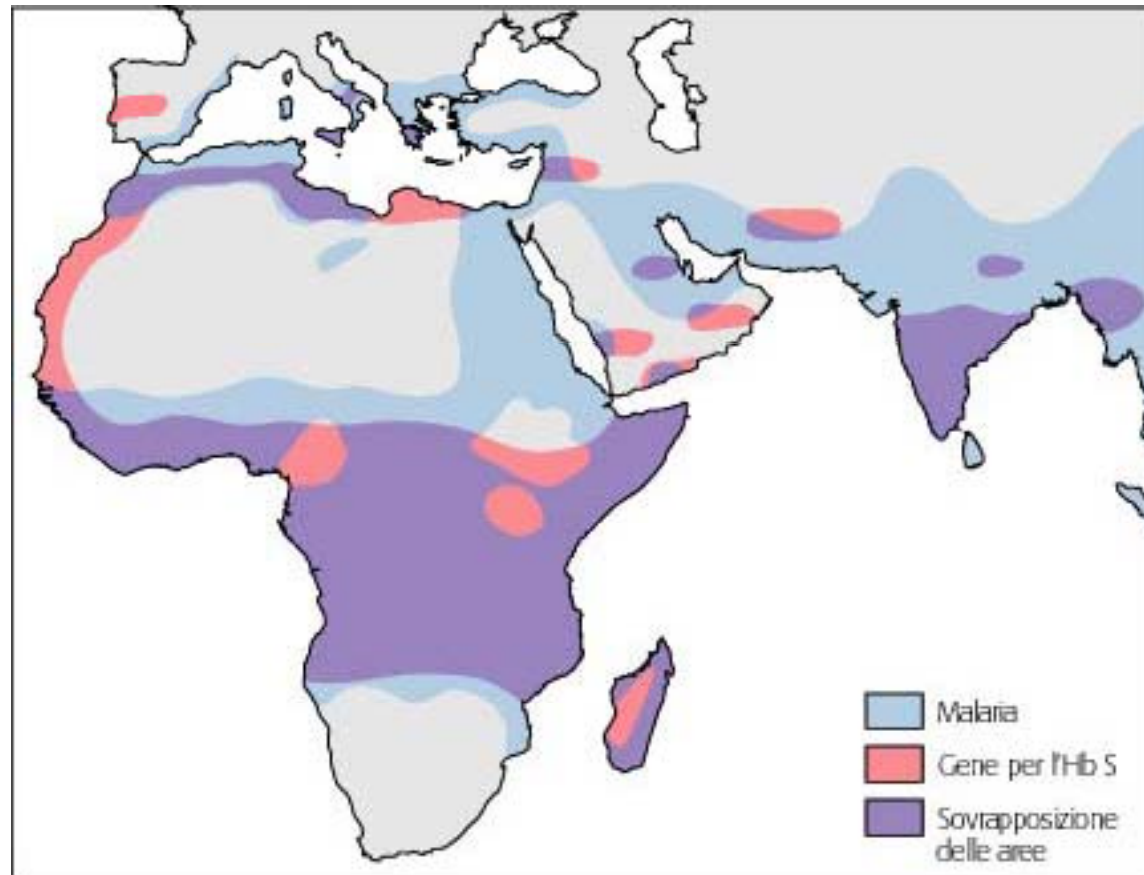
HbS

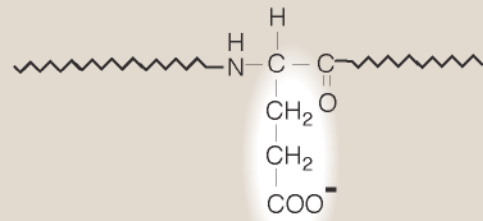


La deossi-HbS polimerizza in filamenti



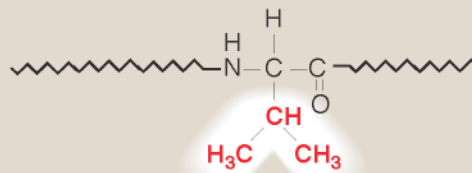
Malaria ed anemia falciforme





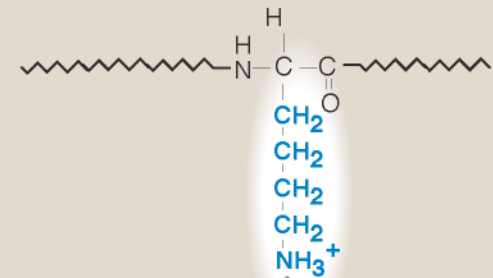
Val · His · Leu · Thr · Pro · **Glu** · Glu · Lys ~~~~
1 2 3 4 5 6 7 8

HbA



Val · His · Leu · Thr · Pro · **Val** · Glu · Lys ~~~~
1 2 3 4 5 6 7 8

HbS

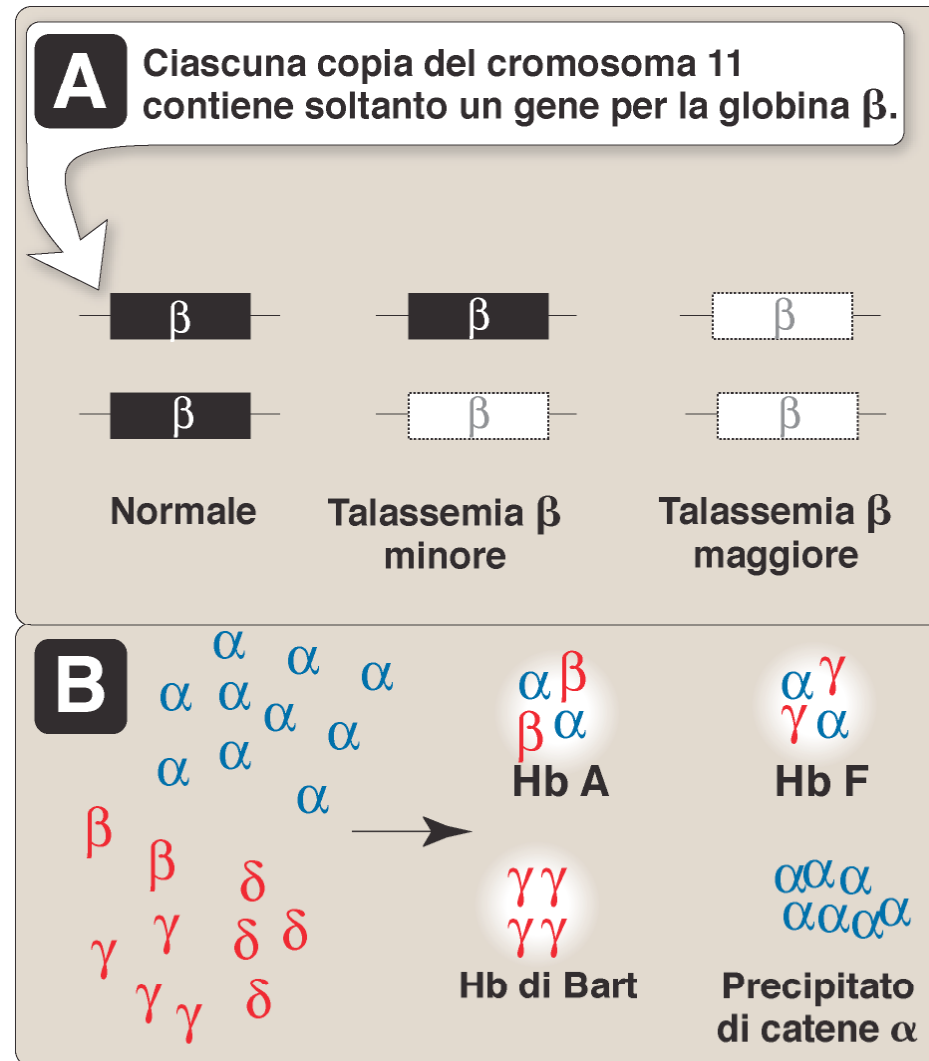


Val · His · Leu · Thr · Pro · **Lys** · Glu · Lys ~~~~
1 2 3 4 5 6 7 8

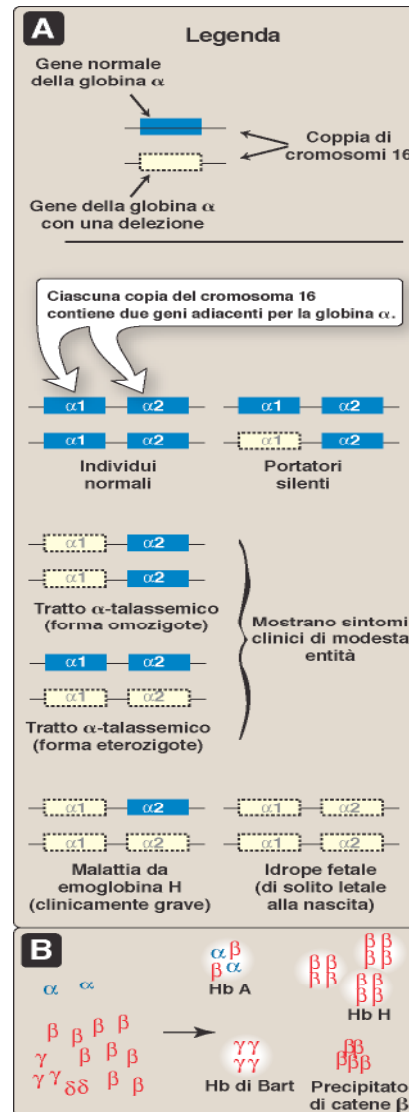
HbC

Effect	Residue Changed	Change	Name	Consequences of Mutation	Explanation
Sickling	$\beta 6$ (A3)	Glu $\longrightarrow$ Val	S	Sickling	Val fits into EF pocket in chain of another hemoglobin molecule.
	$\beta 6$ (A3)	Glu $\longrightarrow$ Ala	G Makassar	Not significant	Ala probably does not fit the pocket as well.
	$\beta 121$ (GH4)	Glu $\longrightarrow$ Lys	O Arab, Egypt	Enhances sickling in S/O heterozygote	$\beta 121$ lies close to residue $\beta 6$; Lys increases interaction between molecules.
Change in O ₂ affinity	$\alpha 87$ (F8)	His $\longrightarrow$ Tyr	M Iwate	Forms methemoglobin, decreased O ₂ affinity	The His normally ligated to Fe has been replaced by Tyr.
	$\alpha 141$ (HC3)	Arg $\longrightarrow$ His	Suresnes	Increases O ₂ affinity by favoring R state	Replacement eliminates bond between Arg 141 and Asn 126 in deoxy state.
	$\beta 74$ (E18)	Gly $\longrightarrow$ Asp	Shepherds Bush	Increases O ₂ affinity by decrease in BPG binding	The negative charge at this point decreases BPG binding.
	$\beta 146$ (HC3)	His $\longrightarrow$ Asp	Hiroshima	Increases O ₂ affinity, reduced Bohr effect	Disrupts salt bridge in deoxy state and removes a His that binds a Bohr-effect proton.
	$\beta 92$ (F8)	His $\longrightarrow$ Gln	St. Etienne	Loss of heme	The normal bond from F8 to Fe is lost, and the polar glutamine tends to open the heme pocket.
Heme loss	$\beta 42$ (CD1)	Phe $\longrightarrow$ Ser	Hammersmith	Unstable, loses heme	Replacement of hydrophobic Phe with Ser attracts water into heme pocket.
Dissociation of tetramer	$\alpha 95$ (G2)	Pro $\longrightarrow$ Arg	St. Lukes	Dissociation	Chain geometry is altered in subunit contact region.
	$\alpha 136$ (H19)	Leu $\longrightarrow$ Pro	Bibba	Dissociation	Pro interrupts helix H.

Talassemie beta



Talassemie alfa



Metaemoglobinemia

- Da Fe^{++} a Fe^{+++}
- Nitrati
- ROS
- Carenza di NADH-citocromo b5 ossidasi
- Cianosi color cioccolato

Emoglobine artificiali: un obiettivo delle biotecnologie

esempi

Emoglobina incapsulata in liposomi

Hb bovina polimerizzata con gluteraldeide (usata in alcuni casi)

Hb umana polimerizzata con diaspirina (tossica)

Hb ad alto peso molecolare mediante peghilazione

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Emoglobinopatie

